Lunan Yan
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Operative Techniques in Liver Resection

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Preface

Hepatectomy has been widely used for the treatment of various liver diseases in recent years. Surgical resection is technically challenging due to the crisp liver and spleen tissues and the rich surrounding blood supply. Intraoperative and postoperative bleeding are the most serious problems in early liver resection.

Recent years have seen the introduction of the use of hepatic blood flow occlusion and technological maturation of the hepatectomy. In addition, new instruments, such as the CUSA system and the Water-Jet, have been widely used and improved the outcomes of hepatectomies. In combination with these advances, the application of hemostatic liver section material has solved the problem of intraoperative and postoperative bleeding. However, the problem of postoperative liver failure remains prominent.

In the past two to three decades, postoperative liver failure prevention and treatment have significantly improved with a deeper understanding of anatomy and physiology, great progress in modern imaging evaluation, better endoscopic techniques, advances in anesthesia, and improved postoperative ICU management.

This book aims to provide a fully updated knowledge in concisely and comprehensively describing the application of hepatectomy to treat various liver diseases.

Most of the authors are experts at the West China Hospital, Sichuan University, who provide their own experiences, norms, and cases and also refer to the latest research and progress in the field. The extensive use of our surgical photos greatly increases readability.

We have invited the well-known Chinese surgeons from Hong Kong, Taiwan, Beijing, Shanghai, Zhejiang, Chongqing, Anhui, and other universities such as Professor Yunyi Liu, Zhaolong Chen, Shusen Zheng, and others to write some chapters on hepatectomy.

The intended readers of this book are clinicians and researchers, especially including hepatopancreatobiliary surgeons, gastrointestinal surgeons, liver disease doctors, interventional and radiologic doctors, and basic researchers.

This book will also be valuable for a broad audience, including general surgeons, epidemiologists, hospital administrators, pathologists, clinical interns, and equipment manufacturers.

Chengdu, China — Lunan Yan

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I strongly wish to show my appreciation of all of those who have contributed to this book, especially to Professor Yunyi Liu, Zhaolong Chen, Shusen Zheng, and others.

I am honored and thankful to my deputy editors, Professor Hong Wu, Professor Jiayin Yang, Dr. Jianyong Lei, and Dr. Wei Zhang, for their help in redrafting, proofreading, and compiling this book.

I am grateful to my secretary, Ms. Fang Liu, for her dedication in typing the manuscript and to Ms. Yiding Fan for her help in the production of the operative photographs.

I am deeply indebted to my wife, Dr. Lin Luo, and my family; without their unfailing support, I would not have finished this book.

Lunan Yan

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Liver Anatomy and the History of Hepatectomy

1

Lunan Yan and Yan Zhong

1.1 Ancient Civilization

An understanding of the liver's anatomy can be traced back to 4000–5000 years ago in the Babylonian Empire, as proven by a hemihepatic model made of mud, which is now preserved at the British Museum.

The liver was described in Huangdi Neijing, which is the earliest literature on Chinese medicine and dates back to 4000 years ago.

Approximately 2500 years ago (450–350 BC), the Greek scientist, Hippocrates recorded the diagnosis and treatment of liver diseases.

1.2 History of Liver Anatomy

Francis Glisson wrote *Liver Anatomy* in 1654, in which he described the distribution and relationship of the portal and hepatic venous systems, establishing the foundation for hepatobiliary surgery.

Frances Kierman described the Glisson sheath in 1833; this term is still used today to describe the connective tissue capsule covering the portal vein, the hepatic artery, and the bile duct.

Cantlie proposed the concept of bilaterality of the liver in 1897, namely, that the plane extending between the gallbladder fossa inferiorly and the left edge of inferior vena cava superiorly, now known as the Cantlie line, divides the liver into the left and right lobes.

Hjortsjo from Switzerland was the first to use perfusion corrosion models to study the intrahepatic biliary system in 1951, thus identifying the liver as a segmental organ and ushering in the thriving era of the hepatobiliary surgery that began in the 1950s.

In 1953, Healey and Schroy proposed an approach to division of the liver that was based on the anatomic structure of the portal vein.

Subsequently, Couinand advocated a numerical system for naming the eight segments of liver in order to accommodate surgical needs. Since then, these anatomic divisions of the liver have been universally accepted.

1.3 History of Hepatectomy

At the end of the twentieth century, hepatectomy took the initial steps as surgical technology advanced.

In 1716, Berta removed a part of the liver that protruded from a patient's abdominal cavity after a knife wound.

In 1870, Brun resected necrotic liver tissue in a patient suffering from traumatic hepatorrhexis.

In 1886, Luis performed liver resection on a patient with liver adenoma for the first time; however, the patient died after the surgery.

In 1888, the noted German surgeon Langenbuch performed the first left hepatectomy.

In 1891, Lucke was the first to successfully resect a left-lobar liver carcinoma.

In 1910, Wendel performed the first right sublobectomy in a patient with liver carcinoma, who survived 9 years after the operation.

In 1940, Cattell was the first to successfully resect liver metastasis of rectal cancer.

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1.4 In the Late 1940s, Hepatobiliary Surgery Developed Rapidly, Presenting the Following Features

1.4.1 An Improved Understanding of Functional Liver Anatomy Led to the Development of Anatomic Hepatectomy in the Late 1940

Kaven performed the first anatomical left lateral hepatectomy in 1948. Left hepatic artery, the left branch of the portal vein, and the left hepatic duct were dissected, ligated, and transected at the root of the round ligament.

Lortat-Jacob performed the first anatomical right hepatectomy in 1952.

1.4.2 Parenchymal Transection

In 1953, Quattlebaum was the first to use scalpel handle to transect the liver.

In 1960, Tianyou Lin from Taiwan first proposed the finger fracture technique.

In 1988, Lvnan Yan proposed the hook-ligature method.

1.4.3 Vascular Occlusion

Total liver inflow occlusion, known as Pringle maneuver, was first introduced by Pringle JH in 1908 and has been widely used ever since.

Healy proposed total hepatic vascular exclusion in 1966. This procedure involves clamping the abdominal aorta below the diaphragm, clamping the hepatoduodenal ligament, and clamping the infra- and suprahepatic inferior vena cava to maintain the liver in a bloodless condition.

Kumada further developed total hepatic vascular exclusion in 1988 by using a biological pump, which forms a bypass from the portal vein and the inferior vena cava into the superior vena cava, in order to avoid stasis of blood and preserve remnant liver function.

Lvnan Yan proposed a convenient hemihepatic vascular occlusion maneuver in 1988.

1.4.4 Development of Liver Transplantation

Starzl et al. performed the first human orthotopic liver transplantation in 1963.

The first orthotopic liver transplantation in China was performed in 1977 by Shanghai Ruijin Hospital and Wuhan Tongji Hospital.

Bismuth and Houssin reported the first reduced-size liver transplantation in 1984.

Pichlmayr reported the first split-liver transplantation in 1988.

Raia from Brazil performed the first pediatric living-related donor liver transplantation in the same year.

Yamaoka reported the first adult-to-adult right-lobe living-donor liver transplantation in 1993.

In 1997, Shangda Fan reported the first adult-to-adult expanded right-lobe living-donor liver transplantation, in which the graft contained the middle hepatic vein.

In 2001, Lvnan Yan performed the first adult-to-adult living-donor liver transplantation in mainland China.

Anatomy in Liver Resection

2

Stephanie H.Y. Lau, Eric C.H. Lai, and Wan Yee Lau

2.1 Surface Markings of the Liver

The position of the liver varies according to the posture of the body. In erect posture in adult male, the edge of the liver projects about 1 cm below the lower margin of the right costal cartilages, and its inferior margin can often be felt in this situation if the abdominal wall is thin. In supine position, the liver recedes above the margin of the ribs and it cannot be detected by palpation. Its position varies with respiratory movements; during deep inspiration, it descends below the ribs; in expiration it rises. In male, the liver weighs from 1.4 to 1.6 kg, while in female, the liver weighs from 1.2 to 1.4 kg.

The upper margin of the right liver, in the midline, is approximately level with the xiphisternal joint; on the right side, the margin arches slightly upward as far as the fifth costal cartilage in the mammary line and then curves down along the right border from ribs 7–11 in the midaxillary line. The upper limit of the left liver also arches slightly upward to the fifth intercostal space 7–8 cm from the midline. The inferior border lies along a line which joins the right lower and upper left extremities. On the right side, the inferior border lies approximately level with the right costal margin while centrally it crosses behind the right upper abdominal wall between the costal margins.

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2.2 Surfaces of the Liver

The liver has three surfaces: diaphragmatic, visceral, and posterior surfaces.

2.2.1 Diaphragmatic Surface

The diaphragmatic surface is covered for the most part in peritoneum, which forms a sheath around the liver, except in places where the ligaments reflect to join the adjacent diaphragm. In the midline of the abdomen and over the anterior convexity of the liver, the falciform ligament is attached and divides the liver into the anatomical right "lobe" and left "lobe." The ligamentum teres, a remnant of the left umbilical vein, runs from the umbilicus in between the two leaves of the falciform ligament to the visceral surface of the liver, where it disappears behind a bridge of either fibrous or liver tissue which connects the right "lobe" with the quadrate "lobe" to end in the left portal vein at the junction between the branches to liver segments 3 and 4. The fundus of the gallbladder peeps below the inferior border of the liver.

2.2.2 Visceral Surface

The sharp inferior border of the liver joins the diaphragmatic surface with the visceral surface which is the inferior surface of the liver. The main structures here are arranged in an H-shaped pattern. The cross-piece of the H is made by the porta hepatis (the hilum of the liver). The right limb of the H is made incompletely by the inferior vena cava posteriorly and the gallbladder anteriorly. The left limb of the H is made by the continuity of the fissures for the ligamentum teres anteriorly and the ligamentum venosum posteriorly. The vena cava lies in a deep groove. On its right side is the bare area and its left side the caudate "lobe."

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2.2.3 Posterior Surface

The inferior vena cava runs in the center of the posterior surface of the liver. A fibrous band called the ligamentum venae cavae (hepatocaval ligament) cover part of the inferior vena cava posteriorly. This fibrous band, sometimes replaced by a bridge of liver tissue, is attached to the bare area on the right side and the caudate "lobe" on the left side. The ligamentum venosum runs in a groove just to the left of the caudate "lobe." The rest of the posterior surface of the liver is made up by the ligaments (the left triangular ligament, the coronary ligament, and the right triangular ligament) which attach the liver to the diaphragm.

2.3 Ligaments of the Liver

The liver is connected to the undersurface of the diaphragm and to the anterior wall of the abdomen by five ligaments; four of these—the falciform ligament, the coronary ligament, and the two triangular ligaments—have been described in the previous paragraph, and the fifth is the round ligament (or ligamentum teres).

2.3.1 Falciform Ligament and Ligamentum Teres

The falciform ligament is a sickle-shaped fold, consisting of two closely applied layers of peritoneum which connect the liver to the diaphragm and to the supraumbilical part of the anterior abdominal wall. At the upper end, the two layers of the falciform ligament separate from each other. The round ligament (its Latin equivalent ligamentum teres) is a fibrous cord resulting from the obliteration of the umbilical vein. It ascends from the umbilicus in the free margin of the falciform ligament to the umbilical notch of the liver, from which it may be traced in its fossa on the inferior surface of the liver to the porta hepatis, where the ligamentum venosum can be traced from the left portal vein in its fossa to the posterior surface of the junction of the trunk of the middle and left hepatic veins.

2.3.2 Coronary and Triangular Ligaments

At the upper end of the falciform ligament, its two layers separate from each other. On the right, the layer forms the upper layer of the coronary ligament, which continues inferiorly to form the right triangular ligament, then the lower layer of the coronary ligament. In between these ligaments is the bare area of the liver. At its left extremity, the lower layer of the coronary ligament passes in front of the lower end of the groove for the inferior vena cava and becomes continuous with the line of peritoneal reflection from the right border of the caudate lobe.

On the left, the other layer of the falciform ligament forms the anterior layer of the left triangular ligament, which turns backward to form the posterior layer. At the upper end of the fissure for the ligamentum venosum, it becomes the anterior layer of the lesser omentum. The posterior layer of the lesser omentum is the line of reflection of the peritoneum from the upper end of the right border of the caudate lobe. This layer then goes around the caudate lobe to join the lower layer of the coronary ligament.

2.4 Functional Anatomy

2.4.1 Concept of Liver Sections, Liver Sectors, and Segments

The concept of functional liver anatomy based on the distribution of the portal pedicles and the hepatic veins is called Couinaud's portal segmentation. This concept (portal segmentation) evolved from Couinaud's study of vasculobiliary casts made by plastic injection of the hepatic and portal veins followed by corrosion of the surrounding liver parenchyma [1–3]. This concept is different from Healey's arteriobiliary segmentation which is also based on corrosive studies of liver casts. However, Healey injected plastic materials into the branches of hepatic arteries and bile ducts. According to Couinaud, the liver is divided by the three hepatic veins into sectors (called suprahepatic segmentation by Couinaud). The middle hepatic vein runs in the main scissura (midplane of the liver) which divides the liver into the right and the left liver (or hemiliver). On the right side, the right hepatic vein runs in the right scissura (right fissure) which divides the right liver into the right anterior sector (right paramedian sector) and the right posterior sector (right lateral sector). It should be noted that in the right liver, Healey's liver sections which he called segments are exactly the same as Couinaud's sectors. On the left side, the left hepatic vein runs in the left scissura (left fissure) which divides the left liver into a left medial sector (left paramedian sector) and a left lateral sector (left posterior sector). However, in the left liver, Healey's liver sections which he called segments are not the same as Couinaud's sectors. Couinaud further subdivided the liver into eight segments (subhepatic segmentation) by using the branches of the portal vein.

In the right liver, as Healey's sections are the same as Couinaud's sectors, the right anterior section (sector) can be divided into segment 8 superiorly and segment 5 inferiorly. The right posterior Healey's section (Couinaud's sector) consists of segment 7 superiorly and segment 6 inferiorly. In the left liver, Healey's sections are not the same as Couinaud's

sectors. The left medial Healey's section lies between the main scissura (main fissure) and the falciform ligament, and it consists of only segment 4, while the left lateral Healey's section consists of segments 2 and 3, being separated by the left hepatic vein which runs in the left scissura (left fissure). For the left medial Couinaud's sector, it consists of segments 3 and 4, lying between the middle hepatic vein in the main scissura, and the left hepatic vein in the left scissura. The falciform ligament/umbilical fissure divides liver segment 4 from 3. The left lateral Couinaud's sector, which lies on the left of the left hepatic vein, consists of liver segment 2 only. The liver segment 1 is the same as the caudate lobe in both the Healey's arteriobiliary and the Couinaud's portal segmentations.

The American surgeons commonly use the terminology proposed by Healey, while the European surgeons commonly use terminology proposed by Couinaud. It must be clearly pointed out that the original Healey's segment is not the same as the Couinaud's segment which is now commonly used throughout the world, and the term "section" used in Healey's arteriobiliary segmentation can be the same, or different from the term "sector" used in Couinaud's portal segmentation. To add things more confusing, there is the term "lobes" which may have different meanings to different people. On the other hand, there are many terms which have been used to mean one thing, e.g., the midplane of the liver which divides the liver into the right and the left hemilivers can also be called the Cantlie's line, midline, principal plane, main scissura, main fissure, main sulcus, main portal scissura (Couinaud), and interlobar plane (American terminology). It is therefore desirable to have a uniform, internationally agreed upon terminology of liver anatomy and liver resections.

2.4.2 The Brisbane 2000 Terminology of Liver Anatomy and Resections

The Scientific Committee of the International Hepato-Pancreato-Biliary Association (IHPBA), at a meeting held in Berne, Switzerland, in December 1998, decided to create a Terminology Committee of international experts to deal with the confusion in nomenclature of hepatic anatomy and liver resections [4–7]. A terminology was sought which was anatomically correct in which anatomical and surgical terms agreed, and which was consistent, self-explanatory, linguistically correct, translatable, precise, and concise. After 18 months, the Committee presented a terminology which was endorsed by the IHPBA at the World Congress of the IHPBA held in Brisbane, Australia. To summarize this terminology, the liver is divided into two parts: the main liver and the caudate lobe (called dorsal sector by Couinaud). There are still some controversies on the terminology of the caudate lobe or the dorsal sector as called by Couinaud.

2.4.3 First-Order Division

The first-order division is based on the branching of the proper hepatic artery into the right and left hepatic arteries. This results in division of the liver into two parts or volumes referred to as right and left livers or hemilivers. The right hepatic artery supplies the right liver and the left hepatic artery supplies the left liver. The plane between these two zones of vascular supply is called a watershed. The first-order division which separates the right and the left liver is a plane that intersects the gallbladder fossa and the fossa for the inferior vena cava and is referred to as the midplane of the liver. Within this plane runs the middle hepatic vein.

2.4.4 Second-Order Division

The second-order division is based on the branching of either the right or the left hepatic arteries each divides into two sectional branches. Each of these sectional vessels supplies a defined volume referred to as a section and so in total there are four hepatic sections. On the right side, there is a right anterior section and a right posterior section. These sections are supplied by the right anterior sectional hepatic artery and the right posterior sectional hepatic artery. The sections are also drained by the right anterior sectional hepatic duct and the right posterior sectional hepatic duct. The plane between these sections is the right intersectional plane. Unlike the midplane and the left intersectional plane, the right intersectional plane has no markings on the hepatic surface. The left liver is divided into a left medial section and a left lateral section. These sections are supplied, respectively, by the left medial sectional hepatic artery and the left lateral sectional hepatic artery and drained by the left medial sectional hepatic duct and the left lateral sectional hepatic duct. The plane between these sections is referred to as the left intersectional plane, and it corresponds to the umbilical fissure and the line of attachment of the falciform ligament to the anterior surface of the liver.

2.4.5 Third-Order Division

The third-order division into the respective segments is based on the branching of the sectional arteries and bile ducts. Each of the right sectional arteries and right sectional bile ducts as well as the left lateral sectional artery and bile duct terminate by dividing into two branches. Each of these two branches supplies one liver segment. Therefore, the right anterior, right posterior, and left lateral sections each contain two liver segments. However, the left medial sectional artery and bile duct terminate into two or more branches and there is no dominant pattern of division. As a result, by convention, the

left medial section has only one liver segment—segment 4. In other words, the level 2 and level 3 volumes (left medial section and segment 4) are identical. The right anterior section is divided into segments 5 and 8, the right posterior section is divided into segments 6 and 7, and the left lateral section is divided into segments 2 and 3. The planes between these segments are referred to as intersegmental planes. The left medial section is designated as a single segment—segment 4 as explained above. For ease of localization of lesions, segment 4 has arbitrarily been divided into segment 4a and segment 4b by a plane passing half way between the superior and inferior limits of the segment.

2.4.6 Caudate Lobe

The caudate lobe is the dorsal portion of the liver lying posteriorly and embracing the retrohepatic inferior vena cava in a semicircumferential fashion. The caudate lobe lies between the major vascular structures in the inferior vena cava posteriorly, the portal triad inferiorly, and the hepatic venous confluence superiorly. There is a series of short hepatic veins which drains directly from the caudate lobe into the retrohepatic inferior vena cava.

The caudate lobe can be divided into three parts: (1) the Spigelian lobe which is located behind the lesser omentum and extends to the left of the retrohepatic inferior vena cava. The ligamentum venosum crosses in front of the caudate lobe as it runs from the left portal vein to the posterior of the common trunk of the middle/left hepatic veins. On the left of the ligamentum venosum is the Spigelian lobe; (2) the paracaval portion lies in front of the retrohepatic inferior vena cava just to the right of the Spigelian lobe, and it is closely attached to the right and middle hepatic veins; and (3) the caudate process which is a small projection of liver tissue between the inferior vena cava and the adjacent portal vein anteriorly, just to the right of the paracaval portion.

The Spigelian lobe is usually supplied by two (which can join to form one) caudate portal triads, most commonly originating from the left pedicle of the portal triad. The paracaval portion is usually supplied by one or two caudate portal triads which originate from the right posterior sectional pedicle. The caudate process receives its blood supply originating from the right pedicle or from the bifurcation of the main portal triad.

The venous drainage of the caudate lobe and caudate process on the right side drains directly through the short hepatic veins into the inferior vena cava. Usually, there are two to four veins of significant size on the right side. The larger short hepatic veins usually emerge from the lower or middle third of the caudate lobe but virtually never from the upper third. Very small branches from the upper third sometimes drain into the right hepatic vein or inferior vena cava—but these are nearly too small to be of surgical significance. On the left side, there are also two to four short hepatic veins. The short hepatic veins are usually arranged on the two sides of the inferior vena cava.

There are usually two to three biliary branches from the Spigelian lobe to join the left bile duct. The paracaval portion is usually drained by two to three biliary branches into the right posterior sectional duct. Occasionally, a biliary branch drains the paracaval portion near to the middle hepatic vein area into the left hepatic duct. The caudate process usually drains into the right posterior sectional duct.

2.4.7 Terminology of Hepatic Resections

The main liver is divided by three orders of division into the livers (or hemilivers), sections or sectors, and segments, respectively. Each segment is an independent unit, with a separate arteriobiliary and portal venous supply and a separate hepatic venous drainage. Thus, each segment can be resected individually, or together with an adjacent segment.

The terminology of hepatic resections is based upon the terminology of hepatic anatomy. Therefore, resection of one side of the liver is called a hepatectomy or hemihepatectomy. Resection of the right side of the liver is right hepatectomy or hemihepatectomy, and resection of the left side of the liver is left hepatectomy or hemihepatectomy. Resection of a liver section is referred to as a sectionectomy. Resection of the liver to the left side of the umbilical fissure would be referred to as a left lateral sectionectomy. The other sectionectomies are named accordingly, e.g., right anterior sectionectomy. Similarly, resection of a sector is called sectorectomy. Resection of the whole right liver plus segment 4 is referred to as a right trisectionectomy. It can also be called a right hepatectomy extended to segment 4. The former is preferred since it implies that all of segment 4 is resected, whereas the latter may or may not. Similarly, resection of the left hemiliver plus the right anterior section is referred to as a left trisectionectomy. Resection of one of the numbered segments is referred to as a segmentectomy. Resection of the caudate lobe can be referred to as a caudate lobectomy or resection of segment 1. It is always appropriate to refer to a resection by the numbered segments. For instance, it would be appropriate to call a left lateral sectionectomy a resection of segment 2 and 3. For details of the terminology, the reader can be referred to the original literature on this subject [4].

2.5 Hepatic Hilar Plate System

2.5.1 Anatomy of Glissonian Sheath

Glisson's capsule covers the liver extends into the liver at the hilus and covers the portal triad, where it is called Glisson's sheath (). Glisson's capsule also covers the Glissonian pedi-

cles inside the liver. Couinaud called this sheath the Valoean sheath, after Valoeus, an anatomist from the Middle Ages who first described the liver capsule. The term "Glissonian sheath" is generally used only to refer to the portion of the Glissonian pedicle inside the liver. In the extrahepatic portion of the "Glissonian pedicle," the portal triads in the hepatoduodenal ligament are also enclosed by connective tissues and peritoneum up to the hepatic hilum. The intrahepatic and extrahepatic portions of the portal triads have the same structures anatomically. In other words, the extrahepatic and intrahepatic portal triads can be considered as part of the same Glissonian pedicle tree.

The common pattern of the intrahepatic Glissonian pedicle tree has been described and used by the Brisbane 2000 Terminology to divide the liver into sections (or sectors) and segments. There are many variations which make dissection of individual structures within the liver difficult and even hazardous. However, if the sheath to a particular segment is taken, it will only contain structures passing to or from that segment. Ligation of an individual sheath is therefore not only simpler, but safer. Sometimes, it is necessary to dissect structures individually within a sheath (this is particularly true for biliary-enteric anastomoses). The bile duct tends to be elliptical rather than round and the inferior aspect usually faces the corresponding artery. The relationship between the three structures within the sheaths follows two general rules of importance for surgeons embarking on biliary-enteric anastomosis. First, the portal vein tends to lie posterior to the bile duct and hepatic artery. Second, the bile duct tends to lie superior to the artery and is always close to it.

2.5.2 Anatomy of the Hepatic Hilar Plate System

Fusion of Glisson's capsule with connective tissue sheaths surrounding the biliary and vascular elements at the inferior aspect of the liver constitutes the plate system. This plate system also contains a large number of lymphatics, nerves, and a small vascular network. Although most workers consider the portal triad to be within the plate system, Couinaud states that the bile ducts and hepatic artery are located within the plate system, but that the portal vein is covered with a separate sheath of loose connective tissue. That is the reason why the plate containing the extrahepatic bile duct and hepatic artery can be separated easily from the portal vein.

The hepatic hilar plate system includes the hilar plate above the biliary confluence, the cystic plate related to the gallbladder, the umbilical plate situated above the umbilical portion of the left portal vein, and the Arantian plate covering the ligamentum venosum.

2.5.3 Hilar Plate

The hilar plate is located in the hilar area of the liver. It is bounded above by segment 4a of the liver (the posterior part of segment 4), on the right by the Rouviere's sulcus (a landmark demarcating the entry of the right posterior sectional portal triad entering into the liver), and is continuous with the cystic plate, and on the left it is continuous with the umbilical plate anteriorly and the Arantian plate posteriorly. The anterior sectional Glisson's sheath to segments 5 and 8 generally runs behind the junction between the cystic plate and the hilar plate, and the posterior sectional Glisson's sheath to segments 6 and 7 runs at the Rouviere's sulcus. As a result, the bile ducts and blood vessels of the right side can be dissected easily without widely opening the hilar plate.

2.5.4 Cystic Plate

The cystic plate is located in the gallbladder bed and is continuous with the capsule of segment 5, segment 4a, and the Glissonian sheath of the anterior segment of the liver. The posterior edge of the cystic plate lies above the midplane of the liver in the hilar area. It has also been observed by Couinaud that in most individual (83 %), the posterior edge of the cystic plate is located on the right side of the right portal vein branch.

2.5.5 Umbilical Plate

The umbilical plate is located along the inferior edge of the ventral surface of the umbilical fissure. It contains the ducts and blood vessels of the segments 2, 3, and 4 and is continuous with the round ligament inferiorly. Thus, the segmental branches of the left liver divide or fuse within the umbilical plate; the upper margin of the umbilical plate can be reached by incising the superior border of the round ligament.

2.5.6 Arantian Plate

The Arantian plate fuses and is continuous with the ligamentum venosum posteriorly.

2.6 Hepatic Artery

The hepatic artery with a high-volume oxygenated systemic arterial flow provides approximately 20–25 % of hepatic blood flow and 30–50 % of its oxygenation [8]. The proper hepatic artery arises from the common hepatic artery and runs alongside the portal vein and the common bile duct to form

the portal triad. The proper hepatic artery branches off the right hepatic artery after the left hepatic artery. The common hepatic artery originates from the celiac trunk in more than 80 % of cases. An aberrant hepatic artery refers to a branch that does not arise from its usual origin. An accessory vessel is described as an aberrant origin of a branch that is in addition to the normal branching pattern. A replaced vessel is described as an aberrant origin of a branch that substitutes for the lack of the normal branch. The liver may receive blood supply directly from the superior mesenteric artery, left gastric artery, aorta, or other visceral branches corresponding to a complete transposition. However, these vessels may be accessory, meaning that they add up to the normal arterial supply which still represents the primary arterial supply to the liver. In 5 % of instances, there is a replaced common hepatic artery, most frequently arising from the superior mesenteric artery. In approximately 10 % of cases, there is an absent common hepatic artery. In such instances, the right and left hepatic arteries originate independently. Further on, the right hepatic artery splits into its anterior and posterior branches and the left hepatic artery splits to supply segments 2 and 3. Segment 4 is supplied by one or more branches originating from the left hepatic artery, right hepatic artery, or both.

The right hepatic artery originates from the proper hepatic artery in more than 80 % of cases. The right hepatic artery crosses underneath the common hepatic duct in 65 % of cases, anterior to it in approximately 10 % of cases, and underneath the common bile duct in approximately 10 % of cases. In approximately 11–20 % of cases, there is a replaced right hepatic artery that arises in most instances from the superior mesenteric artery. Whereas the right hepatic artery usually courses anterior to the right portal vein, the replaced right hepatic artery runs posterior to the main portal vein in the portacaval space and classically ascends posterolateral to the common bile duct. In slightly more than 5 % of individuals, there is an accessory right hepatic artery that may arise from the superior mesenteric artery. Replaced and accessory right hepatic arteries can be identified by palpating the posterior right portion of the hepatoduodenal ligament, with one finger inserted into the foramen of Winslow. The left hepatic artery arises from the hepatic artery proper in more than 80 % of instances. In approximately 10–20 % of cases, there is a replaced left hepatic artery that most frequently arises from the left gastric artery. The replaced artery can be seen running through the lesser sac entering the liver via the fissure for the ligamentum venosum, into the umbilical fissure. An accessory left hepatic artery may be seen in up to 35 % of individuals. Replaced and accessory left hepatic arteries can usually be detected by palpation of the gastrohepatic ligament. Rarely, the right or left hepatic arteries originate independently from the celiac trunk or branch after a very short common hepatic artery origin from the celiac, and the gastroduodenal artery may originate from the right hepatic artery.

2.7 Portal Vein

The portal vein is formed in the retroperitoneum by the confluence of the superior mesenteric vein and the splenic vein, behind the neck of the pancreas and courses behind the duodenal bulb [9]. In its most common branching pattern, it divides at the porta hepatis into the right and left portal veins. As it courses cranially, the right portal vein first gives off collateral branches to the caudate lobe and then divides into anterior and posterior branches, further subdividing into superior and inferior segmental branches to supply the right liver. The left portal vein first has a horizontal course (pars horizontalis) to the left and then turns medially toward the ligamentum teres (pars umbilicalis, i.e., the vertical part), supplying the lateral segments (segments 2 and 3) of the left liver. It displays a wide anterior concavity ending up at the superior and inferior segmental branches of segment 4.

Branching anomalies of the main portal vein (PV) at the hepatic hilum are known to be less frequent (10–20 % of cases) than those of the hepatic arteries and hepatic veins. The most common patterns are represented by: (a) trifurcation of the main portal vein (7.8–10.8 %); in these cases, the main portal vein divides into three branches after entering the porta hepatis; a right anterior sectional vein, a right posterior sectional vein, and a left portal vein; (b) origin of the right posterior sectional branch directly from the main portal vein (4.7–5.8 %), where the main portal vein gives rise to the right posterior sectional vein, then continues to the right for a short distance and divides into the right anterior sectional branch and the left portal vein; (c) origin of the right anterior sectional branch from the left portal vein (2.9–4.3 %). In these cases, the main portal vein divides into the right posterior sectional vein and the left portal vein. The right anterior sectional vein originates from the left portal vein.

2.8 Hepatic Vein

The three main hepatic veins (right, middle, and left) drain into the inferior vena cava [10]. The right hepatic vein commences near the anteroinferior angle of the liver on the right and it has a long course, largely in the coronal plane in the liver. It runs in the intersectional plane between the right anterior and posterior sections of the liver, receiving venous drainage from usually all of segments 6 and 7 and some of segments 5 and 8. Near to its termination it lies almost horizontally. It enters the inferior vena cava at above the same level as the upper pole of the caudate lobe, and this level is a few milliliters lower than the entry of the trunk of the middle and left hepatic veins into the inferior vena cava. It may receive very small branches from the upper part of the caudate lobe.

The middle hepatic vein arises from the confluences of two veins. The vein from segment 4b is long, tenuous, sagit-

tal, and enters the middle vein on its left side. It is joined by the vein from the right side draining segment 5. In 25 % of cases, a substantial amount of venous drainage from segment 6 drains into the middle hepatic vein. The middle hepatic vein runs in the midplane of the liver receiving venous drainage from parts of the right and left livers. The branch from segment 8 is large, and it usually runs transversely into the right side of the middle hepatic vein. The middle hepatic vein ends as a single trunk in the inferior vena cava in only 3–15 % of cases. In approximately 85 % of cases, it forms a common trunk with the left hepatic vein. This trunk is usually 5 mm or less in length, but there can be a common wall between the middle and the left hepatic veins. Therefore, it should be a surgical maxim that there are only two major hepatic veins entering the inferior vena cava—the right and the common trunk of the middle and left hepatic veins. Any attempt trying to dissect the middle hepatic vein from the left hepatic vein extrahepatically is dangerous as a hole made in the trunk or the common wall can result in torrential bleeding.

The left hepatic vein drains segments 2 and 3. It runs in the intersegmental plane between segments 3 and 2. It then runs in the posterior part of the fissure for the ligamentum venosum which forms part of the intersectional plane between segment 4 and segments 2 and 3. The left hepatic vein is situated in the cranial 2 cm of this fissure which divides segment 4 from segment 2, and it makes up part of the posterior edge of the liver. At this level, the vein is covered only by connective tissues of the left triangular ligament. The vein then travels transversely and posteriorly to the right in the direction of the vena cava, following the superior edge of segment 1. It terminates in the inferior vena cava, usually receiving the middle hepatic vein to form a common trunk before it does so. The left hepatic vein receives two main branches within the liver, an umbilical vein which runs in the umbilical fissure draining parts of segments 4 and 3. This vein is inconstant, happening in less than 60 % of cases. Another vein, the accessory segment 4 vein, or the segment 4 vein by some authors, drains into the left hepatic vein in 57.5 % of cases. It is important not to confuse the umbilical portion of the left portal vein with the umbilical vein; the latter is a tributary of the left hepatic vein that normally drains the most leftward and part of segment 4. It is also important not to confuse the umbilical vein which exists in utero but becomes obliterated after birth to form the ligamentum teres with the umbilical vein branch of the left hepatic vein.

2.8.1 The Right Hepatic Vein and Its Anomalies

The prevailing pattern of the right hepatic vein is a long trunk, with only small branches draining all of segments 6 and 7 and some of segments 5 and 8. In rare occasions, the right hepatic vein has only a short trunk and branches off a posterior branch which drains all of segments 6 and 7, and an anterior branch which drains some of segments 5 and 8.

The right hepatic vein may be small and drains only all of segments 7 and parts of segments 6 and 8 under the following three anomalies.

A small right hepatic vein, being compensated by a well-developed middle hepatic vein.

A small right hepatic vein and an accessory inferior right hepatic vein which arises from the inferior vena cava; this happens in about 15 % of cases.

An accessory right hepatic vein (also called dorsal hepatic vein) which drains directly into the inferior vena cava.

2.8.2 The Trunk of the Middle/Left Hepatic Veins and Its Anomalies

The prevailing pattern of the common trunk of the middle and left hepatic veins is that the trunk is directed to the right. In rare occasions, the common trunk is directed to the left, or the trunk can be completely absent. In the latter situation, the middle and the left hepatic veins branch from the inferior vena cava in a Y pattern.

2.8.3 Venous Drainage of Segment 4 and Its Anomalies

The venous drainage of the cranial (or posterior) portion of segment 4 (called segment 4a) is mainly by a short hepatic vein or veins that drain into the middle and/or the left hepatic vein. Segment 4a is small and it represents only 20 % of the segment 4 in the studies by Couinaud in 1957. The quadrate lobe is considered by some authors to be segment 4b and it is drained by a long, tenuous, and sagittal vein that enters the middle vein on the left side in the prevailing pattern. This vein is called segment 4 vein or accessory segment 4 vein by some authors. This segment 4 vein can drain into the middle hepatic vein (commonest or prevailing pattern), into the trunk of the middle/left hepatic veins, into the left hepatic vein, or even directly into the inferior vena cava.

2.9 Biliary Anatomy

The individual biliary drainage system is parallel to the portal venous supply [11]. The right hepatic duct has two major branches: a posterior or dorsocaudal branch draining the posterior section (or sector, segments 6 and 7), with an almost horizontal course, and an anterior or ventrocranial branch draining the anterior section (or sector, segments 5 and 8),

with a more vertical course. The right posterior duct usually runs posterior and fuses with the right anterior duct from a left (medial) approach to form the right hepatic duct. The left hepatic duct is formed by segmental tributaries draining segments 2–4. The bile duct draining the caudate lobe usually joins the origin of the left or right hepatic duct. The right and left ducts exit from the liver and join to form the common hepatic duct. Usually, only a short portion of the right hepatic duct, about 1 cm, is in an extrahepatic position. The left hepatic duct has a much longer extrahepatic course than the right bile duct. Usually, a 2–3 cm length of the left hepatic bile duct is in an extrahepatic position. By convention, the common hepatic duct changes its name to the common bile duct at the point of entry of the cystic duct. The common bile duct then runs down anterior to the portal vein and at the right of the hepatic artery in the free edge of the lesser sac and passes behind the first part of the duodenum, to the right of the gastroduodenal artery and behind or in the pancreas, before it curves to the right where it is joined by the pancreatic duct and enters the ampulla of Vater in the middle of the second part of the duodenum. The arteries of the supraduodenal bile duct arise from the retroduodenal artery, gastroduodenal artery, right branch of the hepatic artery, and cystic artery. There is on average eight small arteries. The most important of these vessels runs along the lateral borders of the duct. The common bile duct receives about two-thirds of its blood supply from below and the rest from small vessels along its course or from above.

Anatomic variations and anomalies of bile duct anatomy are common, with the most common sites of involvement at the hepatic bifurcation and in the insertion of the cystic duct. Although most are of no pathologic significance, an understanding of these variations is important to avoid misinterpretation.

2.9.1 Triple Confluence of the Right Anterior and Posterior Sectional (Sectoral) Ducts and the Left Hepatic Duct

There is a triple confluence of the right anterior and posterior sectional (sectoral) ducts and the left hepatic duct in 10–15 % of individuals, and a right sectional (sectoral) duct joins the main bile duct directly in 20 %. In 16 %, the right anterior sectional (sectoral) duct, and in 4 % the right posterior sectional (sectoral) duct, may approach the main bile duct in this fashion.

2.9.2 The Insertion of a Right Sectional (Sectoral) Duct into the Left Bile Duct

The right posterior sectional (sectoral) duct inserts with the left bile duct in 20 % of patients and the right anterior sectional (sectoral) bile duct does so in 6 %. In both cases, there is no right hepatic duct as both join the left duct, one to the left of the midline and the other in the midplane. A right sectional (sectoral) bile duct inserting into the left bile duct to the left of the midplane is in danger of injury during left hepatectomy.

2.9.3 The Insertion of a Right Bile Duct into the Biliary Tree at a Lower Level than the Prevailing Site of Confluence

Low union may affect the right hepatic duct, a sectional (or sectoral) right duct (usually the anterior one), a segmental duct, or a subsegmental duct. The right hepatic duct may join the main hepatic duct below the normal confluence in 25 % of cases (9 % the anterior and 16 % the posterior). A right bile duct unites with the common hepatic duct below the prevailing site of confluence in about 2 % of individuals. Sometimes the duct unites with the neck of gallbladder or the cystic duct and then with the common hepatic duct.

2.9.4 Hjortsjo Crook

The Hjortsjo crook occurs in the majority of the population [12]. As the right posterior sectional (or sectoral) bile duct courses superiorly, dorsally, and inferiorly to the right branch of the portal vein and hooks over the origin of the right anterior sectional (or sectoral) portal vein, resection of the anterior right section (or sector) of the liver (segments 5 and 8) can damage the right posterior sectional (or sectoral) duct if the resection is done too close to the bifurcation of the right portal vein into the anterior and posterior sectional (or sectoral) branches. The correct procedure is to stay away from the bifurcation of the right portal vein.

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Assessment of the Patient Before Liver Resection

3

Tianfu Wen, Chuan Li, and Lei Li

3.1 Assessment of the Patient's General Condition

In patients with liver cancer, the Eastern Cooperative Oncology Group (ECOG) performance status scale is often used to assess the patient's general condition before hepatectomy. The ECOG scale rates the physical state of the patients on a scale of 0–4 (Table 3.1). In general, patients undergoing an elective liver resection should not have an ECOG score greater than 2. The patient's nutritional status should also be assessed before surgery, commonly by measuring albumin levels.

However, patients with a Child's score of A who are undergoing liver resection can have normal preoperative albumin levels. Some scholars believe that prealbumin levels are a more appropriate assessment of nutritional status in patients with cirrhosis.

3.2 Assessment of Cardiovascular Function

Preoperative hypertension should be controlled, with blood pressure maintained with medication at 160/100 mmHg or less. A careful list of medications should be obtained from patients who are taking oral antihypertensive drugs. For patients who take reserpine to control blood pressure, reserpine must be replaced with other antihypertensive drugs preoperatively; elective surgery must be delayed for at least 1 week after stopping reserpine.

Preoperative routine electrocardiogram is necessary. Patients with arrhythmias should have 24 h of Holter monitoring. When necessary, patients with a history of structural heart disease should have an echocardiogram. Patients who are suspected of having severe coronary artery stenosis or occlusion must undergo coronary CT or angiography, when necessary. For these patients, a joint assessment by anesthesia and cardiovascular specialists before surgery could help to improve the perioperative outcomes.

3.3 Assessment of Pulmonary Function

Preoperative routine chest X-rays can identify pulmonary parenchymal disease or pleural abnormalities. In smokers and patients with previous lung disease or who are older than 60 years, preoperative pulmonary function tests should be considered. In patients with severe impairment of lung function, elective surgery should be performed with caution. Smokers should stop smoking before surgery; 1–2 weeks of smoking cessation leads to recovery of mucociliary function and reduced sputum volume. Quitting for 6 weeks can improve lung capacity. For patients with acute respiratory infections, elective surgery is best delayed for 1–2 weeks; in cases of emergency surgery, antibiotics should be used, and inhaled anesthetics should be avoided to the extent possible.

Table 3.1 US Eastern Cooperative Oncology Group performance status scale

Grade 0	Unrestricted activity; able to perform all pre-diagnosis activities
Grade 1	Strenuous physical activity is limited, but able to move around freely and engage in less intense physical activity or seated work, including housework and general office work
Grade 2	Able to move around freely and perform self-care, but has lost the ability to work. Active less than half of the day
Grade 3	Can only participate partially in self-care; spends more than half the time during the day in bed or chair
Grade 4	Disabled. Cannot take care of self. Bedridden

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3.4 Coagulation

A thorough preoperative inquiry into the patient's medical history and family history is very important. In patients with known coagulation disorders or hemophilia, a hematologist's assistance should be enlisted. Conventional coagulation panels and platelet counts should be obtained. Patients who are taking warfarin should stop taking it preoperatively; warfarin should be replaced with low-molecular-weight heparin, which can be stopped the night before surgery. For patients undergoing emergency surgery, vitamin K can be used to counteract the effects of warfarin. Patients with obstructive jaundice before surgery should receive routine supplements of vitamin K.

3.5 Blood Glucose

Diabetes can increase the risk of postoperative infection, liver failure, and other complications. Also, diabetic patients may have asymptomatic coronary artery disease or renal dysfunction. Patients with diet-controlled diabetes do not require special preoperative care. Oral hypoglycemic agents should be continued until the night before surgery. Long-acting hypoglycemic agents should be discontinued for 2–3 days before surgery, and short-acting insulin should be used to control blood glucose. Patients using insulin should stop taking insulin on the morning of surgery. The target blood glucose value is less than 11.2 mmol/L.

3.6 Assessment of Liver Function and Liver Reserve

The Child-Pugh classification is the most commonly used method for the clinical assessment of liver function and includes the following five parameters: total bilirubin level, albumin level, the presence of ascites, the presence of hepatic encephalopathy, and clotting time (Table 3.2). Each parameter is scored according to severity on a scale of 1–3 points; the five scores are summed for a minimum score of 5 points and a maximum score of 15 points. Patients are then divided into classes A, B, and C (class A – 5–6 points; class B – 7–9 points; and class C – 10–15 points. The Child-Pugh score is a semiquantitative method for determining the prognosis of patients with cirrhosis. Patients with Child class A liver disease have a 1-year rate of liver failure-related mortality of <5 %. Child class B liver disease is associated with a 1-year liver failure-related mortality rate of 20 %. Child class C disease represents severe decompensation of liver function, and the 1-year mortality rate due to liver failure is 55 %. According to the Child-Pugh classification standards [1], hepatic resection is well tolerated in class A patients and can be tolerated in class B patients with adequate preparation. However, there is still some risk in these patients. Class C patients tolerate surgery poorly, contraindicating hepatectomy.

Table 3.2 Child-Pugh classification score criteria

Clinical and biochemical indicators	1	2	3
Hepatic encephalopathy (grade)	None	1–2	3–4
Ascites	None	Mild	Moderate, severe
Total bilirubin (μmol/L)	<34	34–51	>51
Albumin (g/L)	>35	28–35	<28
Coagulation time (s)	<4	4–6	>6

However, the Child-Pugh classification does not accurately reflect the patient's liver reserve. Impaired liver reserve may still exist in patients with a Child class of A. Therefore, these patients require further quantification of liver function, which can be assessed by measuring the ability of the liver to remove certain exogenous compounds. The main quantitative tests of liver blood flow include the following: the indocyanine green (ICG) excretion test, the galactose clearance test, and the sorbitol clearance test. The main microsomal liver cell function tests include the caffeine clearance test and the antipyrine clearance test. These compounds are only processed by hepatic metabolism; if the liver reserve capacity is decreased, the clearance rate for these compounds is also decreased, and retention rates are increased.

3.6.1 Indocyanine Green Clearance Test

Currently, the most common clinical assessment of a patient's liver reserve capacity is the ICG excretion test, which measures the 15-min indocyanine green retention rate (ICGR15) and the maximum clearance rate (ICG max) to reflect the patient's liver function reserve.

Indocyanine green is a photosensitive material that rapidly combines with human serum proteins after injection. It under goes greater than 90 % cell uptake by the liver and is then secreted into bile in its free form; it does not enter the enterohepatic circulation. There is no organized extrahepatic clearance and no toxic side effects. Its clearance rate depends on the amount of hepatic blood flow and bile duct patency hepatocytes. Hepatic blood flow may reflect liver perfusion and hepatocyte metabolism. ICG excretion by the liver is more significantly affected by blood flow velocity; therefore, any factor that affects hepatic blood flow (such as portal vein thrombosis) will affect its clearance rate. Biliary excretion disorders (such as obstructive jaundice) can also obstruct ICG removal. In these circumstances, the ICG excretion test will not accurately reflect the hepatic functional reserve. Generally, in patients with Child class A disease, patients

with an ICG R15 <10 % can tolerate resection of up to four hepatic segments. When the ICG R15 is 10–19 %, patients can tolerate resection of two to three liver segments, and when the ICG R15 is 20–29 %, only one segment can be safely resected.

When the ICG R15 is 30–39 %, only a conservative partial liver resection can be tolerated. When the ICG R15 is ≥40 %, only tumor enucleation can be performed [2].

3.6.2 Artery Ketone Body Ratio (AKBR)

The liver is the main site of energy metabolism. The hepatic mitochondrial NAD +/NADH ratio reflects the energy metabolism of the liver. The NAD +/NADH ratio of liver ketone bodies (acetoacetate/β - hydroxybutyrate) and the NAD +/NADH = acetoacetate/β - hydroxybutyrate × β - hydroxybutyrate dehydrogenase equilibrium are constant. When hepatocyte function is impaired, the chain of liver mitochondrial respiration is damaged, and the AKBR value is decreased. It is generally believed that if AKBR is > 0.7, the liver mitochondrial function is normal, and the liver can produce enough ATP to maintain normal reserve function and withstand most types of surgery. If the AKBR is 0.4–0.7, mitochondrial function is impaired, and insufficient ATP is generated; such patients can only tolerate partial hepatic resection or resection of the tumor only.

When AKBR is <0.4, the mitochondrial function is severely impaired, and the liver cannot produce ATP; these patients cannot tolerate any type of liver resection [3].

3.6.3 Oral Glucose Tolerance Test (OGTT)

Glucose metabolism in the liver requires normal structure and function of the liver cells. Hepatic glycogen synthesis is an energy-consuming process, and the OGTT curve type may reflect the hepatic energy reserve. An early-morning OGTT test is performed by measuring fasting blood sugar in approximately 2 ml of venous blood. Then, 75-g anhydrous glucose dissolved in approximately 250 ml of water is consumed within 5 min. Blood glucose levels are subsequently measured at 30, 60, and 120 min (using 2-mL samples for each measurement). Based on these values, an OGTT curve is generated; the OGTT curve can be divided into the following three types:1) Normal/parabolic (P-type) – the OGTT curve peaks at 30 or 60 min after the glucose load, after 120 min, glucose has decreased to normal; 2) Linear (L-type) curve – glucose continues to increase after 60 min, or remains elevated 120 min after the glucose load, reflecting poor glucose tolerance; and 3) the Intermediate (I-type) is somewhere between these two, where the curve peaks at 60 or 90 min, but blood glucose does not return to normal after 120 min. When the liver energy reserve is normal, blood glucose normalizes 2 h after the load, yielding a P-type OGTT curve. In patients with hepatitis or cirrhosis, progressive disease impairs the normal function of the liver cells and decreases glycogen synthase and hepatic mitochondrial cytochrome a + (a3) content, causing decreased production of ATP. In this situation, the liver cannot quickly synthesize glycogen from blood sugar, and the OGTT curve can change to type I or L from a P-type. It is generally believed that P-type OGTT reflects good liver reserve and an ability to tolerate surgery, while an L-type OGTT suggests diminished liver reserve capacity in patients with poor liver function, creating considerable risk with liver resection [4].

3.6.4 Assessment of Liver Volume

Patients undergoing liver resection require complete resection of the tumor and need sufficient remaining liver tissue to prevent postoperative liver failure. Therefore, preoperative assessment of residual liver volume is very important. However, the optimal residual liver volume in patients with baseline postoperative liver failure is controversial and is affected by the presence of underlying liver disease, weight, and other factors. Shirabe et al. [5] found that in patients with a remaining liver volume after hepatectomy of less than 250 ml/m^2 (m^2 refers to the patient's body surface area), the probability of occurrence of postoperative liver failure was as high as 38 %. Therefore, they recommend a minimum residual liver volume of 250 ml/m^2 for a safe hepatectomy. In patients with liver cirrhosis and chronic liver disease, Schindl et al. [6] showed that a residual liver volume of 26.6% was the critical value predicting for liver failure after hepatectomy. However, studies suggest that a residual liver volume of greater than 25 % is sufficient to prevent postoperative liver failure [7, 8]. Kishi [9] even contends that a residual liver volume of > 20 % permits safe liver resection. However, in patients with impaired liver function cirrhosis, residual liver volume must increase correspondingly. Sudaet al. [10] studied patients with biliary tumors and obstructive jaundice and concluded that these patients require an increased residual liver volume of 40 % in order to avoid postoperative liver failure. For patients with cirrhosis, residual liver volume is generally recommended to be 40–50 % in order to avoid postoperative liver failure [11, 12].

CT volumetric analysis is the main method for performing liver volume measurements. However, this method can only be used to measure liver volume and does not effectively evaluate the function of the remaining liver cells. Especially in patients with cirrhosis, this method may overestimate function because of the poor-quality remnant liver, so patients are at risk of liver failure. Asialoglycoprotein receptor (asialoglycoprotein, ASGP) is only present in mam-

malian cells and has specific receptors in the liver. The intravenous injection of technetium-labeled asialoglycoprotein receptor and its analogs galactosy l human serum albumin (galactosy l human serum albumin-diethylenetriaminepentaacetic acid, TcGSA) can quickly allow measurement of hepatic ASGP. GSA clearance rates may reflect hepatic reserves. Kokudo [13] used logistic regression analysis in a study of relevant factors in patients with liver failure after liver resection. The amount of residual liver ASGP was a meaningful indicator; when it was less than 0.05 mmol/L, there was a postoperative liver failure rate of 100 %. This technology can be used in patients with jaundice and in ICG-intolerant patients [14].

3.7 Assessment of Portal Hypertension

Varying degrees of cirrhosis are present in 80–90 % of patients. Surgery is higher risk in patients with liver cirrhosis. Therefore, accurate preoperative assessment of patients with cirrhosis and portal hypertension is necessary to reduce operative risk. At present, the gold standard for the diagnosis of portal hypertension is a measurement of the patient's hepatic venous pressure gradient (HVPG). The measurement is obtained by threading a catheter into the internal jugular vein or femoral vein, then into the inferior vena cava, and subsequently into the hepatic vein. Then the catheter balloon is inflated, blocking hepatic venous return, and manometry is performed. In this case, the measured parameter is wedge hepatic venous pressure (WHVP). Free hepatic venous pressure (FHVP) is measured again after the balloon is deflated. The following equation expresses the relationship among these values: HVPG=WHVP-FHVP. Under normal circumstances, HVPG is 3–5 mmHg; an HVPG >5 mmHg is considered to indicate the presence of portal hypertension [15]. An elevated HVPG in patients undergoing liver resection is considered to be associated with a higher incidence of postoperative complications and a higher risk of liver failure [16, 17]. However, in many recent studies, portal hypertension was not considered an absolute contraindication to liver resection; Child class A patients with portal hypertension did not have a higher postoperative complication rate than liver cancer patients without portal hypertension [18–20]. Even in patients with significant splenomegaly and hypersplenism, concurrent splenic resection is also safe and can improve the prognosis of patients with hepatocellular carcinoma [18].

However, the need for more rigorous preoperative evaluation of liver morphology, liver functional reserve, and residual volume in such patients should be emphasized. Recent advances have identified ultrasound as a noninvasive method for detecting cirrhosis and portal hypertension. Transient ultrasound elastography is a noninvasive method of measuring liver stiffness and has been used in many centers. Cescon and other investigators [21] have shown that liver stiffness > 17.6 kpa was an independent risk factor for liver failure after liver resection (sensitivity = 91.43 %; specificity = 60.0 %). In this study, patients without postoperative liver failure had a liver stiffness ≤14.8 kpa [21]. Wong et al. [22] showed that liver stiffness of ≥12.0 kpa (sensitivity of 85.7 % and specificity of 71.8 %) was associated with a significantly increased risk of severe postoperative complications (33.3 % vs. 4.3 %).

3.7.1 Assessment of Tumor Size and Location

Advances in surgical techniques and perioperative management in patients undergoing liver resection have ushered in an era where no disease site presents a contraindication to resection. However, the relationships among the site of the tumor, major blood vessels, and bile ducts remain very important. Overall, the preoperative assessment of patients for liver resection should include determining whether there will be enough residual liver, as well as assessments of the patency of the portal vein, hepatic artery, and hepatic vein. At the same time, we need to consider whether postoperative biliary drainage will be unobstructed.

3.7.2 Assessment of Patients with Obstructive Jaundice Undergoing Liver Resection

Clear reasons for biliary obstruction in patients with obstructive jaundice include intrahepatic obstruction of the bile ducts, hilar bile duct tumors, and pancreatic cancer. The need for preoperatively reducing jaundice in patients with hilar cholangiocarcinoma (Huang) is currently controversial. Early studies showed that preoperative treatment of obstructive jaundice can reduce the risk of surgery. Preoperative biliary drainage can reduce obstructive jaundice and liver cell damage, which are conducive to the recovery of liver function. However, the recovery of liver function after preoperative drainage takes a long time.

In patients with jaundice, 4–6 weeks is needed to reduce serum bilirubin levels to 2 mg/dl. Preoperative jaundice is also associated with infection and other complications. The latest systematic evaluation noted that the presence of jaundice before conventional surgery was not associated with increased mortality of patients, but was associated with an increased incidence of postoperative complications [23].

In our clinical work, we do not recommend routine treatment of preoperative jaundice, except in cases of severe jaundice (bilirubin >500μmol/L), elderly in patients with poor blood clotting function, in patients with biliary tract infections, or in patients with poor general condition, when surgery may be beneficial.

3.8 Preoperative Assessment for Living-Donor Liver Transplantation

In order to avoid unnecessary complications, living-donor liver transplantation must include a rigorous assessment of the donor. Donor age requirements differ among the various transplant centers. Some transplant centers accept donors up to 65 years old, while others require donors to be 55 years old or younger [24]. The use of older donors must be carefully evaluated. Increased age presents an increased risk for degenerative diseases such as atherosclerosis and liver fibrosis, which increase the risk to both donor and recipient. The minimum donor age varies according to national and regional laws.

However, most donors are between 16 and 20 years of age. In mainland China, the donor must be an immediate family member of the recipient (within three generations) [25]. In some countries and regions, friends and relatives more distant than three generations are also permitted to act as donors.

A detailed medical history is the first step in a living-donor evaluation.

Donors should be asked about a history of diabetes, hypertension, cancer, infectious diseases, kidney disease, asthma, and cardiovascular and cerebrovascular diseases. Furthermore, it is important to evaluate allergies, past surgical history, reproductive history, drug abuse, alcoholism, smoking, and in women, the menstrual history. A psychological assessment of the patient's mental state is also essential. In our clinical work, we have occasionally encountered donors who do not have full mental capabilities due to mental illness or criminal behavior. In this situation, the decisions of the potential liver donor are not legally recognized. The donor's height and weight are also very important. The estimated standard liver volume (ESLV) and the body mass index (BMI) of the donor should be calculated. For patients with high BMI, clinicians should be alert to the potential for liver steatosis. Also, excessive BMI values (>30) are associated with increased surgical difficulties. After potential donors have passed the first steps of the assessment, the second step of laboratory assessment can be performed. Laboratory examinations include blood panels, liver and kidney function tests, blood coagulation parameters, pretransfusion tests, blood lipid levels, blood glucose levels, Epstein-Barr and cytomegalovirus titers, and electrolytes. As the liver is an immunoprivileged site, preoperative tests do not need to cross-check for line cytotoxicity; transfusion principles are only required for the recipients. Female donors' preoperative hemoglobin levels are often lower than the normal value. Menstrual disorders can lead to anemia before surgery, but a detailed preoperative screening history before surgery is required, and gastrointestinal endoscopy should be performed if necessary.

Individuals who are hepatitis B surface antigen (HBsAg) positive or hepatitis C antibody positive cannot in principle be living donors for liver transplants. However, in recent years, many studies have reported that it is safe to use HBsAg-positive donors [26]. Postoperatively, these patients should be treated for hepatitis B with nucleoside analogs and immune globulin. However, in most recipients, postoperative serum HBsAg remains positive, and only a few cases of postoperative serum HBsAg seroconversion have occurred. Hepatitis B core antibody-positive patients (HBcAb) can be donors, but in HBsAg-negative recipients, preoperative and postoperative hepatitis B infection may occur. A systematic evaluation noted that in HBsAg-positive recipients with an HBcAb-positive donor, the postoperative hepatitis B recurrence rate was 11 %, and in HBsAg-negative recipients with an HBcAb-positive donor, the rate of new-onset hepatitis B infection is approximately 19 % [27]. For HBsAg-positive recipients with HBcAb-positive donors, measures to prevent the postoperative recurrence of hepatitis B must be adopted. We believe that since living-donor liver transplantation is extremely valuable, the opportunity to perform surgery must not be lost; we therefore still use lamivudine and hepatitis B immune globulin for postoperative prophylaxis against hepatitis B infection.

After laboratory testing, ECG and radiographic assessments should be performed. CT examination can evaluate the anatomy of the hepatic vein, the portal vein, and the hepatic artery anatomy and can be used to calculate the liver volume. However, for the assessment of biliary anatomy, we believe that preoperative MRCP is better.

CT scan can show the donor's portal vein anatomy clearly. Typically, the portal vein is divided into the left and right branches; sometimes, three branches are present. However, this variant is not a contraindication to surgery. It is noteworthy that on occasion, a donor's V and VIII portal vein segments are separated by the left portal vein. This anatomical variation prevents left-sided liver donation because once the left side of the liver is resected, the donor's remaining V and VII segments will lose portal perfusion. Another rare case is the presence of only one portal vein in the donor. Although we have not yet encountered this situation in our clinical work, this anatomical variation is a contraindication to surgery.

CT image reconstruction technology can clearly outline the shape of the hepatic artery. Variations in the hepatic artery often occur. Sometimes, the right hepatic artery branches from the superior mesenteric artery, or the left hepatic artery branches from the left gastric artery. In both cases, since the donor can retain the long hepatic artery, it is easy to reconstruct an anastomosis. Also, as the contralateral hepatic artery is not affected, this situation is beneficial to both donor and recipient. Sometimes, one side of the hepatic artery may have two parallel branches. Under normal

circumstances, collateral circulation is present between the two branches.

This situation is not a contraindication for surgery. However, in some cases, one side of the hepatic artery has two or more branches, which can be too small to create the hepatic artery anastomosis and may cause difficulties. If the intrahepatic trafficking branch cannot be determined, the affected side of the liver cannot be donated. Although hepatic arteriography is currently the gold standard for assessing the donor's hepatic arterial anatomy currently, the procedure has risks, including contrast-induced nephropathy or intimal injury of the hepatic artery in the potential donor. Therefore, hepatic arteriography is not recommended for routine use.

CT also can measure the donor's liver volume. It is generally believed that the donor's residual liver volume should be 30–35 % of the whole liver in order to maximize postoperative survival. For recipients, the volume of the graft is generally recommended to be at least 40 % of the estimated standard liver volume (ESLV) or at least 0.8 % by weight of the recipient liver's weight [28, 29]. However, many studies suggest that if the recipient is in generally good condition, a graft that is slightly smaller than 0.8 % by weight of the graft is safe. Currently, many formulas are available for preoperative evaluation of the donor liver volume in addition to CT. These formulas have been obtained in different ethnic groups. Therefore, the formulas may not be universally applicable in patients of different races. In our center, we usually use the standard liver volume to assess Huaxi donors' liver volumes, the Huaxi standard liver volume [30] (ml) = 11.5 × donor body weight (kg) +334. Preoperative evaluation of the donor's biliary anatomy is also very important. Variations in bile ducts may create contraindications to liver donation. Currently, we use magnetic resonance cholangiopancreatography (MRCP) to evaluate the donors' biliary trees. Compared with CT, MRI has a lower risk of renal toxicity and allergic reactions. Some scholars believe that preoperative biliary endoscopic retrograde cholangiopancreatography examination (ERCP) is better than MRCP [31]. However, ERCP carries the risk of acute pancreatitis and biliary tract infections. We believe that in a completely healthy donor, the costs of ERCP complications are potentially enormous. Therefore, in our clinical work, we do not use ERCP to assess donor biliary anatomy.

Routine performance of a preoperative liver biopsy precursor is currently controversial. Some centers advocate routine liver biopsy as BMI does not accurately reflect the degree of fatty liver in the donor, and imaging may miss the presence of pathological changes in the liver. A liver biopsy can therefore preoperatively identify unexpected pathological changes in the liver. In our center, we have adopted more liberal policies regarding liver biopsy. For patients in whom radiologic examination reveals severe fatty liver disease, we will immediately rule out liver donation surgery. For HBcAb-positive patients, as well as those with unexplained bilirubin and/or transaminase elevations or a BMI > 27, we will perform a preoperative liver biopsy.

Patients with fatty liver disease have poor tolerance to ischemia-reperfusion injuries and poor regeneration. The presence of fatty liver disease in the recipient increases the risk of surgery for both donor and recipient. However, the acceptable upper limit of steatosis varies among different centers. The acceptable upper limit at our center is 20 %. For donors with fatty liver disease, we have noted that fatty livers are larger than normal livers, and the preoperative computed liver volume may be larger than the realistic residual liver volume. During preoperative evaluations, the effects of fatty liver disease should be considered. We believe that, for non-emergent surgeries, it is safe for donors with fatty liver disease to engage in proper preoperative physical exercise for weight loss. We also need to distinguish between fatty liver and steatohepatitis before surgery. Patients with steatohepatitis already have chronic liver damage, and physical exercise, medication, and other interventions cannot affect the irreversible damage of steatohepatitis; patients with this condition are therefore not fit to be liver donors.

Once the above assessments are completed, donors and recipients need to have separate preoperative conversations. Doctors and anesthesiologists need to inform the donor and recipient about surgical risks, including morbidity and mortality. We have encountered cases where, after being informed of the surgical risk, the donor did not agree to liver surgery.

At the same time, we need to inform donors and recipients and their immediate families of the possibility of encountering previously undiagnosed anatomic variations or liver pathologies requiring intraoperative termination of the liver donation procedure. We have summarized 290 cases of liver transplantation and found that there were five cases of abnormal intraoperative findings in the donor that forced us to terminate surgery [32]. Of these, one patient had a residual liver volume that was significantly smaller than that predicted by imaging; one patient had >30 % fatty liver; another had undiagnosed cirrhosis due to schistosomiasis; and there were two cases of biliary tract variations that were not found before surgery. In living-donor liver transplantation, these situations should attract our attention. Therefore, intraoperative donor liver biopsy and cholangiography are also indispensable. For pre-liver transplant recipients who have a history of multiple surgeries or in patients with a history of multiple episodes of spontaneous bacterial peritonitis, it may be difficult to separate the adhesions or to control intraoperative bleeding, requiring the termination of surgery. For some patients, the surgical strategy may be adjusted preoperatively for the first recipient operation. Unnecessary surgical risks should be avoided. However, if the recipient fails to complete liver transplant, which can occur for various reasons, the recipient has a poor prognosis, and patients and relatives

should be informed of the situation before surgery. Awkward situations can result for patients who are in critical condition, especially in cases of serious illness or death in the recipient. Methods of addressing an ownerless or "orphan" graft are affected by various national and regional laws.

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The Application of CT and MRI in Hepatectomy

4

Weixia Chen and Shu Shen

4.1 CT Examination Technology with Respect to Its Use in the Liver

Routine and multiphase enhancement scan (including arterial, portal vein, hepatic vein, and delayed phases). Data collected from the multiphase scan can be used for both routine diagnosis and detailed, powerful 3D image post-processing. The data from different phases are used to form a 3D reconstruction, which can provide anatomical information on the liver.

A multiphase scan is used to dynamically observe and analyze the lesion's blood supply and to clarify the nature of the lesion (Figs. 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 4.10, 4.11, 4.12, 4.13, 4.14, and 4.15).

4.1.1 The Application of 3D Reconstruction in Hepatectomy

A 3D reconstruction provides a comprehensive display of the anatomical location of the lesions. This method shows the relationship between the lesions and the vasculature (including the hepatic artery, portal vein, hepatic vein, and inferior vena cava (IVC)), hilar bile duct, diaphragm, and gastrointestinal tract (Figs. 4.16, 4.17, 4.18, 4.19, and 4.20). Because the anatomy adjacent to the liver is complicated,

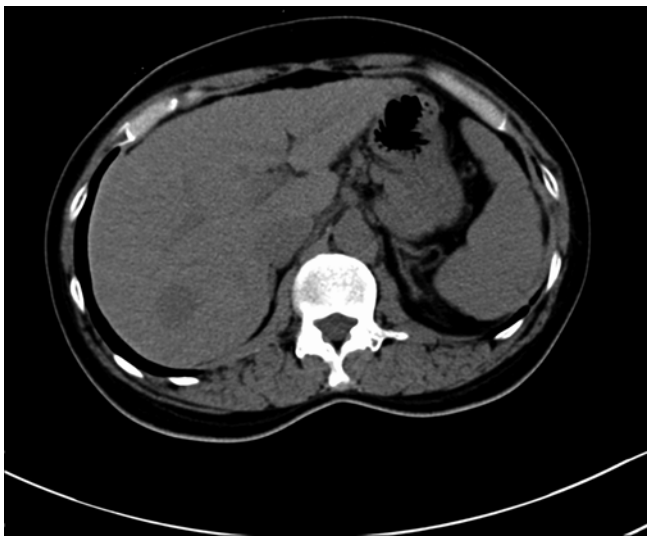

Fig. 4.1 Routine scan of HCC

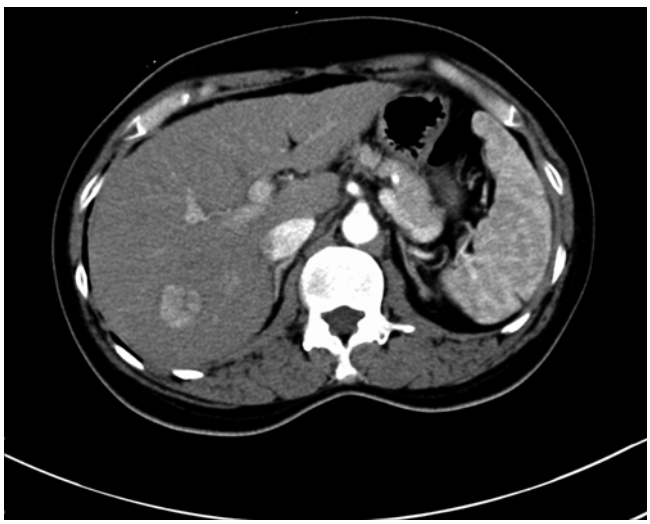

Fig. 4.2 Arterial phase images of HCC

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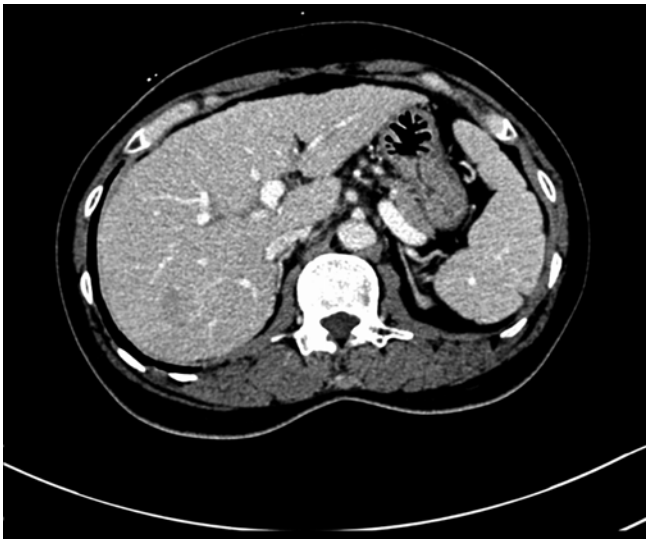


Fig. 4.3 Portal venous and arterial phase images of HCC

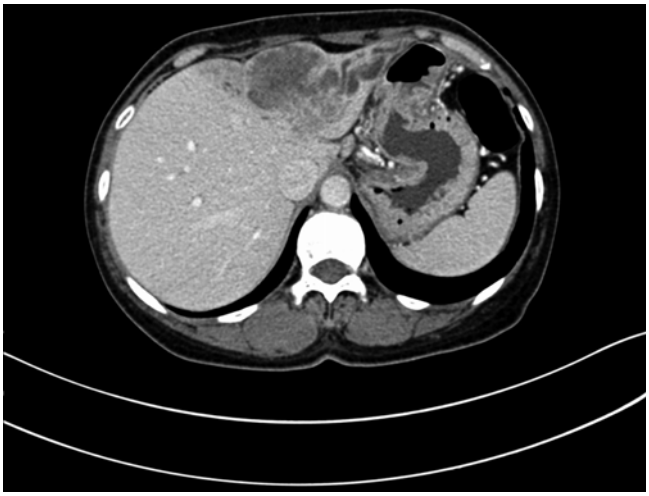


Fig. 4.6 Portal venous images of ICC

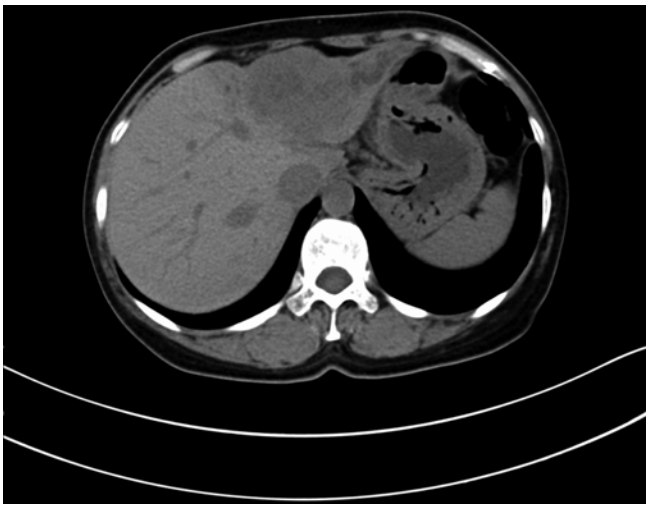


Fig. 4.4 Routine scan of ICC

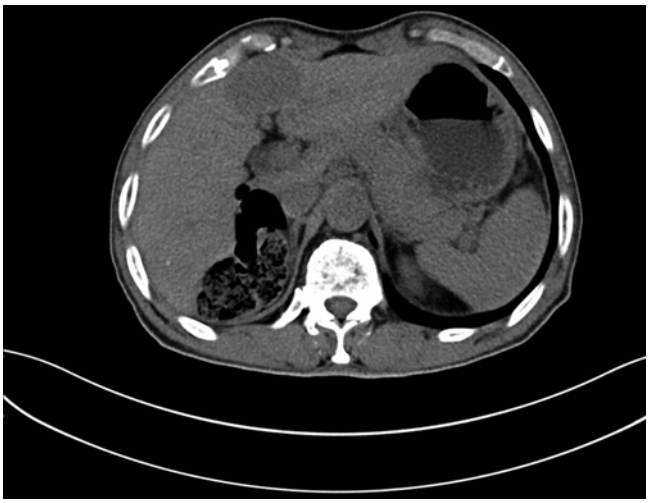


Fig. 4.7 Routine scan of liver hemangioma

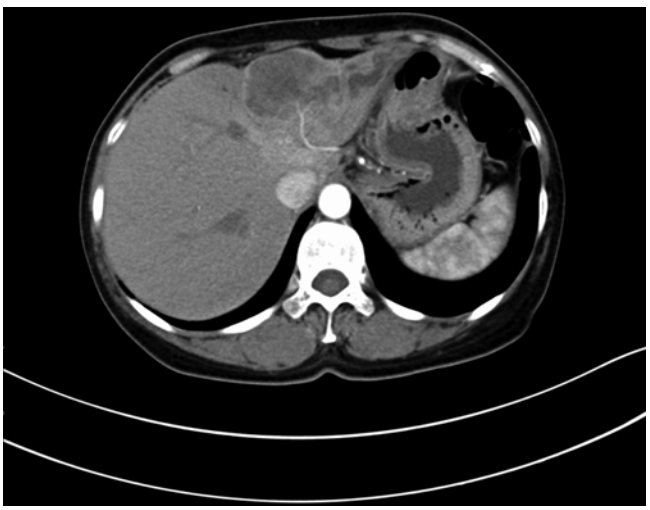


Fig. 4.5 Arterial phase images of ICC

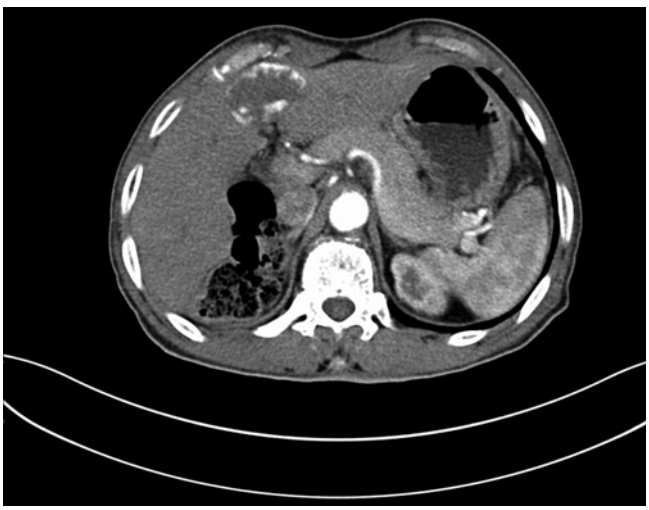


Fig. 4.8 Arterial images of liver hemangioma

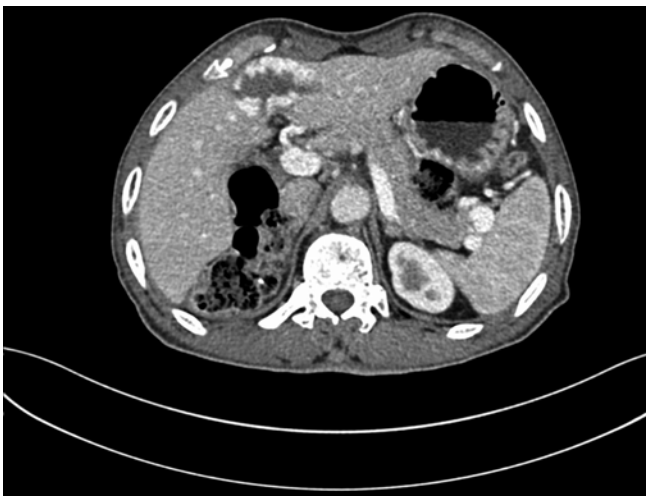


Fig. 4.9 Portal venous images of liver hemangioma

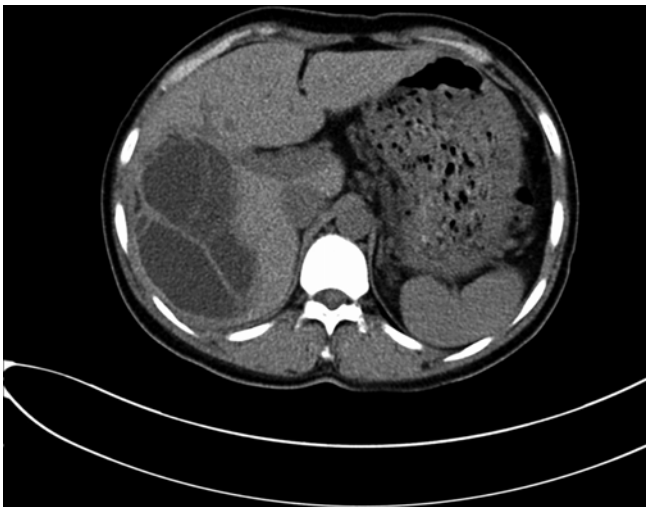


Fig. 4.10 Routine scan of liver hydatid

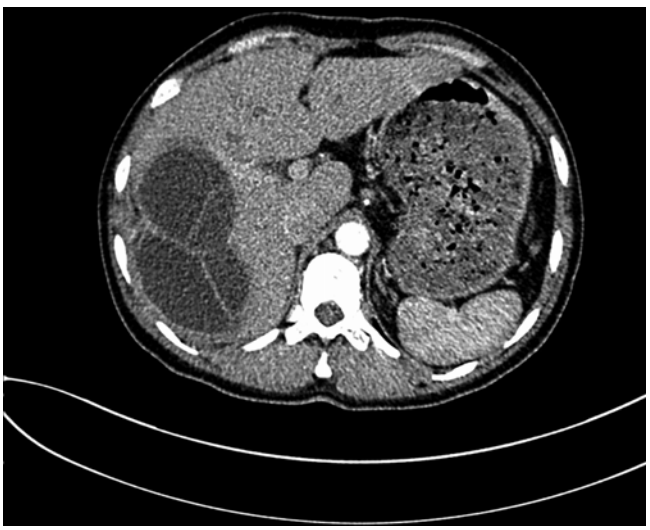


Fig. 4.11 Arterial phase images of liver hydatid

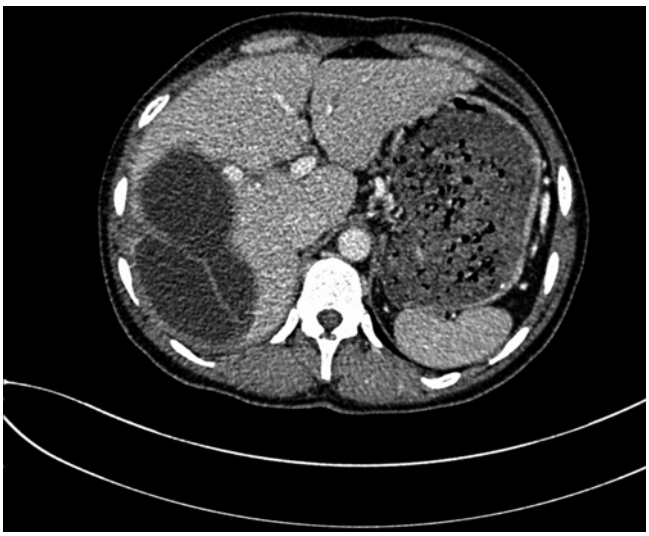


Fig. 4.12 Portal venous images of liver hydatid

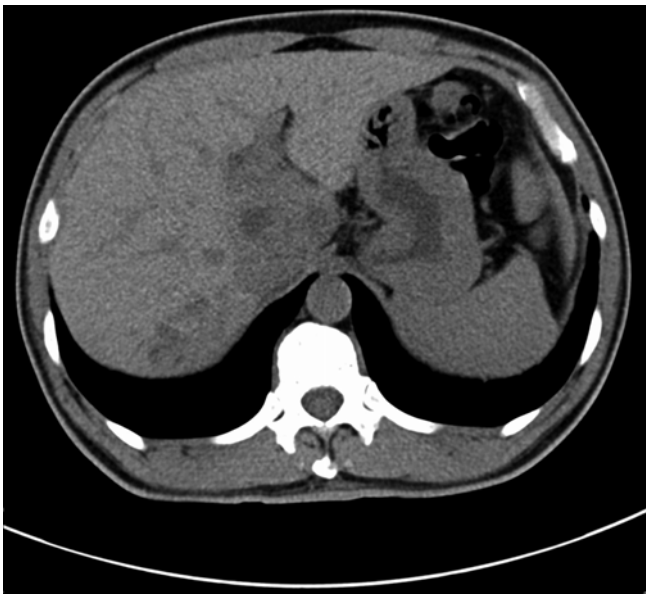


Fig. 4.13 Routine scan of hepatic pulmonary fluke

care should be taken to differentiate between (i) the bare area of the right lobe of the liver and the right adrenal or perirenal glands (Figs. 4.21, 4.22, 4.23, 4.24, and 4.25); (ii) the left lobe of the liver and the stomach, the liver-stomach interface, and the spleen (Figs. 4.26, 4.27, 4.28, 4.29, 4.30, and 4.31); and (iii) the caudate or left lobe of the liver and the enlarged lymph node in the portacaval space, the pancreas, and adjacent tissues (Figs. 4.32, 4.33, 4.34, 4.35, and 4.36).

4.1.1.1 The Anatomy of the Liver Vasculature

Hepatic artery: Imaging can reveal the origin and branch of the hepatic artery and the presence of the aberrant hepatic artery (Figs. 4.37 and 4.38).

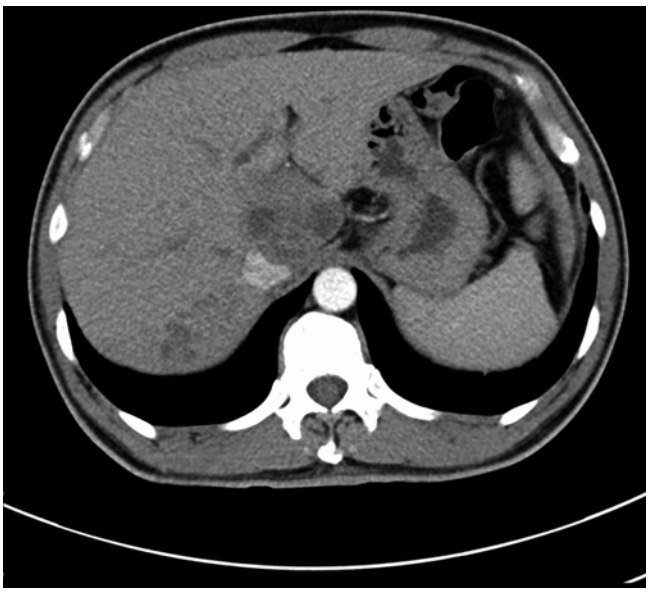


Fig. 4.14 Arterial phase images of hepatic pulmonary fluke

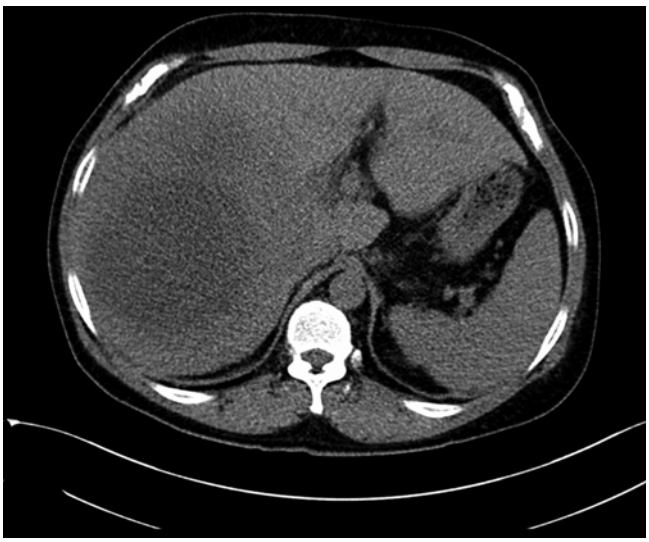


Fig. 4.16 Routine scan of HCC with thrombosis of right branch of the portal vein, while the hepatic vein and IVC suspected involvement

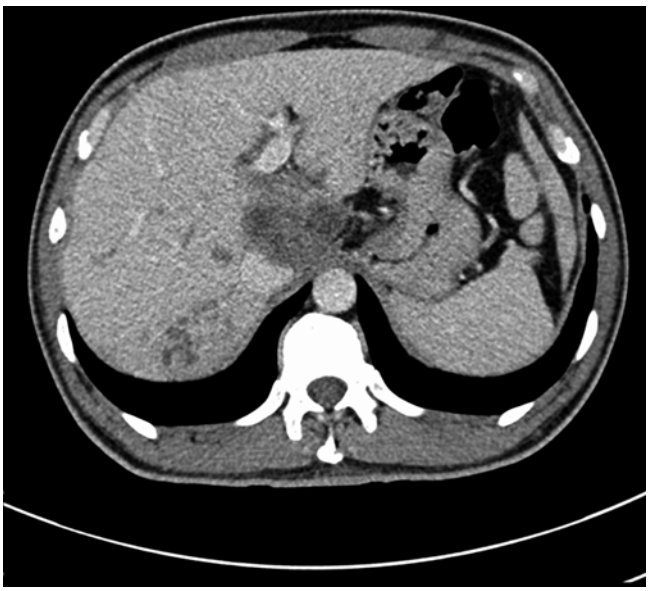


Fig. 4.15 Portal venous images of hepatic pulmonary fluke

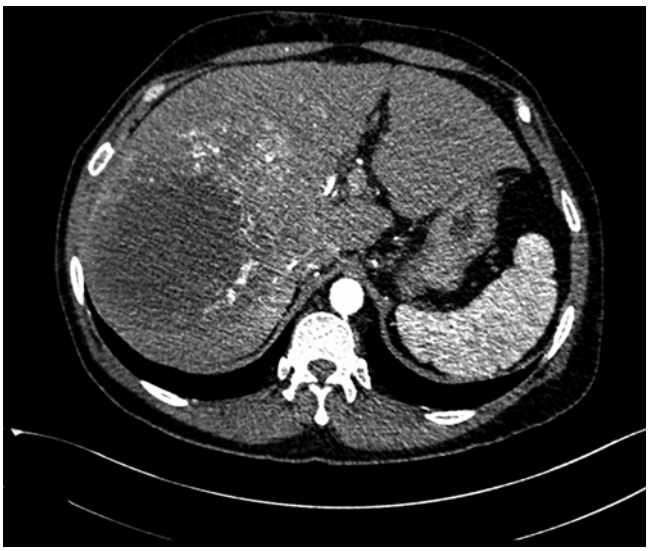


Fig. 4.17 Arterial phase images of HCC with thrombosis of right branch of the portal vein, while the hepatic vein and IVC (suspected involvement)

Portal vein: Imaging shows the branch characteristics of the portal vein, including the left and right branches or the left middle and right branches. The branch and the blood supply area are also observed (Figs. 4.39, 4.40, and 4.41).

Hepatic vein: Imaging reveals how the left, middle, and right hepatic veins empty into the IVC, including the three hepatic vein confluences and the left and right hepatic vein confluence (Figs. 4.42 and 4.43). Moreover, common anatomic variations include an accessory right hepatic vein in the first hepatic portal plane, where there is commonly only one (Fig. 4.44). Multiple hepatic vein scan empty into the IVC in the second hepatic portal plane. The hepatic venous drainage area can be accurately determined in cross-sectional images (Fig. 4.45).

4.1.1.2 Calculating the Liver Volume

The use of software on CT images allows for convenient and rapid calculation of the volume of the liver, the liver segment, and the tumor (Fig. 4.46). These data can help provide a plan for the operation by providing detailed information. Meghan Get al. reported five different

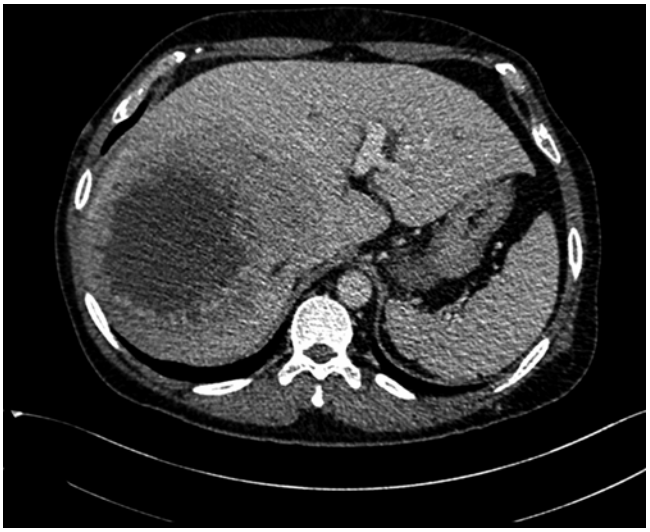


Fig. 4.18 Portal venous images of HCC with thrombosis of right branch of the portal vein, while the hepatic vein and IVC (suspected involvement)

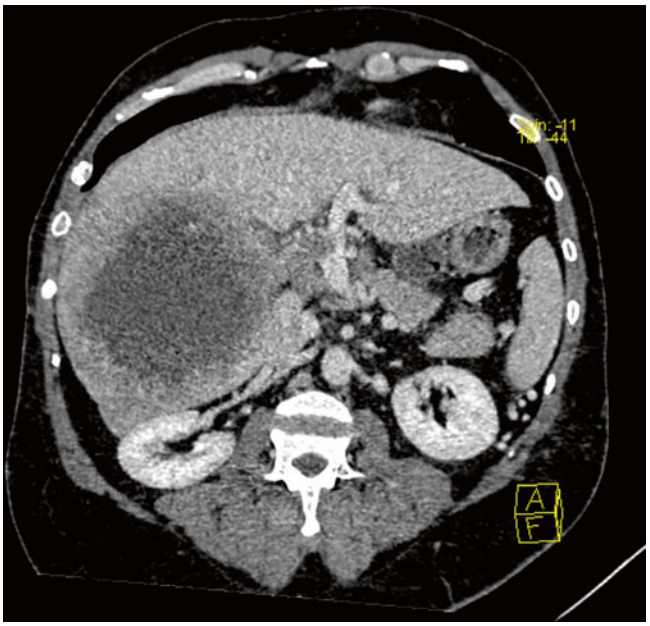


Fig. 4.19 CT reconstruction of the right branch of portal vein thrombosis

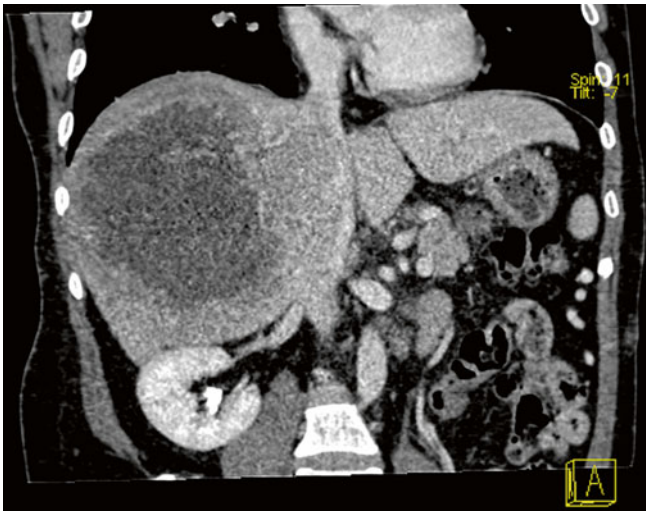


Fig. 4.20 CT reconstruction of the right hepatic vein and IVC (suspected involvement)

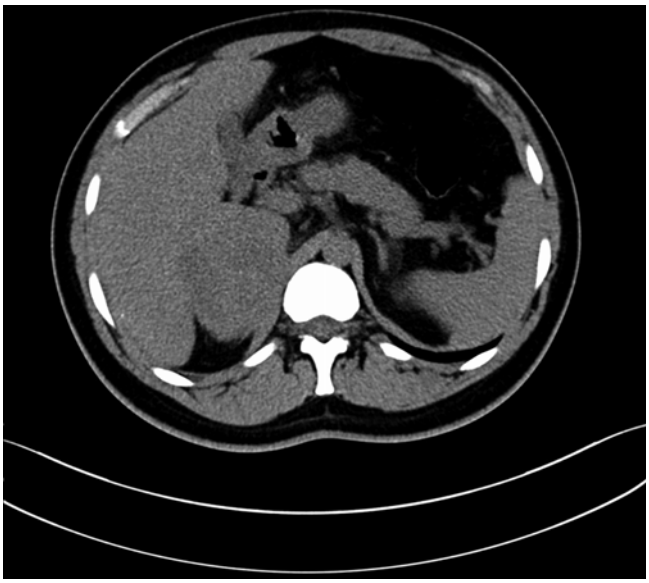


Fig. 4.21 Routine scan of right lobe lesions (hydatid) involving the right adrenal gland

measurement software programs. The authors compared the volume provided by the model with the actual volume. The result shows that there is a large difference between the software program and the actual volumes (8.0 % ± 7.5–16.9 % ± 13.8 %). These variabilities require clinical study [1].

Imaging shows the volume of the tumor before and after ALPPS, the resected liver, and the residual liver. These values can help assess the possibility of surgery (Figs. 4.47 and 4.48).

4.1.2 Liver CT Perfusion Imaging

CT imaging can show not only the morphological characteristic of the liver and tumors but also the anatomical spatial relationship of the blood vessels and organs near the tumor. Functional imaging, such as CT perfusion imaging, can show the features of hepatic perfusion, such as the proportional infusions of the hepatic artery and portal vein in cirrhotic patients. Liver function can be assessed in this manner. Biochemical detection, such as biochemical tests and IgG measurements, evaluates the state of the entire liver, which

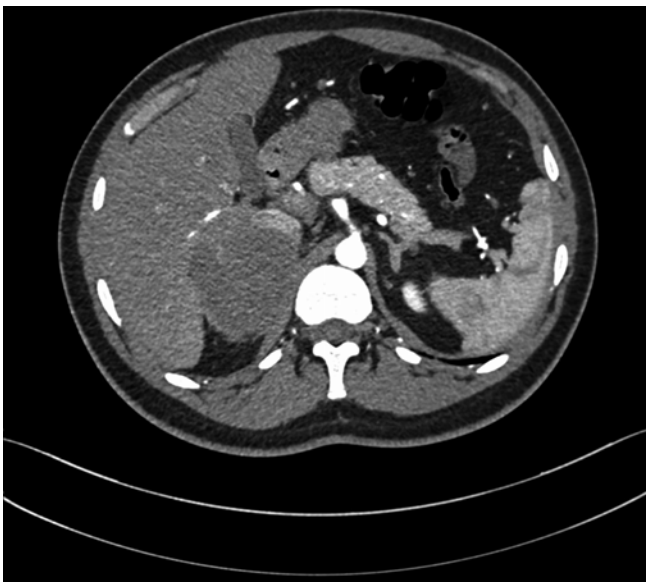


Fig. 4.22 Arterial phase images of right lobe lesions (hydatid) involving the right adrenal gland

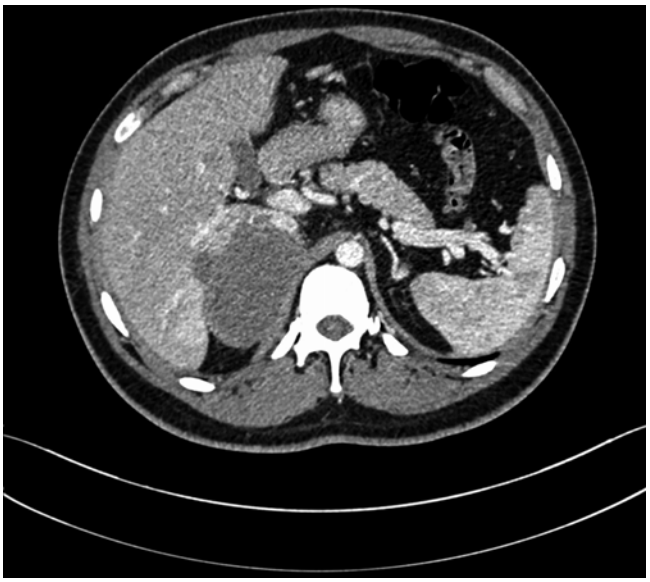


Fig. 4.23 Portal venous images of right lobe lesions (hydatid) involving the right adrenal gland

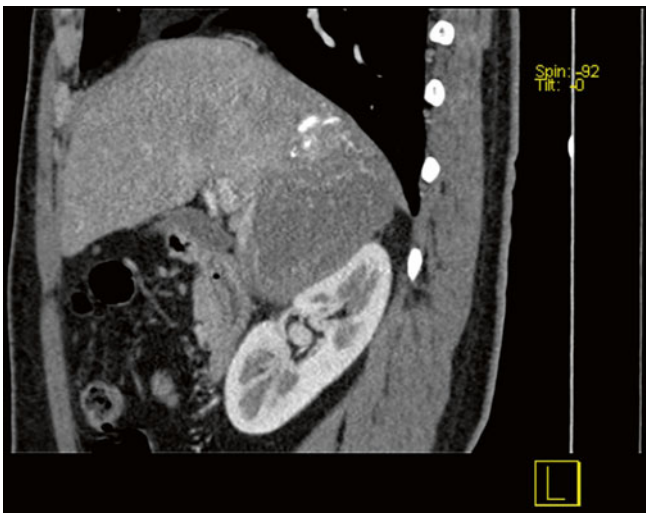


Fig. 4.24 CT reconstruction of right lobe lesions (hydatid) involving the right adrenal gland

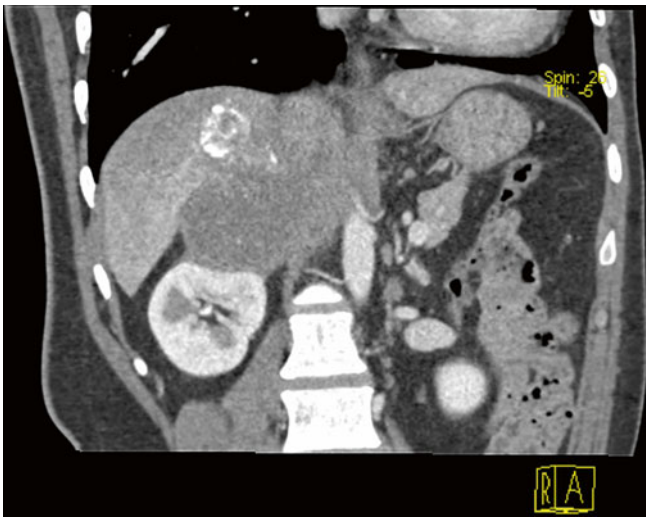


Fig. 4.25 CT reconstruction of right lobe lesions (hydatid) involving the right adrenal gland

4.1.3 The Application of 3D Image Post-processing When Planning Liver Resection

can be influenced by other organs. Additionally, CT perfusion imaging, which is less influenced by blood flow from other organs, can assess the blood perfusion of the full liver as well as a liver segment and lobe (excluding patients with heart failure and hypovolemia, for whom there is little possibility of resecting the liver). Thus, perfusion imaging can provide more detailed and accurate information for liver resection.

The liver volume, especially the residual liver volume, the blood supply range of the hepatic portal vein, the drainage area of hepatic vein, and variations in the arteries and veins and their anatomical relationship of the resected tumor and hilar bile ducts and blood vessels should be obtained. Using these measurements, the liver cutting edge, the necessity of accessory right hepatic vein and IVC anastomoses, and the tumor-negative margins of the cutting edge are confirmed before the surgery.

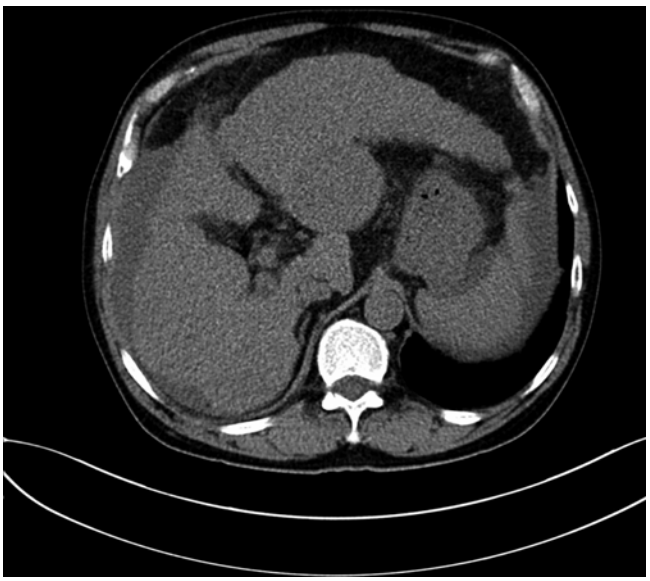


Fig. 4.26 Routine scan of hepatic left lateral lobe lesions

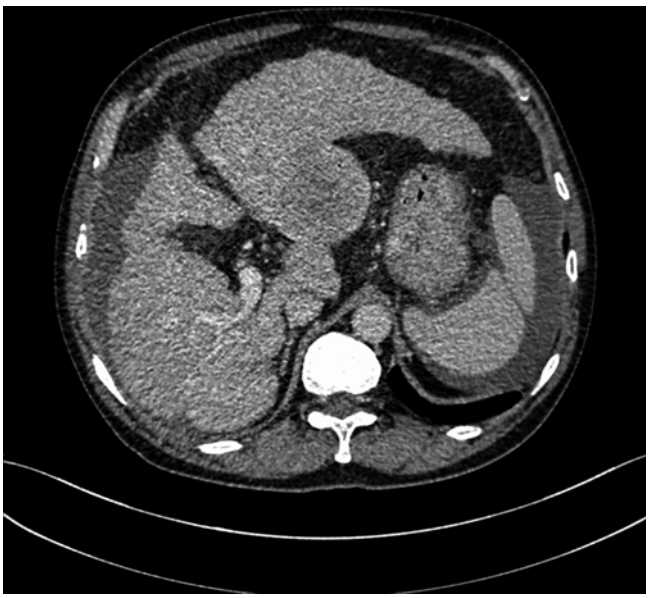


Fig. 4.28 Portal venous images of hepatic left lateral lobe lesions

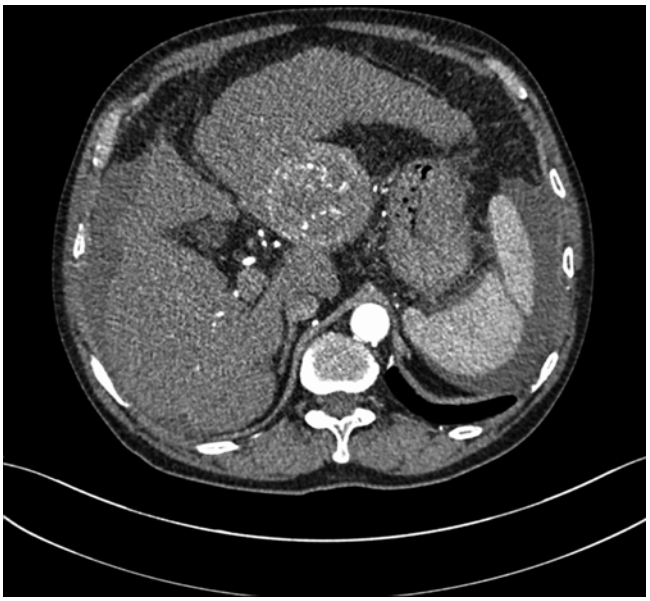


Fig. 4.27 Arterial phase images of hepatic left lateral lobe lesions

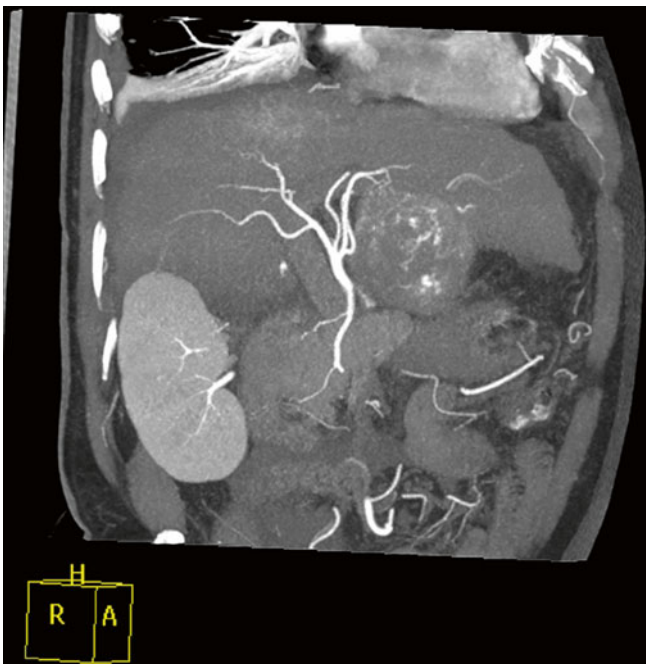


Fig. 4.29 MIP of hepatic left lateral lobe lesions

3D CT Imaging of Biliary Ducts

3D imaging can display the anatomical details and their relationship with a tumor of the hilar biliary duct, the presence of anatomic variation and dysplasia of the hilar biliary duct and vasculature, and whether the hilar biliary duct and vasculature have been invaded by the tumor. These factors can help in making a detailed operation plan, such as the number of bile ducts in the liver section, the necessity and method of biliary duct reconstruction, and the necessity of vascular anastomosis. Knowledge of these factors can help avoid intraoperative exploration and injury and reduce the risk of injury and postoperative complications. Such assessments also help to determine the cause of biliary calculi, especially intrahepatic bile duct stones, such as the exact site of biliary strictures, and make a detailed and rational resection scheme to treat the disease and prevent recurrence after operation.

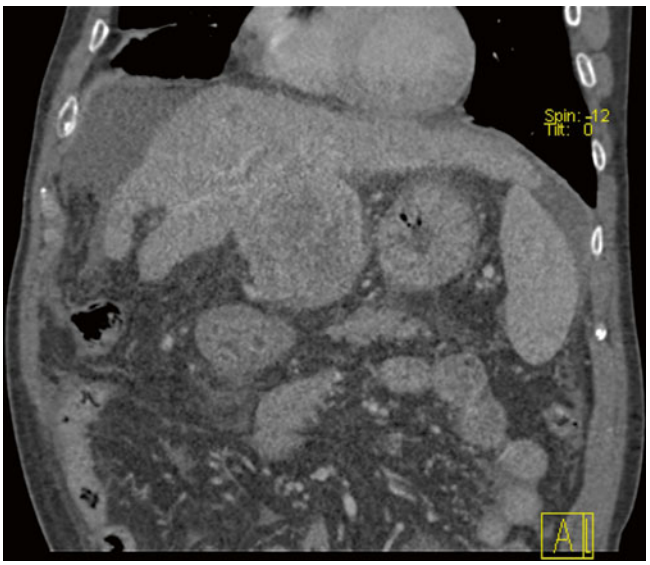


Fig. 4.30 Coronal reconstruction of hepatic left lateral lobe lesions

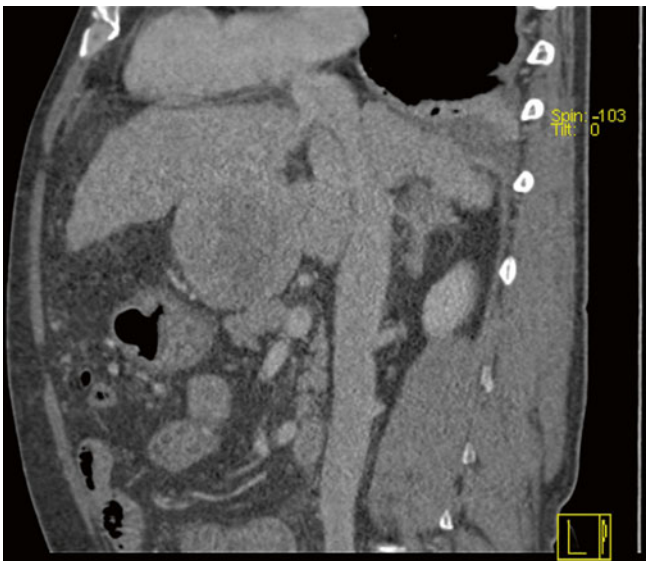


Fig. 4.31 Sagittal reconstruction of hepatic left lateral lobe lesions

4.1.4 Advantages and Disadvantages of CT in Hepatectomy

4.1.4.1 Advantages

The spatial resolution is high. Specifically, it can display the liver vasculature and the branching thereof. The scanning speed is fast and is only slightly influenced by breathing movement. The equipment is used frequently and requires little human manipulation.

4.1.4.2 Disadvantages

Ionizing radiation has a potential risk for the patient, and two imaging sessions are not recommended within a short

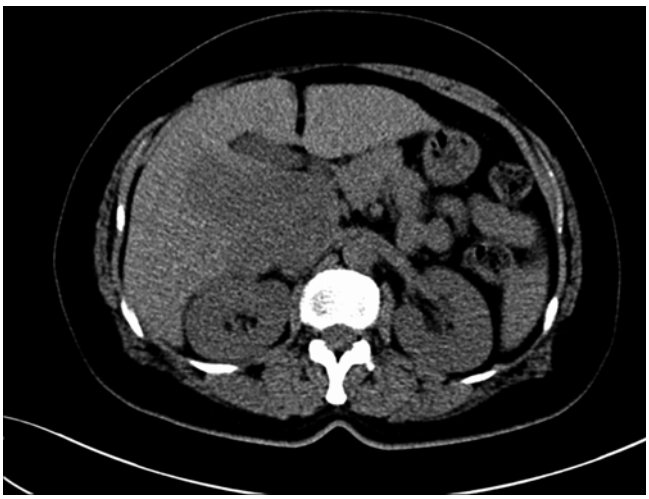


Fig. 4.32 Routine scan of caudate lobe lesions

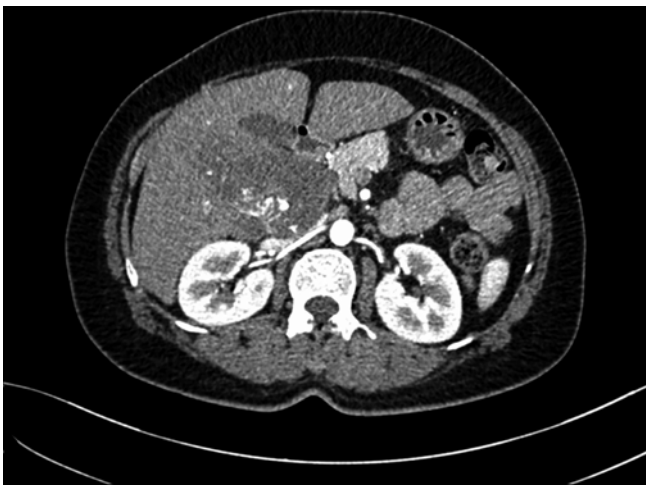


Fig. 4.33 Arterial phase images of caudate lobe lesions

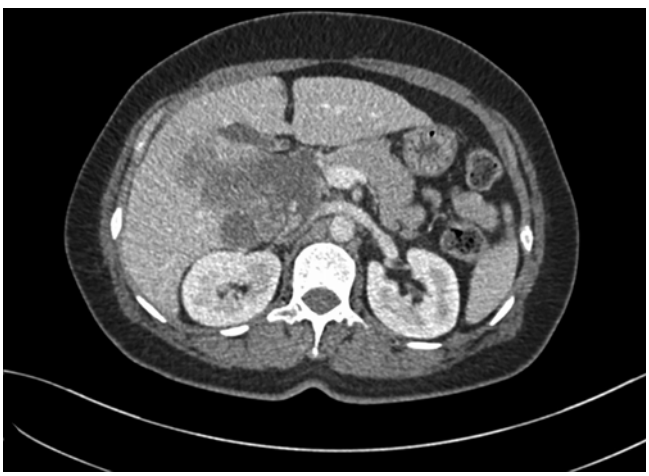


Fig. 4.34 Portal venous images of caudate lobe lesions

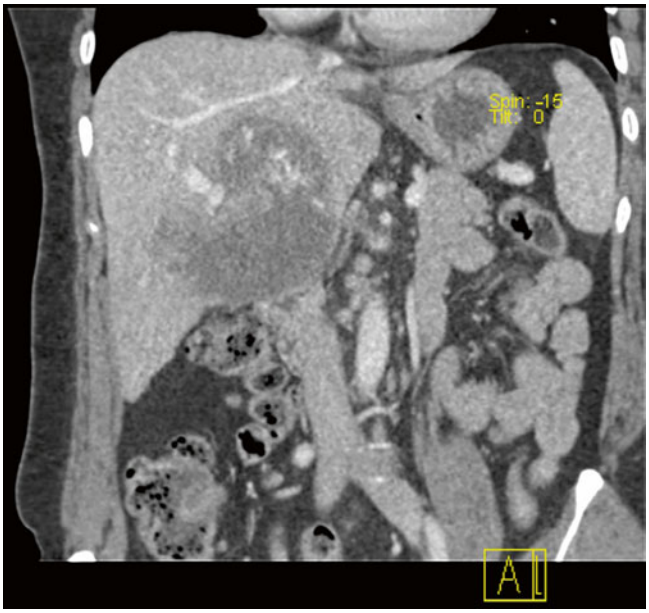


Fig. 4.35 Reconstruction of caudate lobe lesions

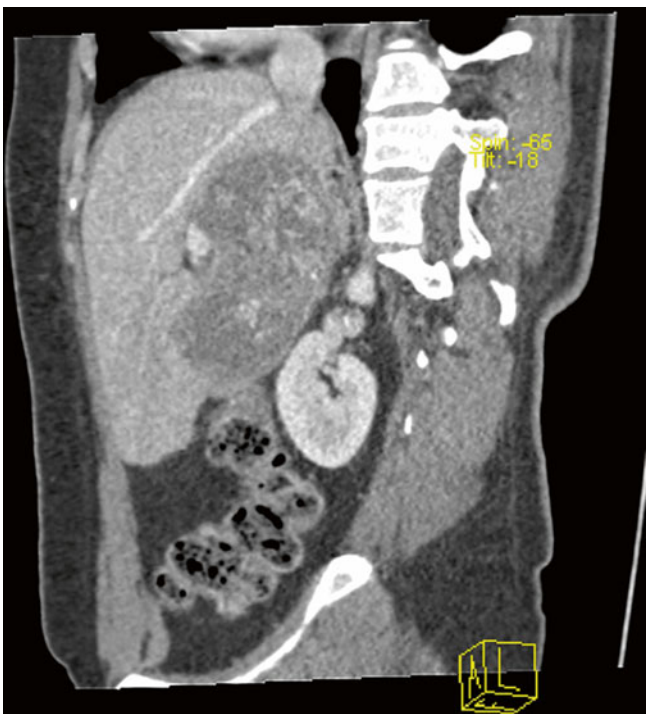


Fig. 4.36 Reconstruction of caudate lobe lesions

period. It is of little use for small liver lesions, especially in the context of liver cirrhosis, such as for SHCC and liver nodules. It is difficult to detect and analyze lesions in fatty livers. It is easy to visualize the lymph nodes but difficult to judge whether metastasis has occurred. CT is not better than MRI when the hilar biliary duct is invaded. The iodine contrast medium that is used in the enhancement

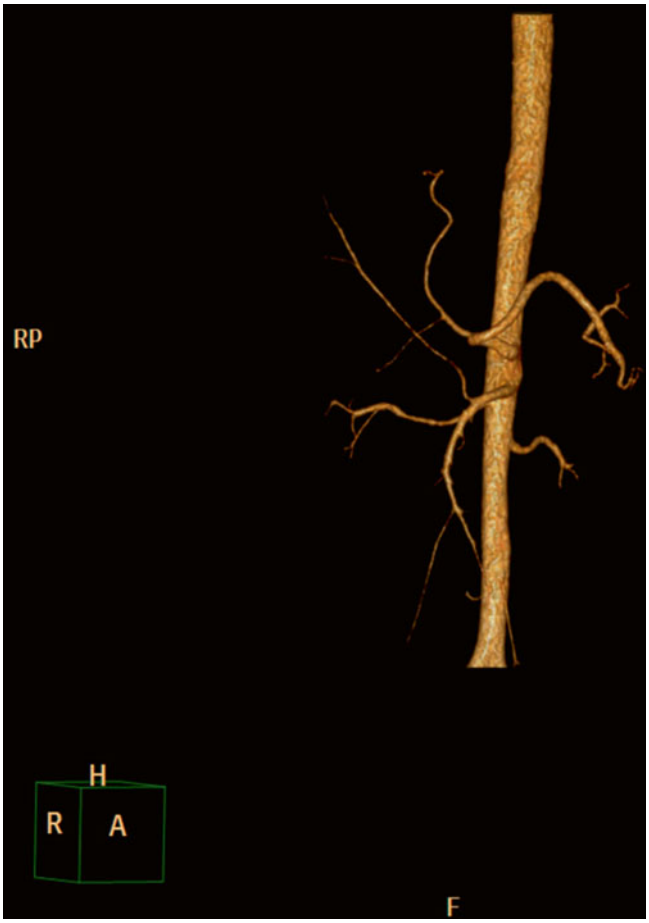


Fig. 4.37 3D image of the right hepatic artery from the superior mesenteric artery

scan can cause side effects in allergic patients. The dye may aggravate kidney dysfunction in patients with renal failure and in perioperative patients with liver failure.

4.2 MRI Technology Used for Hepatectomy

4.2.1 For the Detection and Diagnosis of Hepatic Lesions

Conventional imaging sequences for the liver include unenhanced T2WI, T1WI, TrueFISP, gadolinium-enhanced dynamic multiphase scans, and MRCP. These common sequences can provide more information than regular CT and enhanced diagnostic scans. In most cases, these modalities meet the demand for disease diagnosis (Figs. 4.49, 4.50, 4.51, 4.52, 4.53, 4.54, 4.55, 4.56, 4.57, 4.58, 4.59, 4.60, 4.61, 4.62, 4.63, 4.64, 4.65, 4.66, 4.67, 4.68, and 4.69).

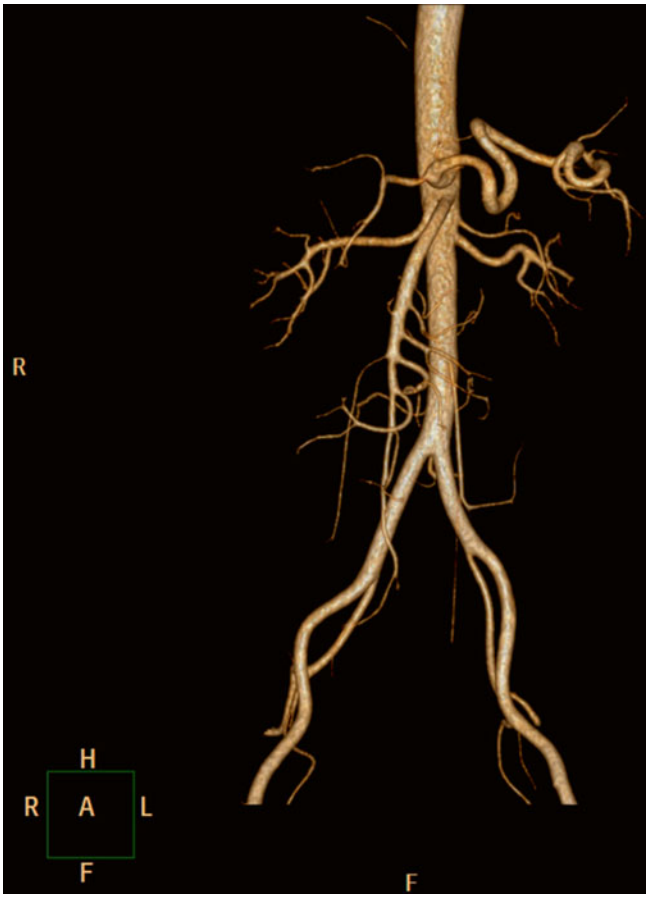


Fig. 4.38 3D image of the left hepatic artery arises from the left gastric artery

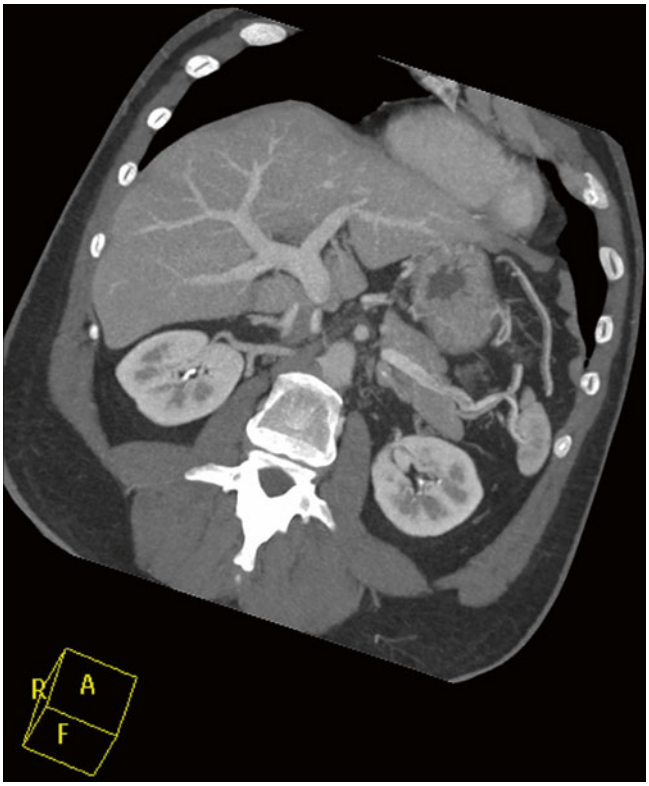


Fig. 4.39 Reconstruction of the left and right and intrahepatic branches and the blood supply area

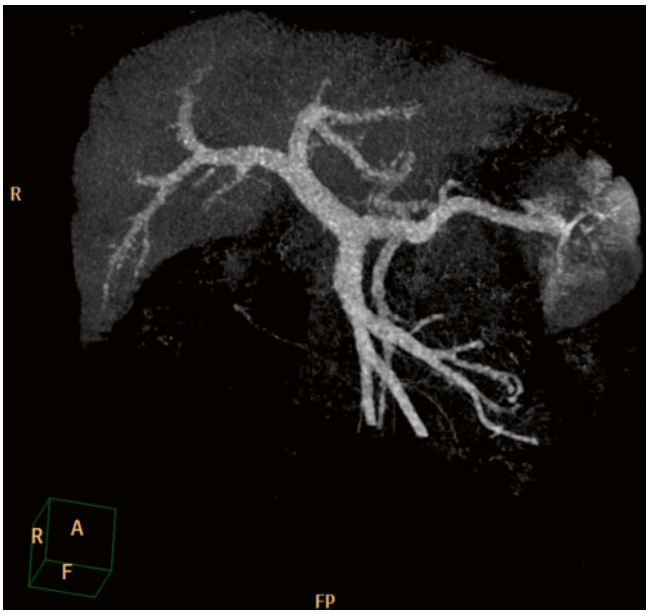


Fig. 4.40 MIP of the left and right and intrahepatic branches and the blood supply area

Using a hepatobiliary-specific contrast agent can help detect smaller lesions, especially multifocal hepatocellular carcinoma, small hepatocellular carcinoma, liver metastases, and small regenerative nodules in the context of diffuse cirrhosis (Figs. 4.70, 4.71, 4.72, 4.73, 4.74, 4.75, 4.76, 4.77, 4.78, 4.79, 4.80, 4.81, 4.82, 4.83, 4.84, 4.85, 4.86, and 4.87). However, even with hepatobiliary special contrast agents, the sensitivity and positive predictive value is still low for the preoperative diagnosis of small hepatocellular carcinoma. MiHye Yu et al. reported the use of gadoxetic acid in the detection and diagnosis of HCC of less and more than 1 cm in size. The sensitivities were 46 % (38.3–54.0 %) and 95 % (90.0–97.6 %), and the positive predictive values were 48% (40.3–55.4 %) and 78 % (71.5–83.3 %) [2].

4.2.2 Enhanced MRA to Evaluate Hepatic Vessels

Similar to the CTA, MRA can also be used to assess liver vascular anatomy characteristics, tumor vascular invasion, etc. The vessels that can be analyzed include the hepatic artery, portal vein, hepatic vein, and the IVC above the liver (Figs. 4.88 and 4.89).

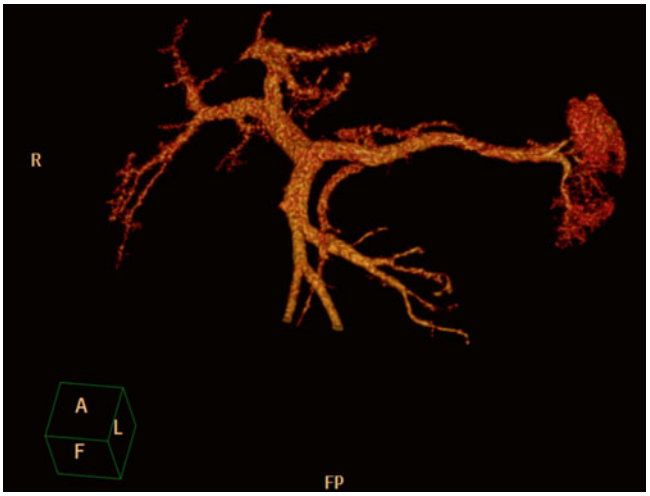


Fig. 4.41 VR of the left and right and intrahepatic branches and the blood supply area

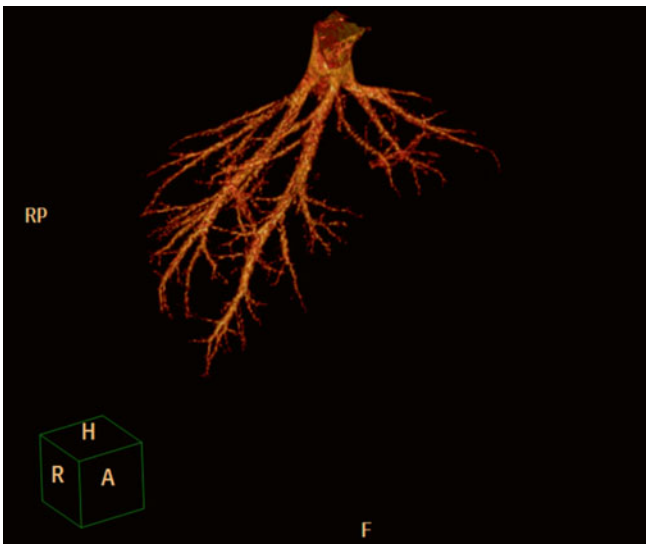


Fig. 4.42 VR of three separate veins draining into IVC

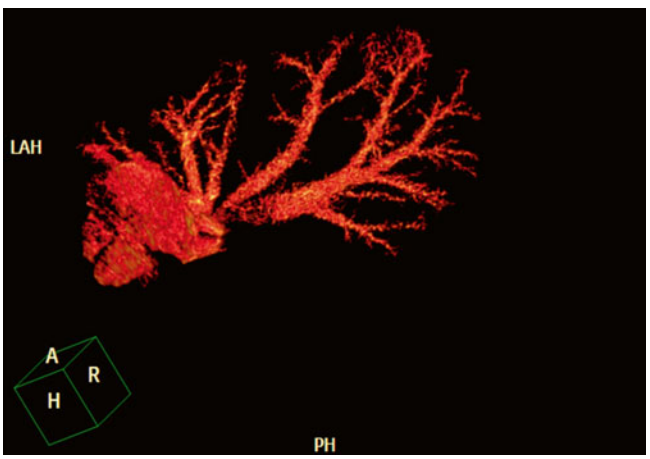


Fig. 4.43 VR of four separate veins draining into IVC

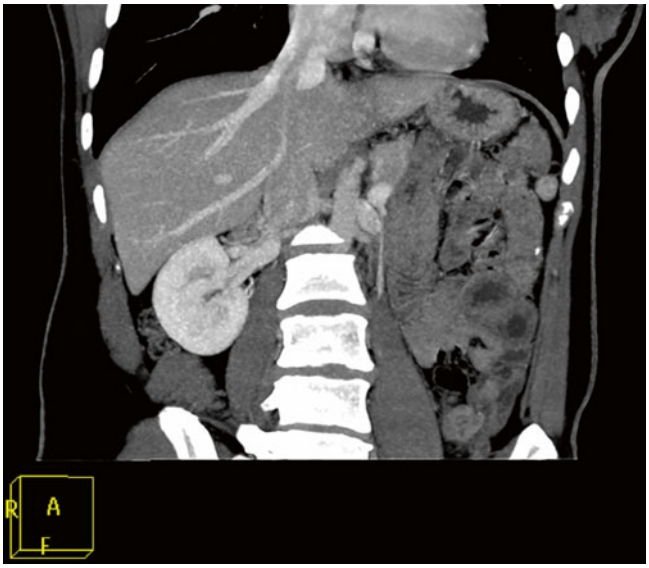


Fig. 4.44 CT reconstruction of the accessory right hepatic vein

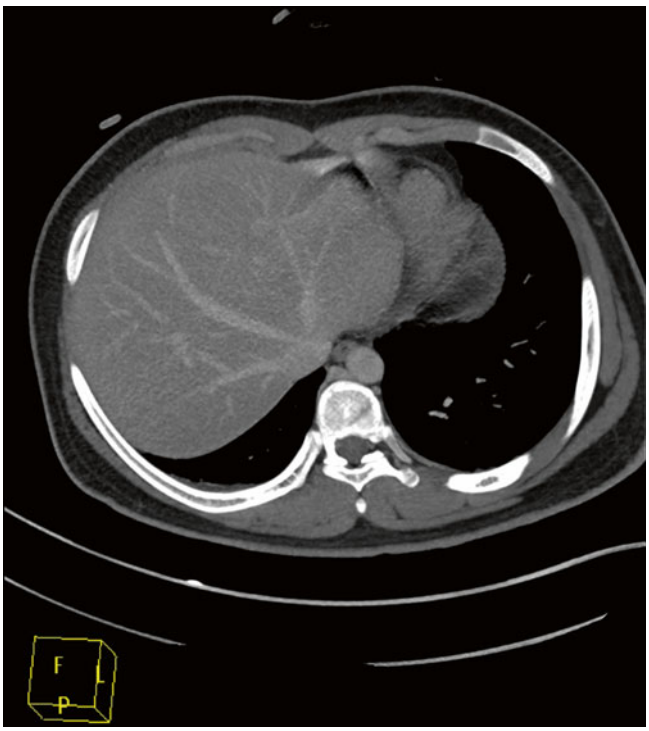


Fig. 4.45 CT reconstruction of the hepatic venous drainage area

4.2.3 MRI Assessment in the Biliary System during Hepatectomy

MRCP is a MR imaging sequence that is frequently used in combination with other imaging sequences (Fig. 4.90). MRCP can clearly show the anatomy of the biliary system and anatomic variations and determine the state and extent of

bile duct stenosis (Figs. 4.91, 4.92, 4.93, 4.94, 4.95, and 4.96). In combination with other sequences, the etiology of biliary obstruction can be determined. This type of imaging provides objective and detailed anatomical information for surgery. In most cases, dynamic MRCP can replace ERCP and help assess the physiological characteristics of bile, pathophysiology, bile reflux, etc. [3].

Using the hepatobiliary gadolinium contrast agent Cypriot gadolinium acid combined with a DWI sequence can improve the assessment of tumor proliferation along the bile duct and invasion of the adjacent liver tissue [4].

Cross-sectional images with 3D MRCP can accurately determine the number of liver bile duct sections before surgery, help develop a detailed operation plan, avoid exploratory surgery and surgical trauma, and reduce postoperative complications.

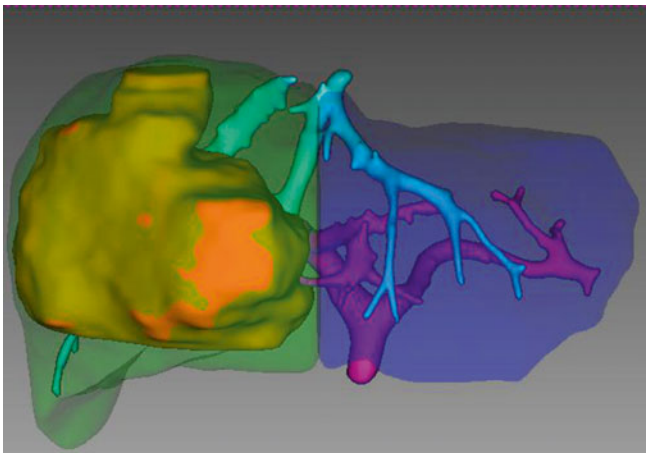
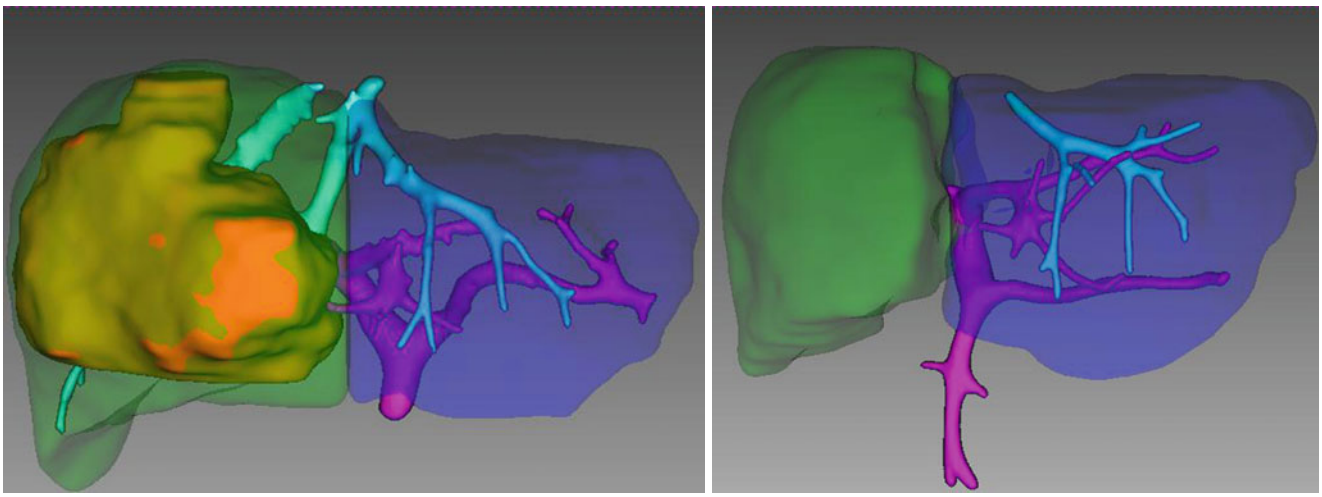


Fig. 4.46 3D images show the total volume of the liver, the lobe volume, the tumor volume, and the residual liver volume measurements

4.2.4 Assessment of Liver Function, Hepatic Fibrosis, and Fatty Liver with MRI

Malignant tumors of the liver, especially hepatocellular carcinoma and cholangiocarcinoma, generally exhibit basic hepatic pathological changes, such as cirrhosis, liver fibrosis, and fatty liver. Moreover, the extent of the basic pathological change is an important factor with respect to whether the liver resection will be performed. Although liver function, liver fibrosis, and fatty liver MRI evaluation are not routinely performed, clinical studies have shown that MRI has great potential in these areas. Numerous studies have shown that MR elastography, susceptibility-weighted imaging (SWI), MR spectroscopy, hepatobiliary contrast agents, Cypriot gadolinium acid, and enhanced scans can be used to test for liver fibrosis, fatty liver, and steatohepatitis. The results of such pathological tests have good consistency and repeatability. MRI can evaluate the whole liver more fully compared with live histopathology. In addition, the specificity of hepatobiliary contrast-enhanced scan can be used to evaluate the function of the whole or partial liver (e.g., a lobe or segment) [5]. Biochemical tests, IgG tests, and others can only evaluate the function of the whole liver, which can be affected by the metabolic function of multiple organs. However, MRI imaging still has limitations for early liver fibrosis and mild fatty liver. For example, for level 2 fibrosis and below, MRI is less sensitive than others. Cypriot gadolinium acid can be used to identify simple fatty liver and hepatitis. However, specificity is still poor for early lesions. Moreover, MRI imaging sequences for evaluating various liver functions, liver fibrosis, fatty liver, and other conditions are noninvasive and fast and have good repeatability and other advantages. Therefore, MRI is far more useful than a liver biopsy with respect to patient acceptance.



Figs. 4.47 and 4.48 3D image shows how the residual liver volume changes between preoperative and postoperative time points

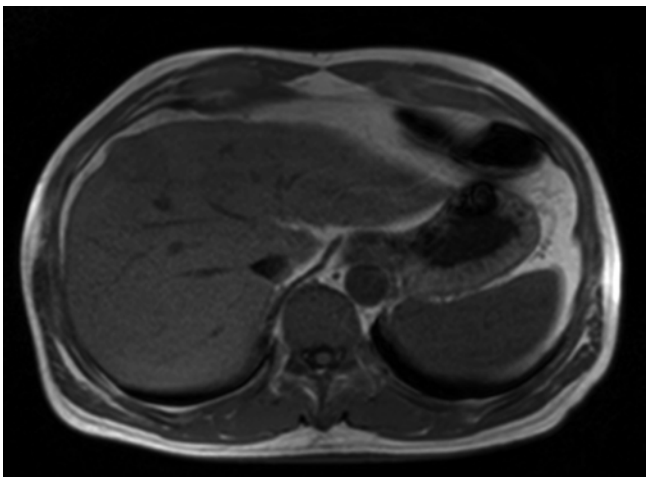


Fig. 4.49 HCC-T1WI

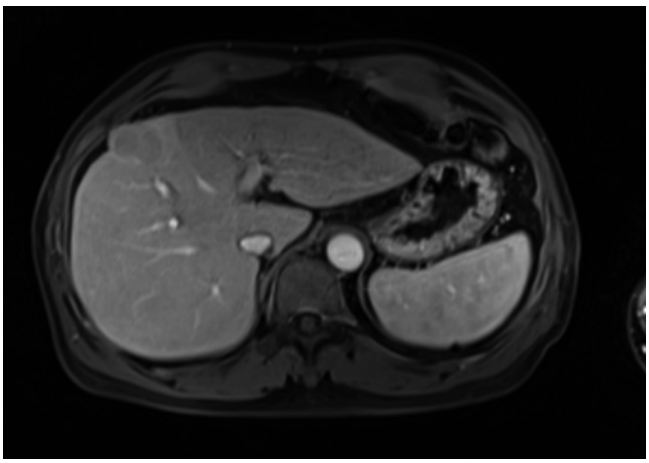


Fig. 4.52 HCC-MRI late arterial phase

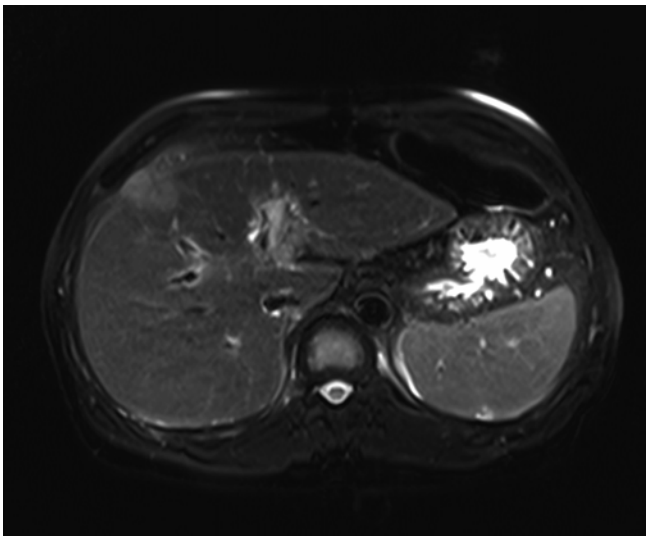


Fig. 4.50 HCC-T2WI

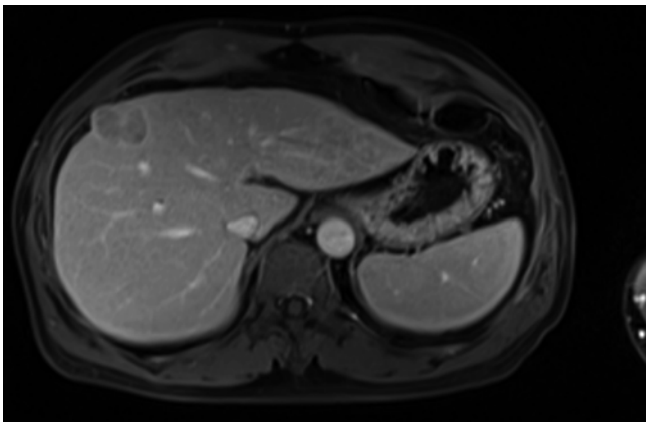


Fig. 4.53 HCC-MRI portal phase

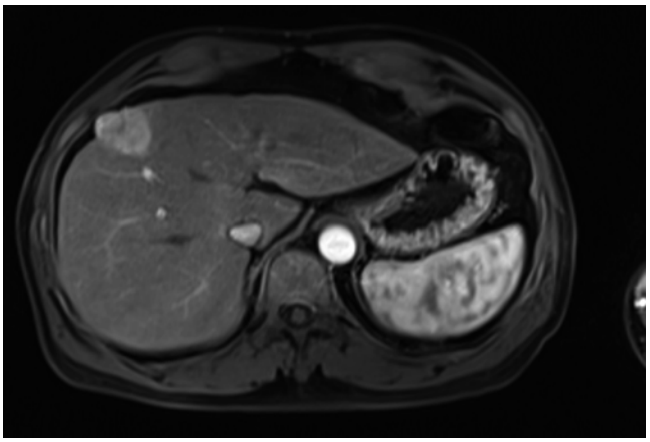


Fig. 4.51 HCC-MRI early arterial phase

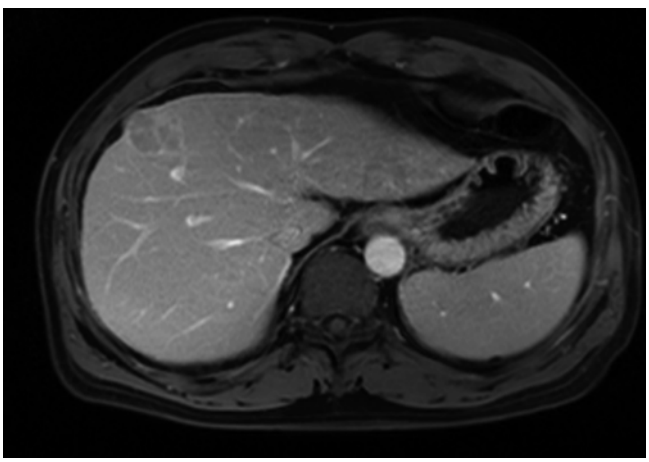


Fig. 4.54 HCC-MRI delay phase

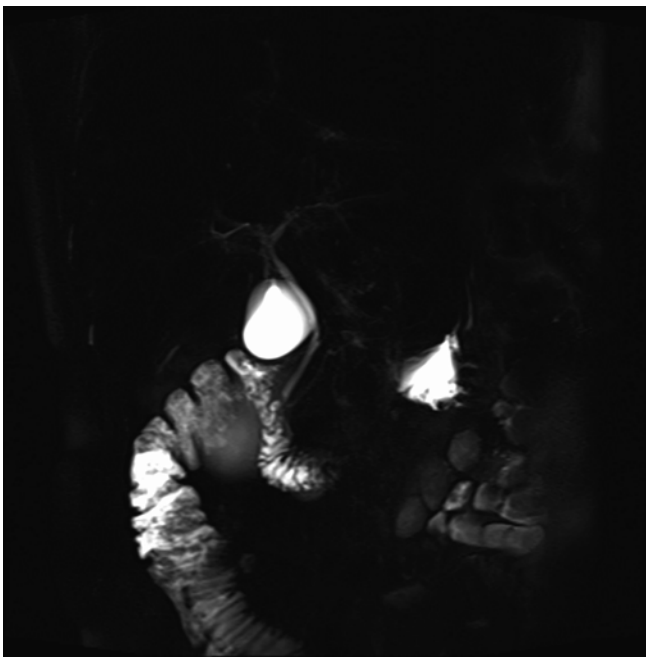


Fig. 4.55 HCC-MRCP

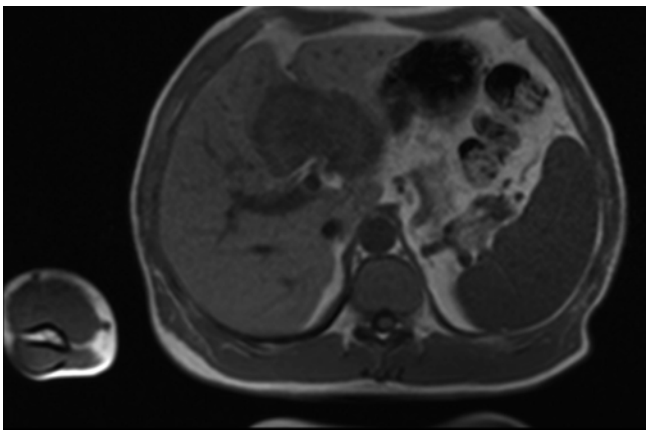


Fig. 4.56 ICC-T1WI

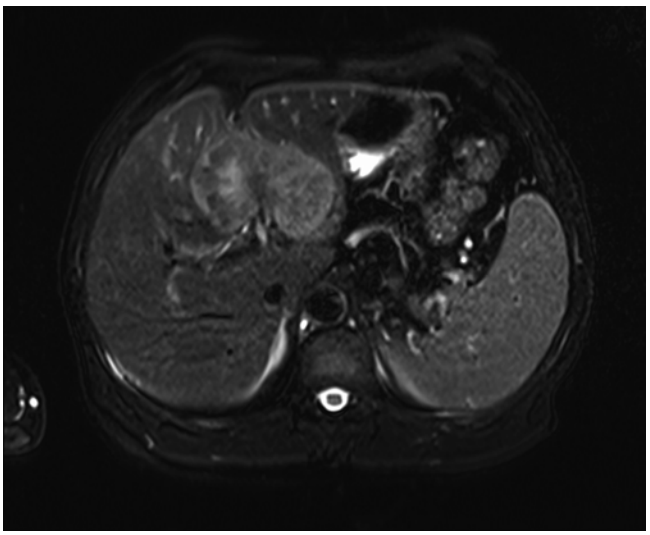


Fig. 4.57 ICC-T2WI

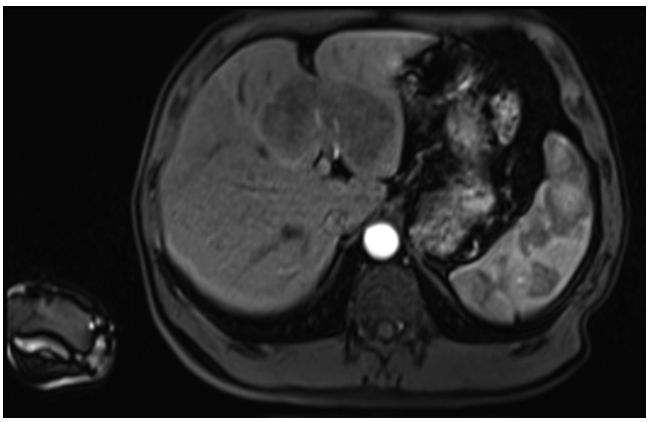


Fig. 4.58 ICC-MRI early arterial phase

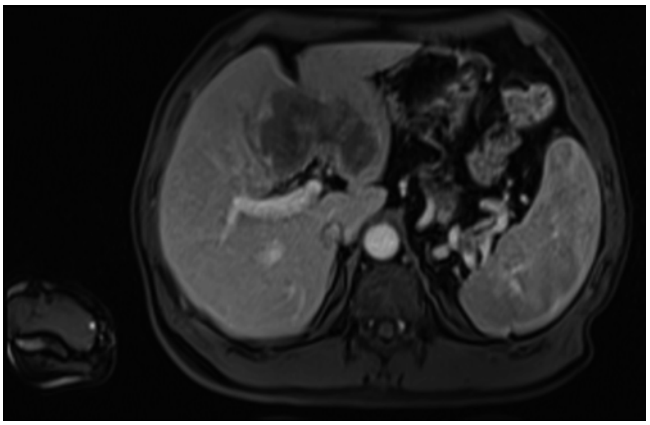


Fig. 4.59 ICC-MRI late arterial phase

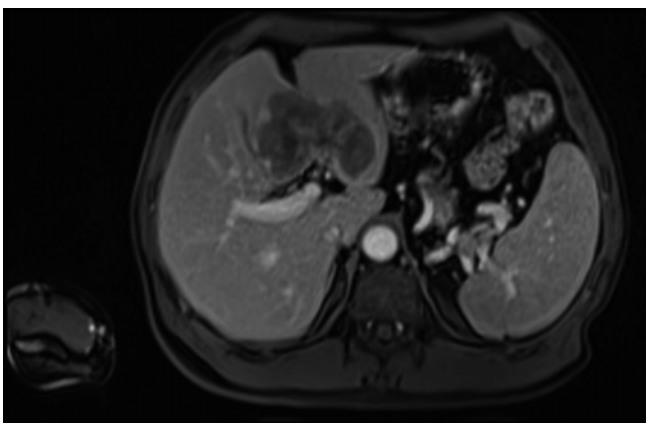


Fig. 4.60 ICC-MRI portal phase

4.2.5 Value of Sequential MRI before Hepatectomy: A Brief Summary

Multiple sequence MRI in liver resection applications include (i) displaying lesion anatomy and spatial relationship of adjacent structures, (ii) determining the nature of disease, (iii) revealing whether there are single or multiple liver lesions, (iv) showing whether the lesions invade the blood

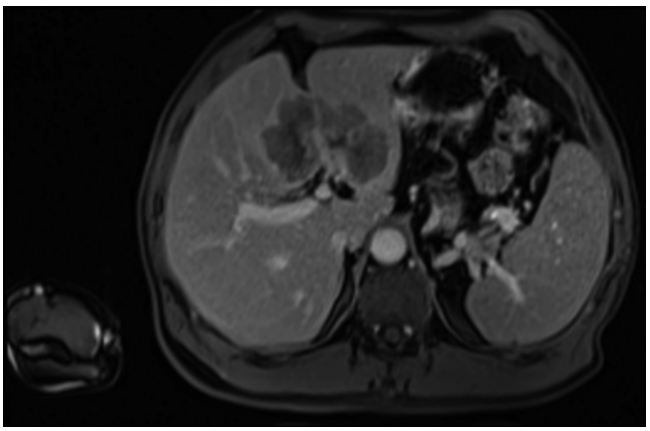


Fig. 4.61 ICC-MRI delay phase

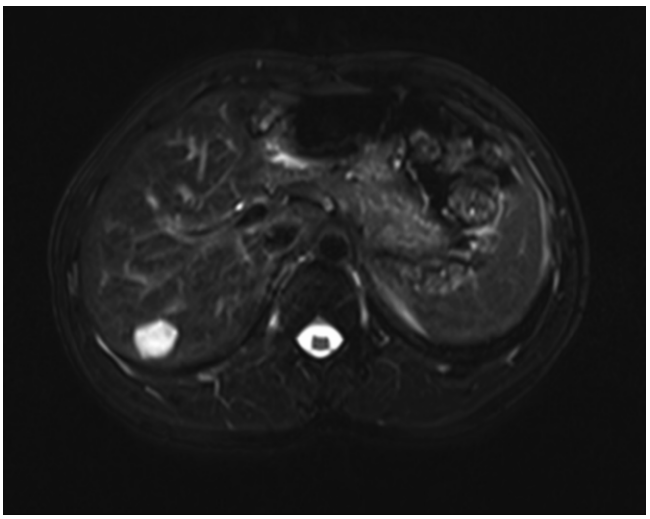


Fig. 4.64 Hepatic hemangioma-T2WI

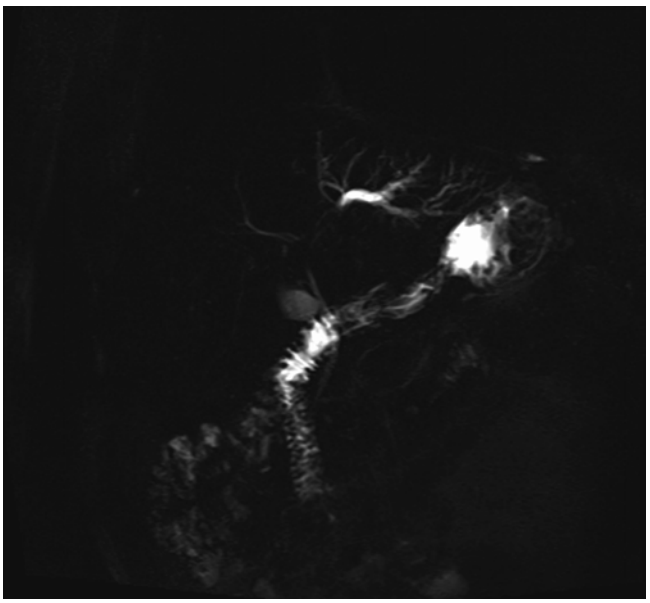


Fig. 4.62 ICC-MRCP

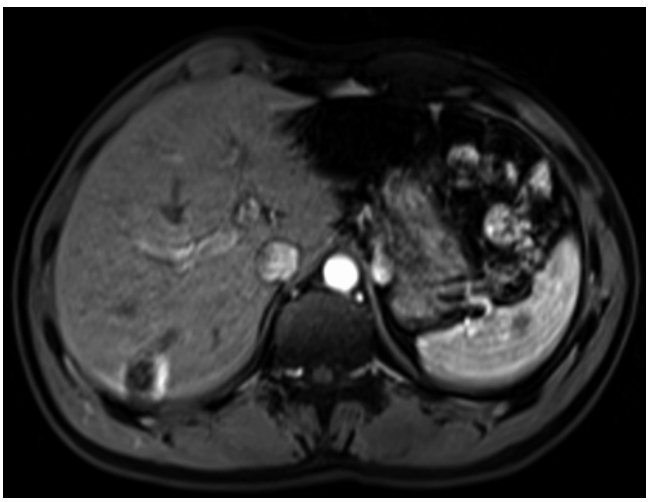


Fig. 4.65 Hepatic hemangioma-MRI early arterial phase

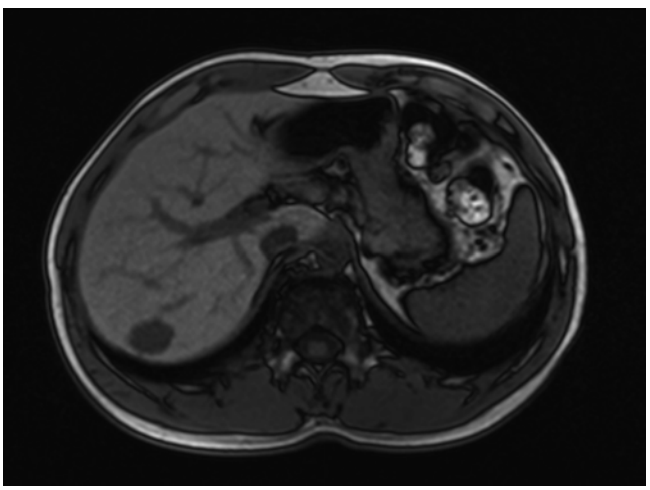


Fig. 4.63 Hepatic hemangioma-T1WI

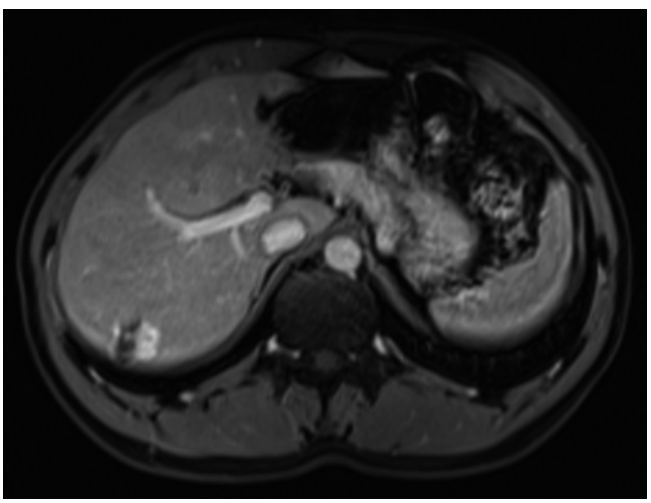


Fig. 4.66 Hepatic hemangioma-MRI late arterial phase

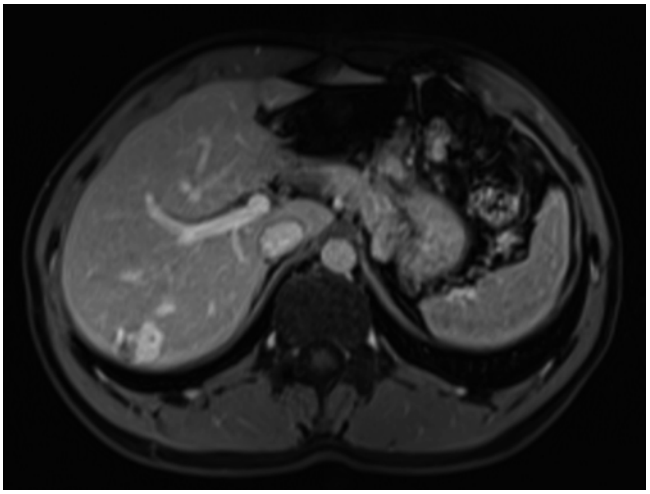


Fig. 4.67 Hepatic hemangioma-MRI portal phase

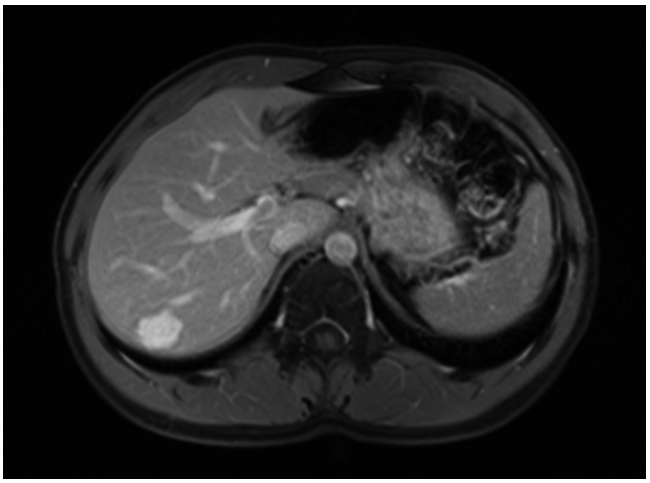


Fig. 4.68 Hepatic hemangioma-MRI delay phase

vessels and bile ducts, and (v) determining the scope of any nonideal factors and whether there are anatomic variations that will affect the operation.

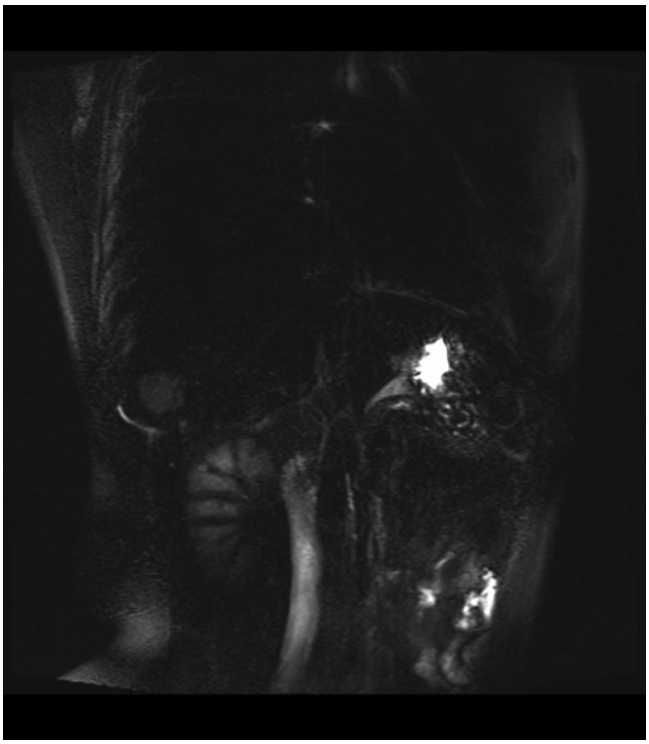


Fig. 4.69 Hepatic hemangioma-MRCP

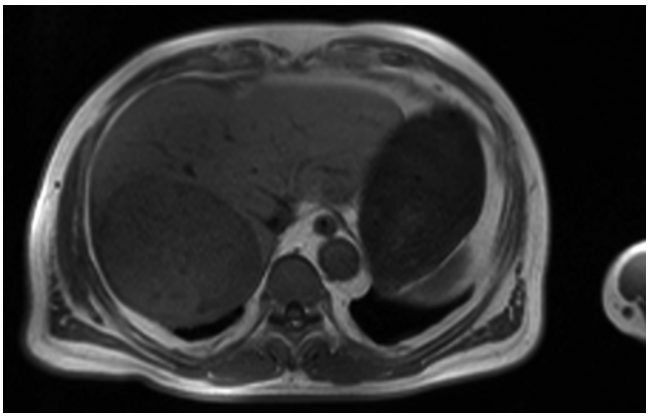


Fig. 4.70 HCC (Primovist)-T1WI

4.2.6 Advantages and Disadvantages of MRI in Hepatectomy

4.2.6.1 Advantages

MRI has high resolution and can be used for multi-sequence imaging, which is better than CT with respect to showing lesions and making a diagnosis. MRI is also better than CT in the detection and diagnosis of small liver lesions, especially in the context of a fatty liver and cirrhosis. In addition, MRI is superior to CT with respect to examining tumor invasion of the hilar bile duct, its proliferation, and its invasion of the adjacent liver tissue along the hilar bile duct. Functional imaging can noninvasively assess liver function, liver fibrosis, and fatty liver. It has no radiation hazard and requires little human manipulation.

4.2.6.2 Disadvantages

The scanning speed is relatively slow and is vulnerable to interference due to respiratory motion. In vivo implants with magnetic metals are contraindications for MR examination. Nonmagnetic metals in such implants will produce artifacts and interference. In a high-field environment, nonmagnetic metal may have higher local SAR values and carry the potential risk of burns. Claustrophobic patients cannot tolerate MR examination. The various MR functional imaging sequences call for more sophisticated hardware and software requirements. Thus far, its popularity is still lower than CT devices.

MR contrast agents have side effects, some of which are serious. For patients with severe renal impairment, there is a risk of inducing nephrogenic systemic fibrosis (NSF).

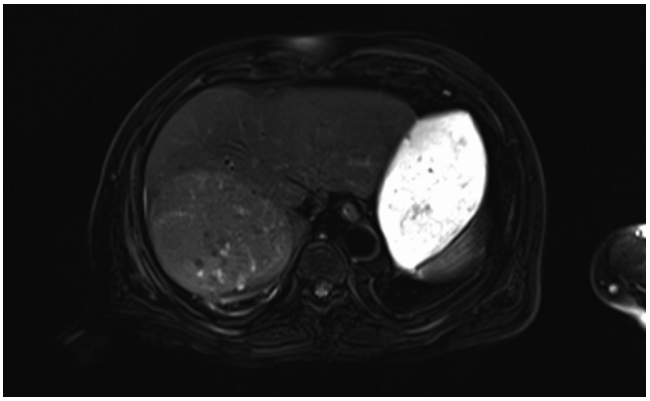


Fig. 4.71 HCC (Primovist)-T2WI

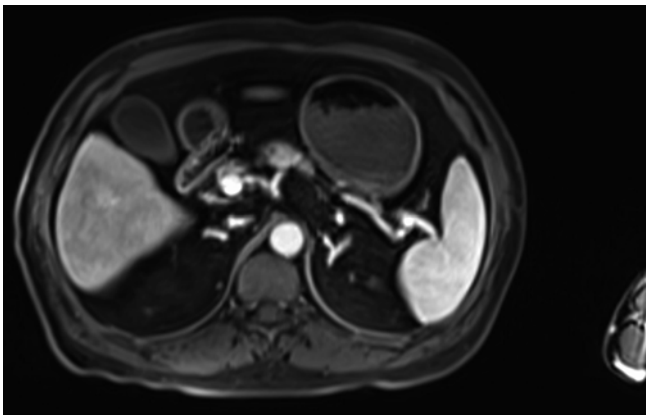


Fig. 4.74 HCC (Primovist)-MRI arterial phase shows the nodule in the right anterior inferior segment of the liver

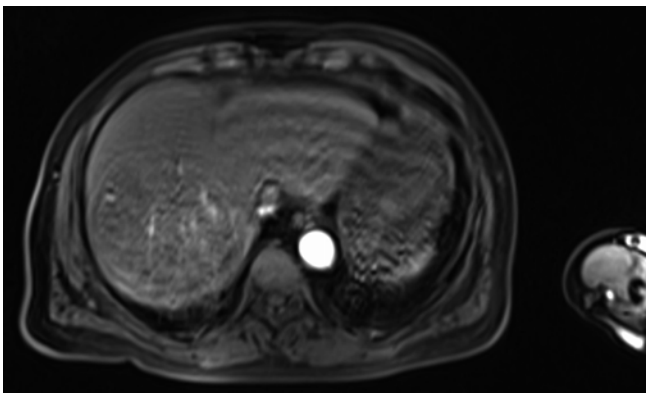


Fig. 4.72 HCC (Primovist)-MRI early arterial phase

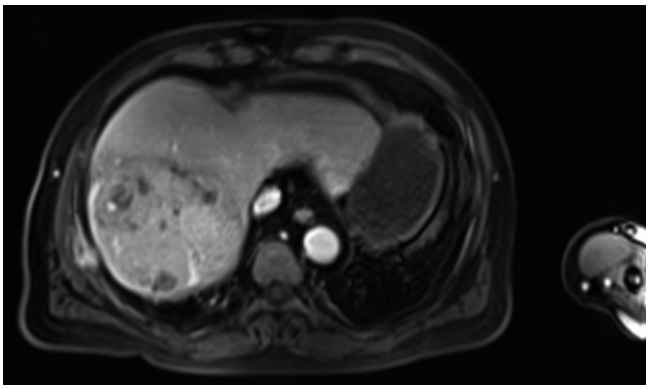


Fig. 4.75 HCC (Primovist)-MRI arterial phase does not show the nodule within the left liver lobe near the diaphragm

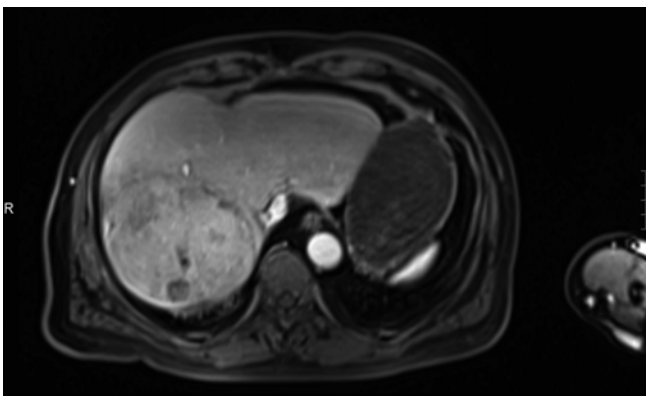


Fig. 4.73 HCC (Primovist)-MRI late arterial phase

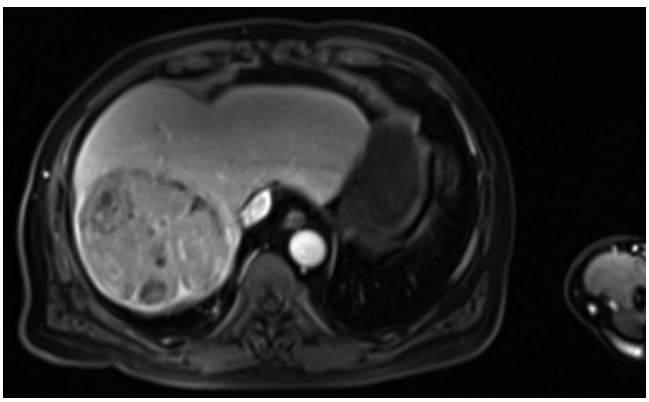


Fig. 4.76 HCC (Primovist)-MRI portal phase

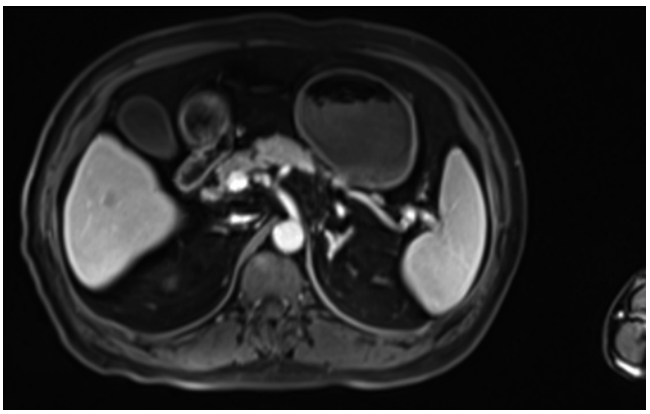


Fig. 4.77 HCC (Primovist)-MRI portal phase shows the nodule in the right anterior inferior segment of the liver

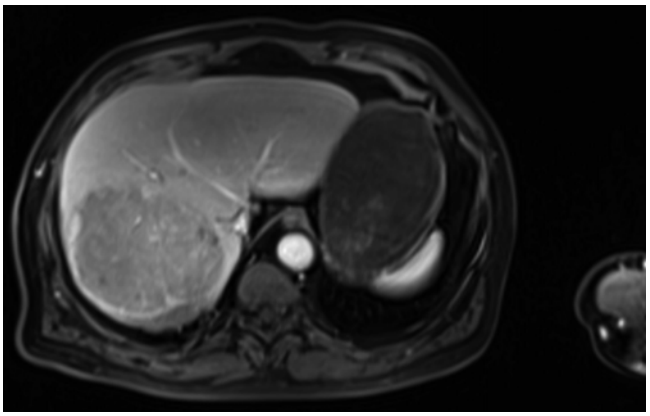


Fig. 4.78 HCC (Primovist)-MRI portal phase shows the nodule in the right anterior upper segment of the liver

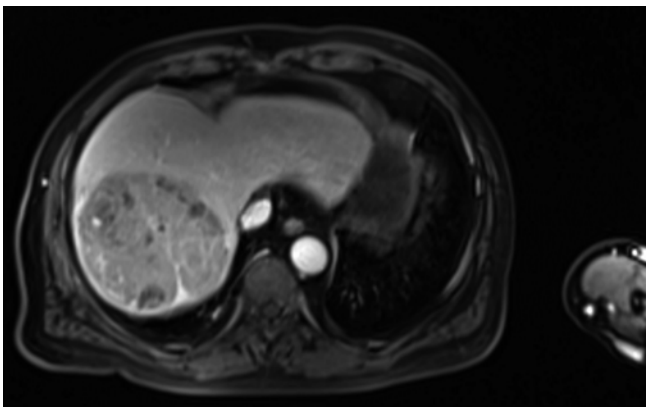


Fig. 4.79 HCC (Primovist)-MRI portal phase does not show the nodule within the left liver lobe near the diaphragm

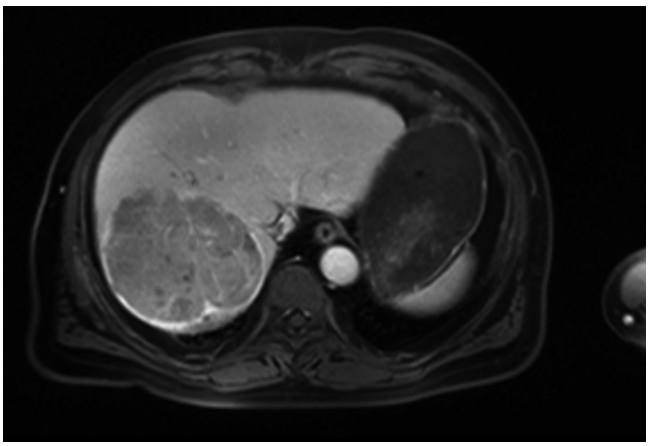


Fig. 4.80 HCC (Primovist)-MRI delay phase

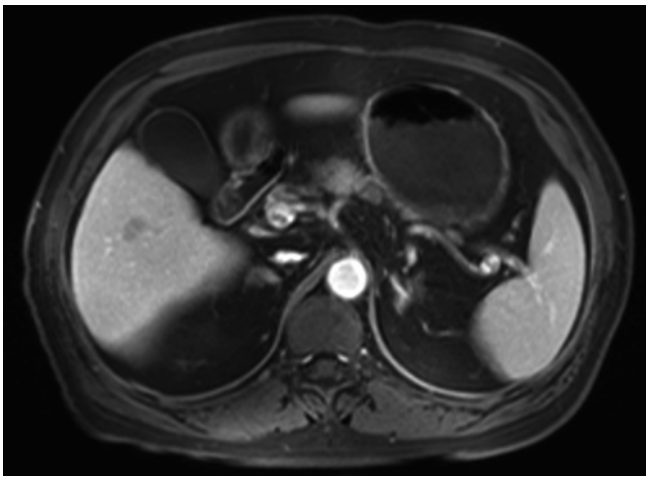


Fig. 4.81 HCC (Primovist)-MRI delay phase shows the nodule in the right anterior inferior segment of the liver

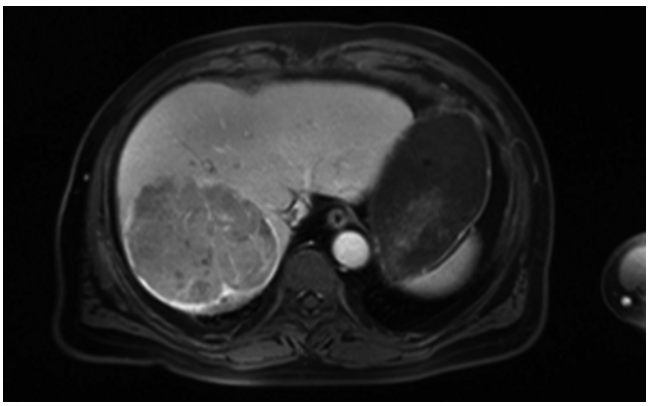


Fig. 4.82 HCC (Primovist)-MRI delay phase shows the nodule in the right anterior upper segment of the liver dimly

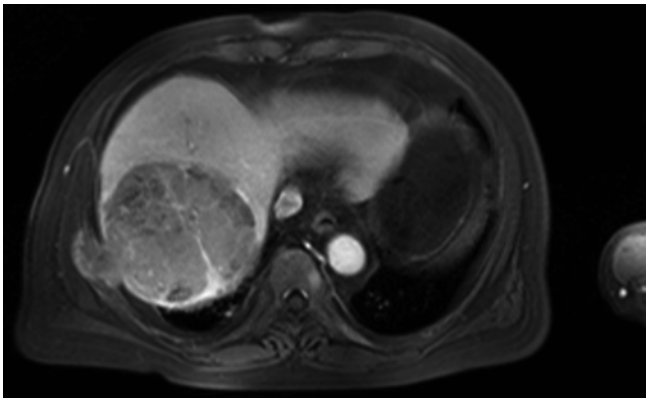


Fig. 4.83 HCC (Primovist)-MRI delay phase does not show the nodule within the left liver lobe near the diaphragm

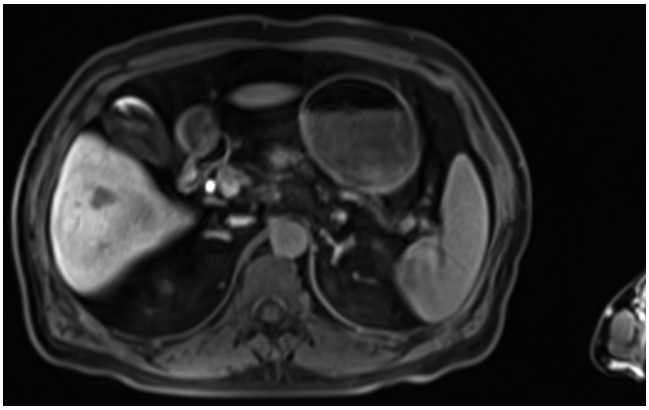


Fig. 4.86 HCC (Primovist)-MRI hepatobiliary phase shows the nodule in the right anterior inferior segment of the liver

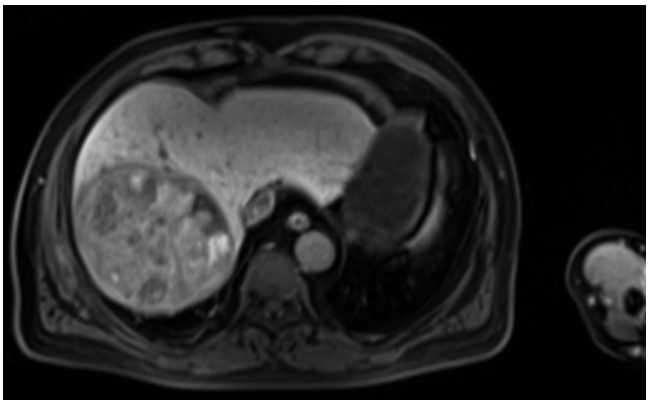


Fig. 4.84 HCC (Primovist)-MRI hepatobiliary phase

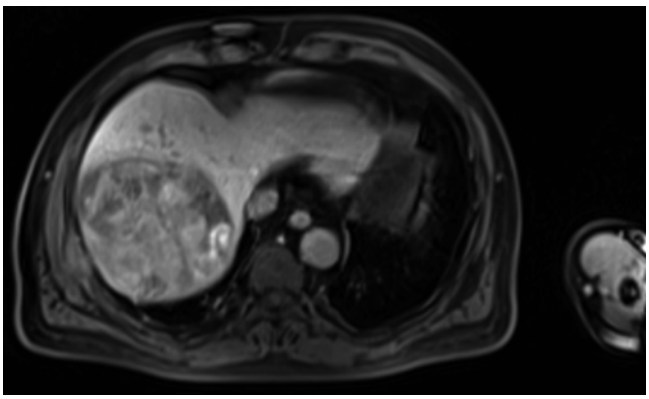


Fig. 4.87 HCC (Primovist)-MRI delay phase shows the nodule within the left liver lobe near the diaphragm

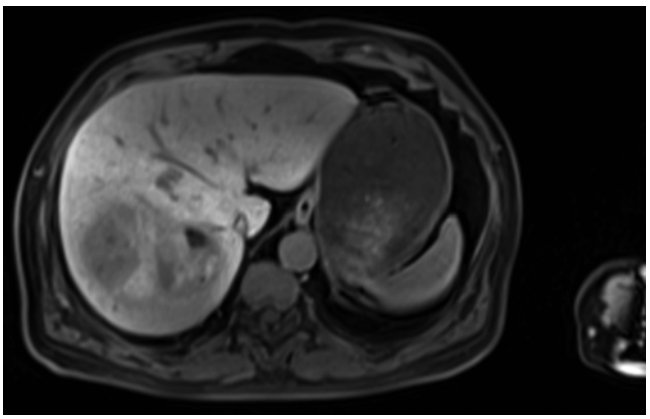


Fig. 4.85 HCC (Primovist)-MRI hepatobiliary phase shows the nodule in the right anterior upper segment of the liver clearly

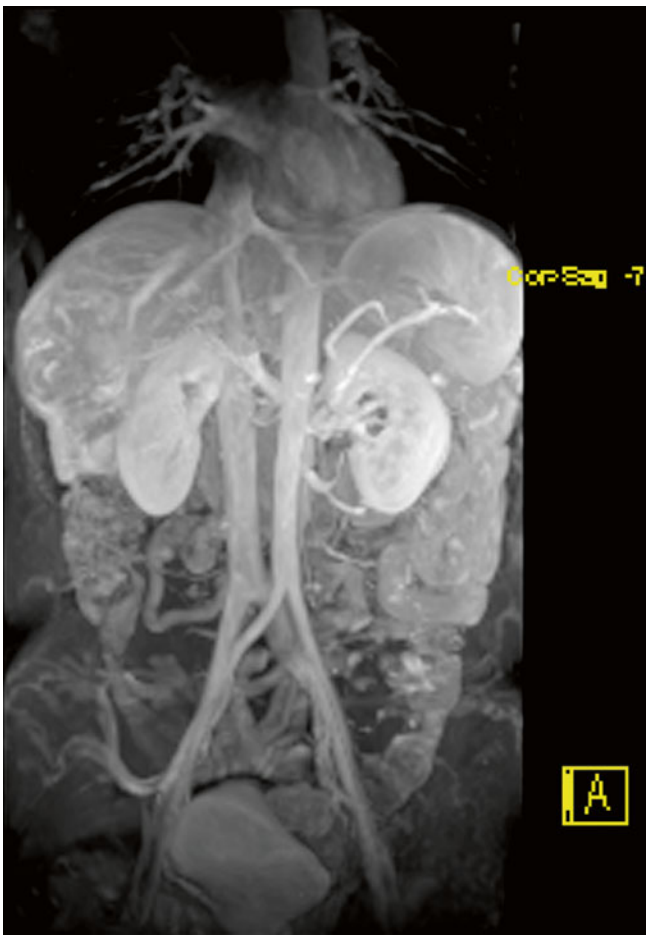


Fig. 4.88 3D images show portal vein thrombosis

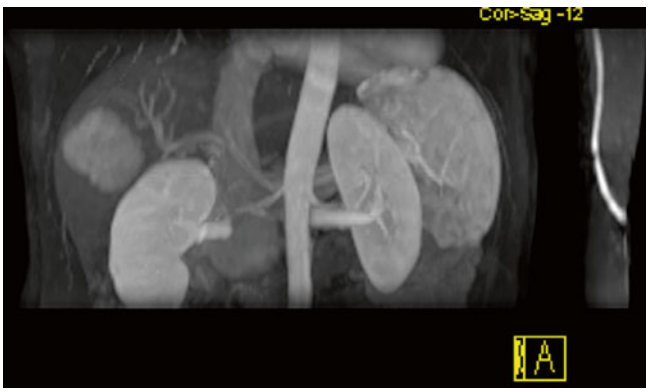


Fig. 4.89 3D images show right hepatic artery blood supply

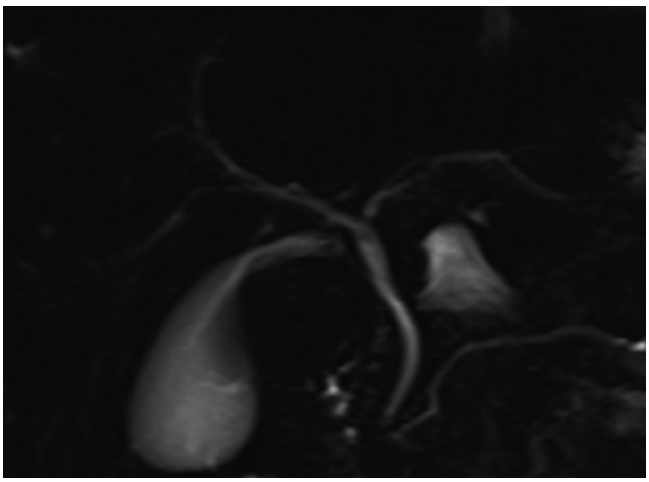


Fig. 4.90 Normal biliary-MRCP

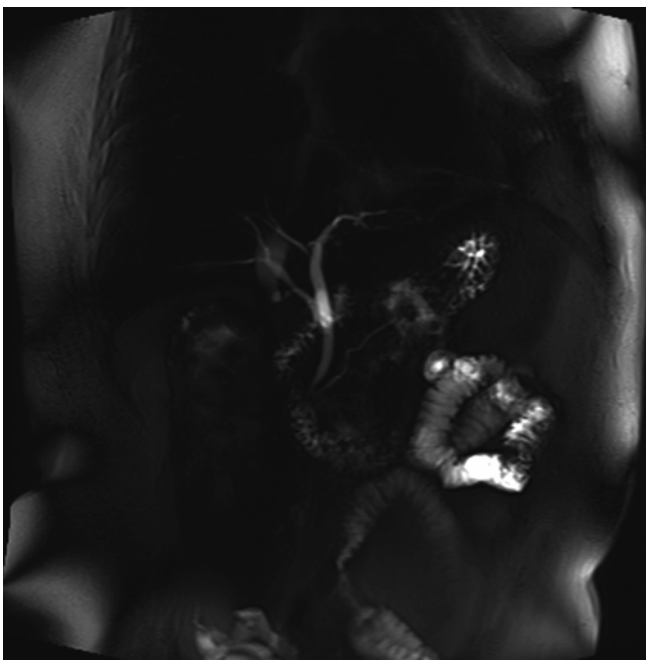


Fig. 4.91 Hilar bile duct confluence variation

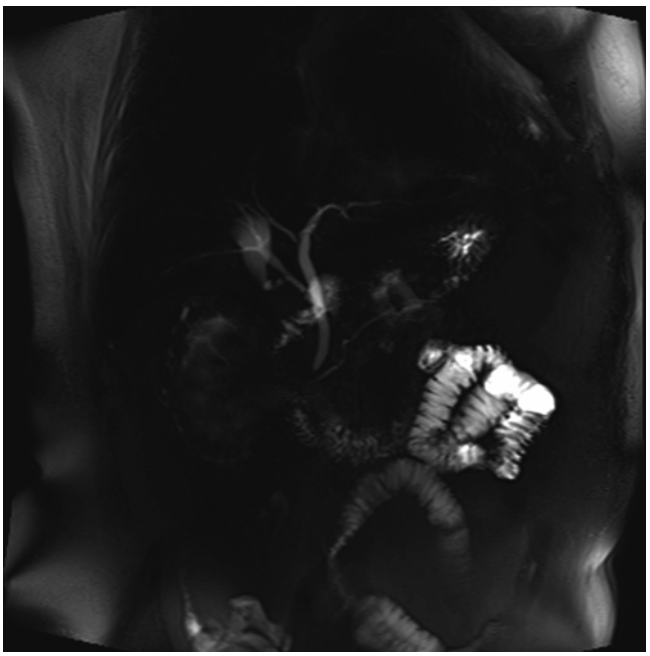


Fig. 4.92 Hilar bile duct confluence variation

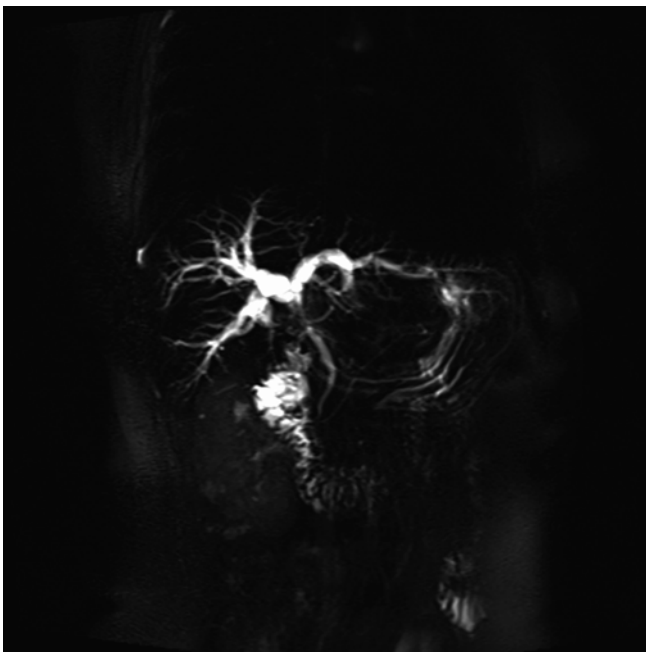


Fig. 4.94 Segmental biliary stricture

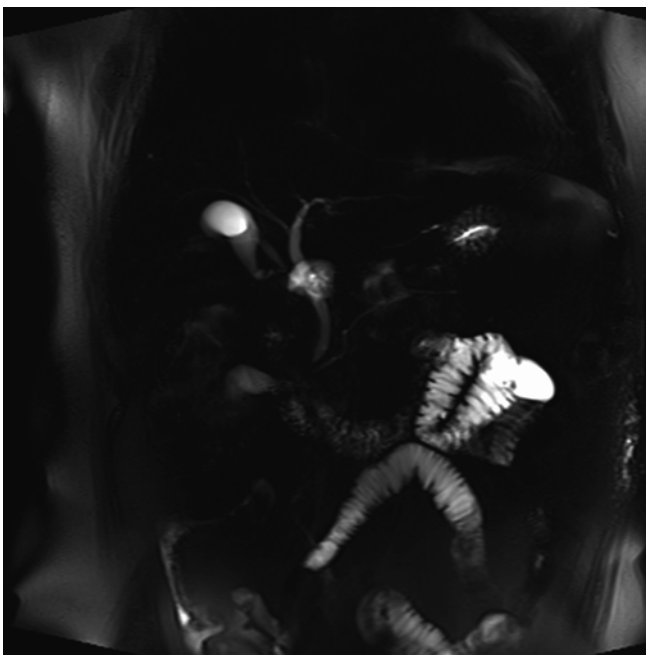


Fig. 4.93 Hilar bile duct confluence variation

Fig. 4.95 Segmental biliary stricture

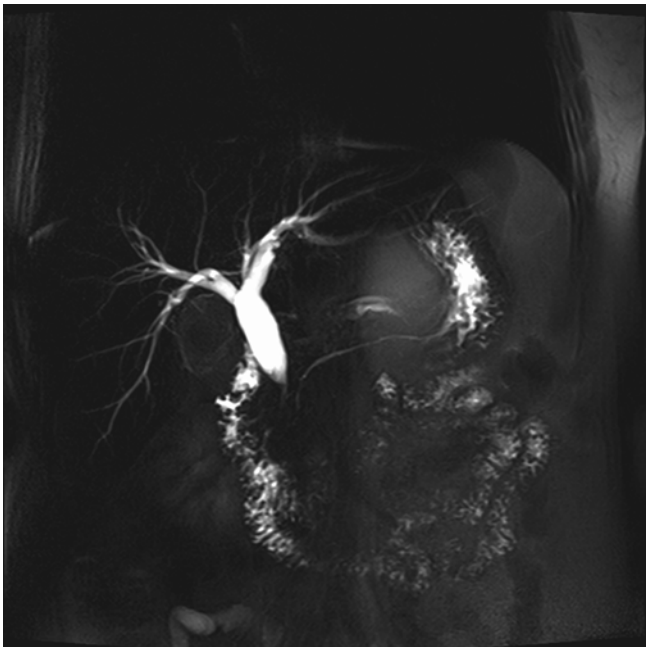


Fig. 4.96 Segmental biliary stricture

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Liver Fibrosis and Its Assessment

5

Guangqin Xiao and Lunan Yan

5.1 The Etiology of Liver Fibrosis

Liver fibrosis is a reversible liver damage – repair response. Almost all chronic liver patients have varying degrees of liver fibrosis. After the amelioration of the factors that lead to acute liver injury, liver fibrosis can possibly occur. If the factors leading to liver cell damage exist persistently, the degree of liver fibrosis will continue to increase, and it will eventually develop into cirrhosis. There are several causes of liver fibrosis, including congenital, metabolic, toxic, and inflammatory causes (Table 5.1).

The pathological features of the liver fibrosis resulting from different causes are not the same. Chronic hepatitis B and hepatitis C viral infection is the major cause of bridging fibrosis, characterized by the junction of lobular hepatitis and portal vein – bridged central vein necrosis, resulting in the formation of portal–central venous fibrous septa. Hepatic sinusoidal or paracellular fibrosis is common in patients with alcoholic or nonalcoholic fatty liver disease. Chronic alcohol-induced liver fibrosis is characterized by the deposition of an extracellular matrix in the space of Disse or in the hepatic sinusoid cells. Biliary fibrosis caused by biliary obstruction accompanied with bile canaliculi hyperplasia and muscle fibroblast proliferation surrounding bile duct results in the formation of portal–portal fibers around the hepatic lobule. Centrilobular fibrosis is mainly caused by a change in hepatic blood flow, characterized by the formation of central–central venous fibrous septa [1].

5.2 Liver Fibrosis, Cirrhosis, and Hepatocellular Carcinoma

Liver fibrosis is a type of occult disease. In most patients, liver fibrosis will eventually develop into cirrhosis after 15–20 years. The main clinical manifestations of cirrhosis include ascites, renal failure, hepatic encephalopathy, gastrointestinal bleeding, and even death. Cirrhosis is a principal cause of death, as well as a risk factor for the occurrence of hepatocellular carcinoma. Hepatic fibrosis may develop into cirrhosis in the short term under certain conditions such as severe alcoholism, subfulminant hepatitis, and cholestasis [2]. The natural development of hepatic fibrosis is influenced by genetic and environmental factors. Epidemiological studies indicated that several genes might influence the progress of human liver fibrosis [3]. The severity of liver fibrosis varies in cohorts who are exposed to the same chronic factors and might be related to different genetic factors.

Cirrhosis is a risk factor for the occurrence of hepatocellular carcinoma. Hepatocytes that persist for approximately 20–30 years in a cirrhotic environment will become cancerous. More than 80 % of hepatocellular carcinoma patients show varying degrees of liver cirrhosis. Annually, there are more than 750,000 new-onset cases of hepatocellular carcinoma worldwide, of which about half are in China [4]. Hepatocellular carcinoma is the sixth most prevalent cancer and has become a threat to human health [5].

Stimulated by chronic causes, liver cell necrosis and the deposition of an extracellular matrix lead to fibrosis.

Table 5.1 The common causes of liver fibrosis

1. Presinusoidal liver fibrosis	**3. Parenchymal liver fibrosis**
Schistosomiasis	Virus infections (HBV, HCV, etc.)
Idiopathic portal liver fibrosis	Drugs and toxins (alcohol, isoniazid, etc.)
	Autoimmune diseases
2. Postsinusoidal liver fibrosis	Metabolic/genetic diseases
Hepatic veno-occlusive disease (Budd–Chiari syndrome, etc.)	Biliary obstruction
	Other causes

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Changes in the hepatic microenvironment promote the release of several cytokines. Changes in the liver cell microenvironment and the release of these cytokines can lead to carcinogenesis [6]. The disorder of collagen cross-linking of proteins and sclerosis of the extracellular matrix play important roles in tumor genesis via the integrin signaling pathway [7]. Changes in the integrin family can promote tumor cell growth, survival, and proliferation. Some integrins, such as α1β1 and α2β1, are associated with tumor cell invasion [8].

5.3 Diagnosis and Prediction of Liver Fibrosis

Early accurate diagnosis of liver fibrosis is necessary because it can help retard disease progression and guide the treatment of chronic liver injury. For patients who need or have received partial liver resection surgery, the assessment of the severity of liver fibrosis is essential. Liver biopsy remains the gold standard for the assessment of liver fibrosis and cirrhosis. However, noninvasive methods are becoming more important. These methods not only mitigate the risk of percutaneous biopsy to provide more security to the patient but also allow easy, dynamic monitoring of the status of liver fibrosis.

5.3.1 Histology and Morphology

Tissue for histology and morphology assessment is generally taken by percutaneous or laparoscopic liver biopsy. Various semiquantitative morphological methods are used to assess the severity of liver fibrosis. These methods are based on the use of HE staining or connective tissue staining such as Masson trichrome, reticulin silver impregnation, or van Gieson staining to evaluate the extracellular matrix of liver tissue. Semiquantitative methods include the Ishak scoring system [9], the METAVIR score [10], Scheuer's scoring system [11], Batts scoring system [12], and other methods [13]. There is good correlation among different fibrosis scoring systems. Liver fibrosis is classified by 4–5 point stages based on the distribution and amount of fibrosis. However, these methods are not entirely accurate if the fibrosis is not evenly distributed.

Immunohistochemistry and in situ mRNA hybridization can be used to identify specific matrix components in experimental research. However, these methods are not necessarily more optimal than the standard method for routine clinical application. The semiquantitative methods and quick polymerase chain reaction can be used to measure a variety of cytokines and matrix components, such as TNF-α and TNF-β1 [14]. This approach has some potential for clinical application. However, it must be carefully controlled to ensure that the amplification is specific and within its linear range. Moreover, even if the results are accurate, this method does not reflect the protein level but rather the mRNA level, and these two are not always related.

5.3.2 Noninvasive Methods

Noninvasive methods for the diagnosis of liver fibrosis allow safe, simple, economical, and dynamic monitoring and have other advantages as well. With noninvasive methods, doctors and patients do not have the anxiety that accompanies invasive methods. Noninvasive methods do not result in severe complications such as hemorrhage and death. Commonly used diagnostic methods for liver fibrosis include blood tests, ultrasound, CT, and MRI. Conventional ultrasound, CT, and MRI have some value in discerning the early and late stages of liver fibrosis. However, these methods cannot accurately distinguish different stages of early liver fibrosis. In recent years, advanced ultrasound, CT, and MRI techniques as well as the assessment of more hematological detection variables have been used in the diagnosis and prediction of liver fibrosis.

5.3.2.1 Blood Tests

Serum markers for assessing liver fibrosis include direct serum markers (that monitor extracellular matrix components) and indirect serum markers (that reflect liver inflammation and function). The ideal serum markers for the diagnosis of liver fibrosis have the following characteristics: high sensitivity and specificity, reliability, security, economy, reusability, and ability for dynamic monitoring. Recently, a growing number of serum markers have been considered valuable for predicting liver fibrosis in clinical practice. Simple serum markers such as transaminases and bilirubin can also be used to predict liver fibrosis. Currently, some serum markers can possibly predict the degree of liver fibrosis and cirrhosis, but the serum markers that can indicate the severity of liver fibrosis remain to be found.

Direct Serum Markers

Many types of direct serum markers that can reflect the degree of fibrosis have been reported. In this chapter, we will introduce four common direct serum markers: hyaluronic acid (HA), laminin (LN), IV type collagen (CIV), and procollagen type III (PCIII).

HA is a type of macromolecule, a glucosamine polysaccharide, that is widely present in the extracellular matrix. It is synthesized by the liver mesenchymal cells and taken up and degraded by endothelial cells. The serum HA level can reflect the status of liver cell damage and liver fibrosis, and it is a sensitive indicator of liver fibrosis and cirrhosis. An

elevated serum HA level can indicate possible liver fibrosis. If the serum HA is progressively increasing, it may indicate that liver fibrosis is uncontrolled [15]. LN is a type of non-collagenous structural protein in the extracellular matrix, and CIV is a fibrous glycoprotein. Both proteins are important components of the basement membrane, and they are mainly distributed in the vessel wall, the bile duct and lymphatic walls, and in other places. LN is mainly synthesized by endothelial cells, stem cells, and fat-storing cells in the liver. When liver cells are damaged, LN and CIV combine to form an endothelial basement membrane, resulting in liver fibrosis. Therefore, the serum LN and CIV levels are two important indicators that indicate liver fibrosis in patients with chronic hepatitis [16, 17]. PCIII is the precursor of the III collagen, and it is mainly synthesized and released in the activated hepatic stellate cells. The serum PCIII level can indicate the condition of III collagen metabolism and severity of liver fibrosis, and serum PCIII level is hardly affected by inflammation [18].

Currently, no single direct serum marker can completely independently represent the synthesis of an extracellular matrix. At different stages in the development of liver fibrosis, various serum markers show different trends, and they can be affected by liver inflammation, liver cancer, and other factors, which cause the results to be nonspecific. When inflammation of the liver cells is at the active stage, a large number of extracellular matrices are formed and decomposed, so the direct serum markers may be abnormally high. However, at an advanced stage of liver fibrosis, the activity of the inflammation of the liver is low, so the direct serum marker levels might be inconsistent with the condition of liver fibrosis as observed by pathology. At the same time, when other organs such as the lungs and kidneys are fibrotic, these indicators may also appear elevated, so these markers lack specificity for diagnosing liver fibrosis. In addition, the serum concentrations of these markers are susceptible to impact by the renal excretion clearance.

Indirect Serum Markers

When liver cells are necrotic to a certain extent, the variables measured by routine blood tests, the coagulation function test, and the liver function test, such as serum transaminase levels, platelet count, coagulation factors, and serum albumin concentration, may change. These indicators reflect the changes of the function of synthesis, metabolism, and reservation in hepatic cells. These simple markers do not directly indicate the production of the liver cell extracellular matrix. Several research groups in China and in Western countries have combined the serum direct or indirect markers to create a model to predict the status of liver fibrosis. Some models even include age or sex. These models are shown in Table 5.2.

Most of the noninvasive models in Table 5.2 are from the United States and Europe, and the population cohorts included are not the same. The main population cohorts in these models are patients with chronic hepatitis C (HCV) infection or patients who abuse alcohol. Most liver fibrosis in Chinese patients is caused by chronic hepatitis B (HBV) infection. The HBV infection rate in the Chinese population

Table 5.2 Noninvasive models for the prediction of liver fibrosis

Noninvasive models	Years	Serum markers
AST/ALT [20]	1988	AST, ALT
Age–platelet index [21]	1997	Platelets, age
Cirrhosis discriminant score [22]	1997	Platelets, AST, ALT, PT, ascites, spider angioma
FibroTest (FibroSure) [23]	2001	Age, α2-macroglobulin, haptoglobin, apolipoprotein, GGT, TB, gender
Pohl index [24]	2001	Platelets, AST, ALT
Forns index [25]	2002	Platelets, Age, GGT, cholesterol
Globulin–albumin ratio [26]	2002	Globulin, albumin
APRI [27]	2003	Platelets, AST
FIBROSpect II [28]	2004	TIMP-1, α2-macroglobulin, hyaluronic acid
MP3 score [29]	2004	MMP-1,PIIIP
FibroMeter [30]	2005	Platelets, AST, age, sex, PT, GGT, urea, α2-macroglobulin
GUCI [31]	2005	Platelets, AST, PT
Hepascore [32]	2005	Age, α2-macroglobulin, hyaluronic acid, GGT, TB, gender
Lok index [33]	2005	Platelets, AST, ALT, INR
Zeng index [34]	2005	Age, α2-macroglobulin, GGT, hyaluronic acid
FIB-4 [35]	2006	Platelets, AST, ALT, age
Fibrosis index [36]	2006	Platelets, albumin
Sabadell NIHCED index [37]	2006	Platelets, AST, ALT, age, PT, post-right hepatic lobe atrophy, splenomegaly, caudate lobe hypertrophy
FibroIndex [38]	2007	Platelets, AST, γ-globulin
HALT-C model [39]	2008	Platelets, TIMP-1, hyaluronic acid
FibroQ [40]	2009	Platelets, AST, ALT, PT
King's score [41]	2009	Platelets, AST, age, INR
Fibro-α score [42]	2011	Platelets, AST, ALT, AFP
Fibrosis–cirrhosis index [43]	2011	Platelets, alkaline phosphatase, bilirubin, albumin
Fibrosis–protein index [44]	2011	α2-macroglobulin, heme-binding protein
Significant fibrosis index [45]	2011	Haptoglobin, α2-macroglobulin, TIMP-1, MMP-2, GGT
Fibrosis routine test [46]	2012	Platelets, AST, age, AFP, albumin
Fibronectin discriminant score [47]	2013	Platelets, AST, albumin, fibronectin

cohort is much higher than that in America and Europe. APRI and FIB-4 are two models that have been validated in HBV patients. The initial population cohorts for these two models are HCV and HCV/HIV-infected subjects. Studies have shown that the AUC values of APRI for diagnosing mild or moderate liver fibrosis and cirrhosis were 0.74, 0.73, and 0.73, respectively, and the AUC values of FIB-4 for diagnosing mild or moderate liver fibrosis and cirrhosis were 0.78, 0.82, and 0.84, respectively, in adult patients with chronic HBV infection [19].

Our medical center staffs collected 2176 cases of chronic HBV-induced hepatocellular carcinoma (including 1682 retrospective subjects and 494prospective subjects). All of these patients have had partial liver resection. We found that the AUC values of APRI and FIB-4 for predicting mild or moderate liver fibrosis and cirrhosis in this population cohort are approximately 0.65.By analyzing the data from our medical center, we found that five simple biomarkers were correlated with severity of liver fibrosis: total bilirubin (TBL), platelet count (PLT), clotting time (PT), fibrinogen (FIB), and serum hepatitis B virus e antigen. After univariate and logistic regression analysis, we have established a new model for the assessment of liver fibrosis (not yet published): {[TBL(μmol/L)*PT(s)]/[PLT(10^9/L)*FIB(g/L)]}*[HBeAg(+)=2,HBeAg(-)=1]. The results demonstrated that the AUC of this model for distinguishing early fibrosis (Ishak Score: 0–4) and cirrhosis (Ishak Score: 5–6) was 0.75.

However, because these models combine a variety of markers to assess liver fibrosis, any false-positive marker will affect the diagnostic accuracy. At the same time, the existing serum markers lack specificity for the liver and can be affected by the kidney excretion function. Additionally, various liver or systemic diseases can cause false-positive results for these markers. Although these models have an ideal high accuracy for distinct mild liver fibrosis and cirrhosis, they are limited for distinguishing different levels of moderate liver fibrosis. Direct and indirect serum markers are simple, noninvasive assessment methods for assessing the severity of liver fibrosis. However, the diagnostic accuracy of these models must be studied and validated. We anticipate the findings for simple blood markers that can accurately reflect the severity of liver fibrosis with various etiologies.

For diagnosing liver disease, no serum marker can replace radiographic examination. Radiographic examinations are commonly used noninvasive methods for the diagnosis of liver fibrosis. Combining serum markers with imaging might improve the diagnostic accuracy of liver fibrosis and allow for monitoring dynamically.

5.3.2.2 Ultrasound Examination

Ultrasound examination is based on high-frequency acoustic information obtained from the human body to diagnose disease. It is noninvasive, inexpensive, easy to repeat, and has other advantages that cause clinicians to prefer this type of diagnostic method. Ultrasonography is a routine imaging diagnostic method and the first choice for diagnosing liver disease.

Conventional Ultrasound Examination

When liver cirrhosis reaches a certain level, the two-dimensional ultrasound image can appear as an uneven echo, showing rough or nodular changes of the liver parenchyma; the liver capsule can also be irregular or wavy, and the liver edge is blunt. Abnormality of other organs is also evident, such as thinness and narrowness in the intrahepatic vein, gallbladder wall thickening, and splenomegaly. Recently, general high-frequency ultrasound has been used in the diagnosis of liver fibrosis. High-frequency ultrasound has some value for diagnosing liver fibrosis and early cirrhosis by observing the changes in the surface morphology of the liver capsule and semiquantitative grading. The ultrasonic tissue characterization method uses a radiofrequency or videographic method to explore the relationship between the acoustic characteristics and ultrasonography. The ultrasonic tissue characterization method provides new quantitative indicators for the clinical diagnosis of liver fibrosis.

Color Doppler and Spectral Doppler Ultrasound Examination

Based on the two-dimensional ultrasound color, Doppler ultrasound uses the Doppler principle of sound and a series of electronic techniques to show a real-time display of the blood flow spectrum of arteries and veins at a point. Spectral Doppler ultrasound uses the information from the ultrasound Doppler effect to detect the speed of blood flow to diagnose disease. When the liver fibrosis or cirrhosis occurs, sclerosis, an abnormality of the liver parenchyma, damages the integrity of blood vessel walls. Color Doppler and spectral Doppler ultrasound examinations can diagnose liver fibrosis and cirrhosis by detecting the dynamics of the blood in vessels in the liver. Hepatic vein spectra include three types: type 0 hepatic vein – a three- or four-phase wave (i.e., two negative phase waves, one or two positive phase waves); type 1 hepatic vein – a low and flat wave, without inverted blood flow; and type 2 hepatic vein – continuous flat wave, similar to the blood flow in the portal vein [48]. Some researchers believe that normal or mild liver fibrosis is characterized by a type 0 hepatic vein, moderate hepatic fibrosis has a type 1hepatic vein, and severe liver fibrosis has a type 2 hepatic vein. However, the hemodynamic changes of color Doppler and spectral Doppler ultrasound examinations are vulnerable to interference from electronic equipment or human error that will bias the results [49].

Liver Contrast-Enhanced Ultrasound Examination

Liver contrast-enhanced ultrasound examination is a new method for diagnosing liver disease. The contrast media are

gas-filled microbubbles that are administered intravenously to the systemic circulation. The microbubbles sequentially flow through heart, lung, liver artery and the portal vein, the liver sinusoid, and then merge into the hepatic vein. After the signal is emitted by the ultrasound probe, the contrast agents produce harmonic resonance to form an image. Combining the trigger and the acoustic densitometry imaging techniques produces more accurate ultrasound images. Contrast-enhanced ultrasound can be used to image blood perfusion in organs. We can use contrast-enhanced ultrasound to monitor the blood flow in the liver to diagnose liver fibrosis. For the small arteriovenous shunt and hyperdynamic state of microvessels in liver fibrosis or cirrhosis patients, it provides a theoretical basis for contrast-enhanced ultrasound to assess liver fibrosis. The commonly used indicators of contrast-enhanced ultrasound for diagnosing liver fibrosis include the rate of blood flow through the hepatic vein, the delay rate in the hepatic artery, the blood perfusion strength in the portal vein, and the blood cycle time in the liver. Several studies indicated contrast-enhanced ultrasound can reflect the degree of liver fibrosis. It is one of the noninvasive methods to diagnose liver fibrosis and cirrhosis [50, 51].

Three-Dimensional Ultrasound Imaging Examination

Three-dimensional ultrasound imaging technology is an emerging discipline in medical imaging. Initial research on three-dimensional ultrasound imaging began in 1970s and now it has entered the stage of clinical application. Its working principle is to create a three-dimensional image via computer using a series of images acquired under certain rules. Three-dimensional ultrasound can show the blood vessels and their positional relationships more clearly than two-dimensional ultrasound for the diagnosis of liver disease. Studies have shown that three-dimensional ultrasound imaging is superior to the two-dimensional ultrasound imaging in many aspects, such as liver morphology, edge of the liver, resolution, continuity of the intrahepatic vessels, and relationship between the liver and blood vessels around the liver [52].

Ultrasound Elastography Examination

Ultrasound elastography is a new noninvasive diagnostic method for the assessment of liver fibrosis. Currently, there are three main methods used in clinical ultrasound elastography, including the following: real-time tissue elastograph (RTE), transient elastography (FibroScan, FS), and acoustic radiation force impulse (ARFI). The physical principles of these three diagnostic methods for assessing liver fibrosis are different. FS and ARFI base on shear wave elastography; however, RTE uses resilience-tissue elasticity to form images. The modulus of liver elasticity is liver stiffness, which is closely related to its pathological state. Several researchers confirmed the close relationship between liver tissue elasticity and the stages of liver fibrosis [53–55]. The ultrasound elastography technique, with its noninvasive and real-time detection of the soft tissue elasticity modulus, provides a new method for the detection of liver fibrosis and cirrhosis. The new technique avoids the significant risks of liver biopsy to assess liver fibrosis, and it is expected to become the ideal method for evaluating liver fibrosis. However, this new diagnostic method is currently in the research stage, and it has not been widely used in clinical practice. Additionally, its diagnostic accuracy for liver fibrosis caused by chronic HBV infection, alcohol abuse, and liver bile obstructive disease must be validated. Moreover, ultrasound elastography is limited to the identification of different stages of mild to moderate liver fibrosis. Furthermore, the cutoff values of the elastic modulus for predicting different fibrosis levels have not been unified. Therefore, more research is necessary to verify the diagnostic capabilities of ultrasound elastography to fully utilize its diagnostic capabilities.

5.3.2.3 Computed Tomography (CT) Examination

Conventional CT Examination

Conventional CT diagnoses liver fibrosis by observing morphological changes in the liver. The observed morphological changes include the liver profile, liver volume, proportion of the liver lobe, the liver split, the density of the liver parenchyma, the spleen size, and the diameter of the portal or hepatic vein. Morphological changes in the liver vary at the early and advanced stages of liver fibrosis. At the early stage of liver fibrosis, the left lateral and caudate lobes of the liver are notably enlarged, and the right lobe and square lobe of the liver are slightly enlarged. At the advanced stage of liver fibrosis, the left lateral and caudate lobes of liver increase relatively and the right and square lobes of the liver are significantly shrunken. The overall liver volume first increases and then shrinks. In advanced liver cirrhosis, a CT scan can clearly show morphological changes in the liver, such as a wavy edge, an imbalance of the liver lobes, a wider liver split, an uneven liver parenchyma, splenomegaly, and portal vein thickening and dilation; meanwhile, portal hypertension symptoms are present such as gastric esophageal varices and ascites. A conventional CT scan cannot be used for staging liver fibrosis, and it is not sensitive to detect early stage cirrhosis. Morphological changes in the liver can be detected by CT examination only after the cirrhosis has progressed to a certain extent. In recent years, Fibro-CT, a quantitative method for assessing liver fibrosis, has been used in clinical practice. It has some value for staging liver fibrosis [56].

Enhanced CT can provide more information for the clinical diagnosis and treatment of liver disease. A liver CT scan can detect changes in liver density and in the blood vessels in the liver as well as other secondary changes, including splenomegaly, ascites, portal hypertension, and collateral

circulation formation. Studies have shown that the enhanced uneven proportion of the liver parenchyma is higher in a liver in the later stages of liver fibrosis [57]. The early radiographic signs of portal hypertension caused by cirrhosis are atypical and easily missed. However, a 256-slice spiral CT with low dose of contrast agent and low radiation dose can clearly reflect portal hypertension and the collateral circulation of the blood vessels [58]. However, an enhanced CT scan still cannot quantitatively predict the early stages of liver fibrosis.

CT Perfusion Imaging

CT perfusion imaging is a type of functional imaging. The selected levels of interest are dynamically scanned continuously after contrast agents have been injected intravenously to obtain a time–density curve for each pixel within the selected levels. Based on this curve, several hemodynamic parameters and blood perfusion images of different organs, such as the local blood flow capacity and the average flowing time and peak time of contrast agents, can be obtained via different mathematical models and computer pseudo-color processing. CT perfusion imaging can more effectively and quantitatively reflect the changes in blood perfusion of the local tissue, and it allows us to understand the blood supply of organs.

Significant abnormal angiogenesis, a reconstruction of hepatic sinuses, dysfunction of sinusoidal endothelial cells, capillary proliferation between hepatic sinuses, an increase in intrahepatic vascular resistance, and the formation of portal hypertension are present in a liver with fibrosis. Liver CT perfusion imaging can perfectly indicate the changes of hemodynamics in the liver. It can predict fibrosis levels by measuring the hepatic artery perfusion volume, the portal vein perfusion volume, the total blood flow in the liver, the hepatic perfusion index, the blood flow, the blood volume, and the average rate of blood flow through the liver [59]. Some studies demonstrated that CT perfusion imaging can identify mild to moderate liver fibrosis [60]. However, the examination time for CT perfusion imaging is long. Patients cannot endure a lengthy examination without moving, which can result in a poor result or even examination failure. Moreover, patients exposed to radiation for a long time can suffer from radiation damage.

Energy Spectrum CT

Energy spectrum CT is based on the principle that different substances have different absorption capacities at different X-ray energies. Compared to a conventional CT scan, energy spectrum CT can provide more imaging parameters and information. Energy spectrum CT does not only show morphological changes but also quantitatively reflects energy differences in tissues. Via enhanced energy spectrum CT scanning, different liver fibrosis levels can be distinguished by measuring the concentration of iodine [61]. Single-energy spectrum CT imaging can show the portal vein more clearly, and it is more accurate for the assessment of portal hypertension. Energy spectrum CT has not yet been widely used in clinical practice as a new diagnostic method for liver fibrosis. The iodine concentration diagram can be used to predict liver fibrosis, but whether the other parameters that are also available can be used to quantitatively assess liver fibrosis must be verified.

5.3.2.4 Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging (MRI) can detect earlier stages of liver fibrosis than a CT scan, and it can be used to quantitatively analyze liver fibrosis. It also has the following advantages: it rarely uses contrast agents, it causes no radiation damage, and it provides high contrast and resolution of soft tissue and a variety of functional imaging. These advantages give MRI great potential in the clinical diagnosis of liver fibrosis.

Conventional MRI

A conventional MRI examination of the liver includes ordinary plain and dynamic contrast-enhanced scans. The general unenhanced MRI scan can diagnose liver fibrosis via liver morphological changes and the grid-like changes in the hepatic parenchyma [62]. The enhanced MRI scans detect liver fibrosis mainly by introducing various types of contrast agents to increase the differences between the injured and the normal tissues. Two types of contrast agents are mainly used. One is the nonspecific extracellular space contrast agents, such as gadolinium-DTPA (Gd-DTPA), which accumulate in the extracellular space to shorten the T1 time of the tissue; consequently, the fibrotic component might show delayed enhancement. The other contrast agent is the cellular specific type. Reticuloendothelial cell-specific contrast agents such as superparamagnetic iron oxide (SPIO) particles can be engulfed by the Kupffer cells in the liver, which cause the signal from tissues reduced on T1 and T2 and the T2 to shorten more significantly. The number of Kupffer cells in the liver is reduced when liver fibrosis occurs, and the function of Kupffer cells is reduced. Therefore, the signals in the fibrotic liver are lower than those in the normal liver tissues. Studies have shown that SPIO-enhanced MRI and double-enhanced MRI are better than a plain MRI scan for detecting liver damage [63]. Although a conventional MRI examination can display changes in liver morphology via a variety of MRI imaging sequences and parameters, it is still insufficient for the clinical diagnosis of liver fibrosis. Conventional MRI cannot quantitatively detect the degree and grades of liver fibrosis. Because the number of Kupffer cells in the liver is extremely less than that in the normal liver cells, it is difficult to distinguish early liver fibrosis from normal liver tissue via an SPIO-enhanced MRI scan. In addition, the process of enhanced MRI imaging is complex, and it is not easily accepted by patients.

Diffusion-Weighted MR Imaging (DWI)

Diffusion-weighted MR imaging (DWI) is a new type of functional MR imaging technique. DWI is very sensitive to molecular Brownian motion and can noninvasively reflect the physiological and pathological features of living tissue. DWI has been widely used to diagnose central nervous system diseases. DWI can dynamically reflect the composition of the spatial organization and the functional status of exchanges of water molecules in pathological tissues. The parameter which describes the amount of diffusion of biomolecules in vivo is the apparent diffusion coefficient (ADC). In recent years, with the progress of studies on the DWI technique in the diagnosis of liver disease, DWI has been increasingly used in the diagnosis of liver fibrosis and cirrhosis. A study found that the ADC value in liver fibrosis is lower than those in normal liver tissue and the ADC value in moderate liver fibrosis is lower than that in mildly fibrotic liver tissue [64]. As a noninvasive functional examination method for predicting liver fibrosis, a DWI MRI scan can detect liver fibrosis earlier, before the traditional morphological changes occur. However, DWI MRI examination has several limitations. The examining time for DWI imaging is long and slightly movement of the subject can affect the ADC value. Fat deposition in the liver can also affect the ADC value. No unified standard for DWI imaging scans exists and there is a lack of comparability of the results. Moreover, a DWI MRI examination is not suitable for the elderly or the patients with liver hemochromatosis.

Perfusion-Weighted Imaging (PWI)

MR perfusion-weighted imaging (PWI) is a form of functional MR imaging. It mainly provides information about the hemodynamics of microscopic tissues. Currently, the commonly used contrast agent in clinical practice is the ionic nonspecific extracellular contrast agent Gd-DTPA. The contrast agent is quickly injected into the peripheral veins with a high-pressure syringe. Then, a rapidly continuous multitemporal scan of the target organs using sufficiently high temporal resolution MR imaging sequences is conducted. Finally, PWI can detect the changes in the signal strength of the blood with contrast agent from the blood that first flows through the subject tissues over time to reflect the hemodynamic information. PWI can provide different hemodynamic status of the pathological liver and the whole liver with perfusion imaging. The liver tissues are reconstructed in the fibrotic liver. Hagiwara et al. found that the liver blood flow, arterial fraction, and the distribution of blood volume of patients suffering from severe liver fibrosis increased significantly compared to those of patients with mild or moderate liver fibrosis. Additionally, the portal perfusion in patients with severe liver fibrosis decreased [65]. However, the diagnostic accuracy is susceptible to stroke volume, fasting status, hepatic congestion, inflammation of the liver, and portal vein blood flow. The liver has a dual blood supply and a complex special micro-loop structure. The existing liver perfusion MR sequence and the analyzing software are inadequate. The current MR-PWI examination is limited for the clinical assessment of liver fibrosis, and it has not been widely used clinically.

5.3.2.5 Magnetic Resonance Spectroscopy (MRS)

Magnetic resonance spectroscopy (MRS) is a method that analyzes a particular nucleus and its compounds via magnetic resonance phenomena and chemical shift effect. It is a noninvasive method to measure metabolism in tissue, biochemical changes, and quantitative analysis of chemicals in living subjects. It is a new functional analytical and diagnostic method based on conventional magnetic resonance imaging. The liver is an active metabolic organ, which allows MRS to be used for basic clinical studies on liver disease. Some researchers found that values of the ratios for phosphomonoesterase/lipid, glutamic acid/lipid, and glycogen/lipid gradually increased with the degree of liver fibrosis, aggravated by using ^{1}H-MRS imaging [66].^{1}H-MRS is an important method to detect the liver fat content and advanced liver fibrosis, and the results have good consistency and relevance with a histological assessment [67]. A trial using $^{31P\text{-}MRS}$ to investigate liver energy metabolism demonstrated that the phosphate monoester and phosphate monoester to phosphodiester ratio increased in patients with liver fibrosis, while phosphodiesters, ATP, and inorganic phosphorus were lower [66]. A study from Noren et al. showed that there are significant differences in concentration of phosphodiester between patients with mild liver fibrosis and cirrhosis by using^{31}P-MRS, and the investigators believed that the phosphodiester content could distinguish early fibrosis and advanced cirrhosis [68]. Currently, liver MRS is a not yet a fully mature examination method, and it cannot be considered as a routine noninvasive diagnostic method for liver fibrosis in clinical practice.

Magnetic Resonance Elastography (MRE)

Magnetic resonance elastography (MRE) is a new noninvasive imaging method for quantitatively measuring the mechanical properties of tissue and is considered a "video palpation." The mechanism is to detect the displacement of tissues or organs under external force by using nuclear magnetic resonance spectroscopy to obtain MRI phase images via a motion-sensitive gradient. We can draw an elasticity map (i.e., the elastography) which reflects the elasticity distribution of each point in a tissue or organ, and the elastic parameters of tissues or organs can be considered as diagnostic markers of disease. The hardness of liver is directly related to the severity of liver fibrosis. The hardness gradually increases with the progression of liver disease, so MRE is also useful as a diagnostic tool for liver fibrosis. Studies

have shown that the difference in hardness of the early fibrosis levels was not obvious by an MRE examination, and there was an overlap between groups with different stages of early fibrosis. However, a significant difference in hardness between the groups with advanced liver fibrosis was present, and there was little overlap between the groups [69, 70]. Compared to DWI, the diagnostic accuracy of MRE is higher [71]. However, MRE has shortcomings. First, the elastic modulus of human tissue overlap in some tissues, as does the elastic modulus of normal tissues and pathological tissues, so false-positive and false-negative results occur when MRE is used to diagnose liver fibrosis. Secondly, the physician must carefully observe the elastic graph and record the hardness data for the tissue region with a reliably transferring wave. If the physician recorded the hardness data for the tissue region without reliably transferring wave, the results obtained would be inaccurate. Furthermore, the image resolution of MRE is not very satisfactory. MRE technology is still in its infancy. With the advances in technology, it is expected to become a new noninvasive method for the clinical diagnosis of liver fibrosis.

Molecular MR Imaging

Molecular MR imaging can qualitatively and quantitatively study changes in cells and intracellular molecules in vivo. The key is to identify the cells or molecules specific for the disease. In liver fibrosis, hepatic stellate cells (HSC) affected by an inflammatory reaction transform to collagen cells and secrete large amounts of collagen, the progression of the disease. Collagens can become the targeted marker. If we measure the collagen, the liver fibrosis can be quantitatively assessed. Some researchers have successfully identified the components of fibrotic collagens in animal liver fibrosis models by the use of collagen-specific probes [72]. Chow et al. [73] conducted a targeted imaging of liver fibrosis in an animal model by using the nanospheres of decapeptide cyclic peptide labeled by targeting the fibronectin–fibronectin complex. The results demonstrated that the targeted contrast agent can accurately detect liver fibrosis and the stage of liver fibrosis. At present, specific molecular MRI molecular imaging of liver fibrosis is still in the experimental stage in animals. Discovery of a highly expressed molecule associated with liver fibrosis will help us to improve the targeting properties of imaging.

5.4 Summary and Expectation

Liver fibrosis is the result of the long-term effects of the causative factors on the liver, which results in liver cell damage. Without early intervention, it will develop into cirrhosis or liver cancer, which can seriously threaten people's health and lives. The early diagnosis of liver fibrosis can provide a basis for early treatment by doctors. It can delay the progression of liver fibrosis. Additionally, for a patient slated for hepatectomy, it is especially important to know the extent of liver fibrosis. It not only helps the surgeon to assess whether the patient can tolerate surgery, but also to assess the risks of surgery and postsurgical recovery. Methods of diagnosing liver fibrosis include invasive and noninvasive methods, each with its own advantages and disadvantages. With the application of genomics, proteomics, and metabolomics in biological and clinical research, these methods are expected to become the new noninvasive methods for the diagnosis of liver fibrosis in the future.

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Ultrasound Elastography in the Assessment of Liver Fibrosis

6

Qiang Lu and Wenwu Ling

6.1 A Brief Introduction of Liver Fibrosis: Its Etiology and Diagnosis

According to the fact sheet released by World Health Organization (WHO), an estimated 240 million people worldwide are chronically infected with the hepatitis B virus (HBV). HBV-related diseases, such as liver failure, liver cirrhosis, and hepatic cell carcinoma (HCC), result in approximately 600 thousand deaths per year [1]. An estimated 150 million people are infected with the hepatitis C virus (HCV), and 350 thousand mortalities per year are HCV related [2]. As one of the most widespread epidemic diseases in China, the positivity rate for the HBV surface antigen is 7.18 % [3]. In addition, epidemiological surveys revealed that in 2006, there were more than 93 million people infected with chronic HBV, of whom approximately 20 million are chronic HBV patients. Common diseases associated with HBV infection include acute and chronic HBV hepatitis, HBV-related liver cirrhosis, and HBV-related HCC. The incidence of HCC in China is approximately 350 thousand per year, accounting for 55 % of global incidences. HCC also ranks the second in cancer-related mortality, compromising the well-being of individuals and causing an enormous financial burden on the family, society, and the country. In China, 95 % of HCC originates from a background of HBV infection, and liver fibrosis plays a major role in the progression from HBV infection to liver cirrhosis and ultimately possible to HCC. Liver fibrosis is not a single disease entity but a common pathological process in almost every type of chronic liver disease. It is characterized by increased synthesis of extracellular matrix proteins, primarily via interstitial cells especially activated hepatic stellate cells, with subsequent excess deposition of fibrous connective tissue in the liver [4]. This increased synthesis and excess deposition result in structural disturbances of the hepatic lobules and the formation of pseudolobules, an effect that gradually advances to cirrhosis and liver dysfunction. The main causes of liver fibrosis are infection with hepatotropic viruses (HBV and HCV), alcohol abuse, and nonalcoholic fatty liver disease. The progression of liver fibrosis is relatively slow, usually taking a decade or even several decades for the initial fibrosis in the portal triads to form fibrous septa, which damage the hepatic lobules and to ultimately progress to cirrhosis. Excluding cirrhosis, liver fibrosis is considered to be reversible under certain circumstances; therefore, early diagnosis and dynamic surveillance of liver fibrosis is crucial. With observation, it is possible to determine the proper starting time for treatment, to evaluate drug efficacy, to stage the disease, and to evaluate its prognosis. Thereby, the accurate staging of liver fibrosis is of great importance.

Liver fibrosis is classified into four stages according to the internationally accepted fibrosis grading system proposed by Scheuer [5]: S0 indicates no fibrosis, S1 indicates portal fibrous expansion with intact lobule structure and no fibrous septa, S2 indicates periportal fibrosis and fibrous septa formation with most of the lobule structure preserved, S3 is defined as lobule structural distortion without cirrhosis, and S4 is cirrhosis. Inflammation together with necrosis is graded into four levels, which are described as follows: G0 represents no inflammation; G1 is portal inflammation without necrosis; G2 is mild piecemeal necrosis; G3 is moderate piecemeal necrosis; and G4 indicates severe piecemeal necrosis and bridging necrosis.

There are primarily three approaches for staging liver fibrosis, including liver biopsy, serum biomarkers, and imaging examinations. Liver biopsy has been considered as the gold standard for diagnosing liver fibrosis; however, liver biopsy has a few limitations that restrict it from dynamic surveillance and long-term follow-up of liver fibrosis. Some patients may reject this procedure owing to its invasive nature and possible severe complications in rare cases. In addition,

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a standard liver biopsy sample represents only 1/50,000th of the entire organ, resulting in sampling error and inaccuracy [6, 7]. The limitations of liver biopsy, an intense demand for noninvasive approaches and a lack of long-term follow-up approaches for liver fibrosis, have led to a search for noninvasive approaches to assess liver fibrosis. Such methods primarily include biomarkers and imaging examinations. The biomarker method uses direct serological markers derived from fibrogenesis and fibrous degradation or combinations of regular serological indicators to estimate liver fibrosis. However, those biomarkers are not liver specific and can be affected by factors unrelated to the liver, compromising their accuracy in assessing liver fibrosis. Imaging examinations, including gray-scale ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI), are noninvasive, objective, and reproducible. Of these techniques, US is widely accepted for the diagnosis of liver diseases for its convenience and low cost. US can detect: (1) liver morphology, (2) echo intensity, (3) the homogeneity of the parenchyma, (4) the smoothness level of the liver capsule, and (5) the presence of nodules in the parenchyma to estimate liver fibrosis or cirrhosis. However, conventional US is limited with respect to grading liver fibrosis and diagnosing early cirrhosis. Recently, with major advances of ultrasound techniques, ultrasound elastography has been widely used to measure the stiffness of soft tissue, playing an important role in the differential diagnosis of benign or malignant tumors in superficial organs, such as the mammary and thyroid glands. The innovation of ultrasonic elastography for deep organs makes it possible to measure liver stiffness, and researchers have already applied this technique to quantitatively assess the degree of liver fibrosis. Guideline regarding the application of ultrasonic elastography in clinical practice was released by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) in 2013. This guideline noted [8] that elastography can be used in the follow-up and surveillance of patients with chronic liver diseases owing to its advantage in assessing liver fibrosis resulting from chronic liver diseases. The EASL guideline of management of HCV infection indicates [9] that when the result of elastography coincides with clinical manifestations, a liver biopsy is not needed for diagnosis. Elastography is well recognized as a valuable and promising method in assessing liver fibrosis resulting from chronic liver diseases.

6.2 Application of Ultrasound Elastography for Assessing Liver Fibrosis

Since the concept of elastography was first introduced by Ophir et al. [10] in 1991, ultrasound elastography has gradually matured. As an emerging technique, ultrasound elastography measures the elastic modulus or stiffness of the tissue, a physical attribute that cannot be obtained by conventional ultrasound. An alteration in stiffness is usually caused by pathological changes in the tissue; therefore, this technique provides us with a new strategy in diagnosis. With broader knowledge and acceptance, ultrasound elastography has become widely used in measuring the stiffness of soft tissue, especially in the differential diagnosis of benign or malignant tumor in superficial organs, such as the mammary gland [11]. Further innovation of ultrasound elastography for deep organs makes it possible to measure liver stiffness, and it has already been applied for the quantitative assessment of liver fibrosis. The currently used ultrasound elastography techniques for estimating liver stiffness include transient elastography (TE, such as FibroScan), acoustic radiation force impulse imaging (ARFI), elastography point quantification (ElastPQ), supersonic shear wave imaging (SSI), and real-time tissue elastography (RTE). However, by using distinct principles in estimating liver stiffness, different elastography techniques may show different abilities in diagnosing and grading liver fibrosis and can be affected by other factors. TE, ARFI, ElastPQ, and SSI belong to shear wave elastography, while RTE belongs to compression elastography or strain imaging. The abovementioned techniques can all be used in noninvasive clinical diagnosis and in the grading of liver fibrosis. These techniques will be discussed in detail in the following paragraphs.

6.2.1 The Application of TE for Grading Liver Fibrosis

The TE technique was proposed by Catheline et al. [12] and Sandrin et al. [13], and FibroScan was developed by the French company Echosens. FibroScan is an example of a one-dimensional TE system and is composed of a probe and a signal processor. An ultrasound transducer probe is mounted on the axis of a low-frequency vibrator. Vibrations of mild amplitude and low frequency are transmitted from the vibrator to the liver via the transducer, inducing a shear wave inside the liver to generate reversible and detectable mechanical alterations. Meanwhile, pulse-echo ultrasound acquisitions track the propagation of the elastic shear wave and measure its velocity, and tissue deformation caused by the shear wave is calculated via a cross-correlation algorithm; this result is the elastic value of the tissue. This technique measures the mean elastic value (kPa) of the region of interest (ROI). The stiffer the tissue, the larger the elastic value, and the faster the shear wave is propagated. This technique is widely used as a noninvasive tool to assess liver fibrosis, evaluate therapeutic efficacy, and prognosticate related complications [14].

At present, most quantitative liver fibrosis assessments in research are performed using the FibroScan technique;

however, various results have been reported. In a meta-analysis including 18 studies and 2772 HBV patients, Chon et al. [14] reported that when using 7.9 kPa as the cutoff value for the diagnosis of moderate or worse liver fibrosis (≥S2), the area under the receiver operating characteristic curve (AUROC) was 0.859. In this analysis, the sensitivity and specificity were 74.3 % and 78.3 %, respectively. Moreover, when using 8.8 kPa as the cutoff value for severe or worse liver fibrosis (≥S3), the AUROC was 0.887, the sensitivity was 74.0 %, and the specificity was 63.8 %. When using 11.7 kPa as the cutoff value of liver cirrhosis (S4), the AUROC was 0.929, the sensitivity was 84.6 %, and the specificity was 81.5 %. FibroScan showed great value in the quantitative diagnosis of liver fibrosis, especially liver cirrhosis. However, there are overlaps in the elasticity values of different grades of liver fibrosis, leading to certain difficulties in distinguishing adjacent grades of liver fibrosis, especially in S0-S2. Myers et al. [15] reported that the elastic values of S0-S4 were 5.5 kPa (4.0–7.7), 6.3 kPa (4.7–9.0), 7.7 kPa (5.7–10.4), 12.0 kPa (8.3–17.3), and 24.3 kPa (13.7–34.6), respectively. The overlap in early liver fibrosis was more prominent, and the AUROCs for diagnosing fibrosis stages ≥S2, ≥S3, and S4 were 0.74, 0.89, and 0.94, respectively. This previous study also suggested that liver stiffness was correlated with multiple factors, such as gender, age, HCV (compared with HBV), alanine aminotransferase (ALT), and aspartate aminotransferase levels. However, stiffness was not correlated with the degree of necroinflammation in chronic hepatitis. Chan et al.'s study [16] indicated that the liver stiffness value was higher in patients with elevated ALT levels than in those with normal ALT levels among patients with the same grade of liver fibrosis; this correlation overestimated liver fibrosis grade, leading to potential false positives. In the diagnosis of liver fibrosis in HBV patients (S0 vs. S1-4), patients with HBeAg positivity had significantly lower AUROCs than patients without HBeAg positivity (0.63 vs. 0.90, respectively). HCV patients with the same liver fibrosis grade showed a higher liver stiffness than did HBV patients. Stebbing et al. [17] reported that the liver stiffness values of HCV patients with grade ≥S2 and S4 liver fibrosis were 8.44 kPa and 16.14 kPa, respectively, which are notably higher than those of HBV patients. This effect might be explained, as some researchers have suggested [18, 19], by the fact that HBV patients had less and thinner fibrous septa than did HCV patients with the same grade of liver fibrosis. Moreover, HBV patients exhibit larger nodules in fibrogenesis than do HCV patients. Therefore, in HBV patients, the pulse more likely propagates along relatively normal parenchyma and causes a lower measurement stiffness value. FibroScan shows significant value in the quantitative assessment in grading liver fibrosis; however, multiple factors should be considered when performing the measurement to acquire more accuracy in this assessment.

FibroScan also has some limitations [20]. Liver stiffness measurements can be difficult to obtain in obese patients because adipose tissue strongly attenuates low-frequency shear and ultrasound waves. The probe cannot be employed in patients with narrow intercostal spaces. In addition, without two-dimensional imaging, it is difficult to avoid intrahepatic vessels and bile ducts, resulting in sampling error. Moreover, FibroScan cannot be applied in patients with ascites because the low-frequency shear wave is unable to propagate in fluid.

6.2.2 The Application of ARFI for Grading Liver Fibrosis

ARFI is an imaging technique performed using a standard ultrasound imaging device within medical power. This method uses focused ultrasound pulses to produce a radiation force that causes tissue dislocation in the ROI. Tissue dislocation generates shear waves that can be measured using ultrasonography. Owing to the rapid attenuation of radiation force outside the ROI, it is possible to measure the propagation velocity (m/s) of the low-frequency shear wave inside the ROI. This velocity increases with the liver parenchyma stiffness; therefore, it is possible to indirectly estimate the tissue elasticity [21, 22]. The Acuson S2000, also known as virtual touch tissue quantification (VTQ) (see Fig. 6.1), was designed by Siemens in 2008 using the ARFI principle and has been widely applied for the noninvasive quantification of liver fibrosis in clinical practice. Studies have shown a positive correlation between the velocity of shear waves and histological grading in assessing liver fibrosis using ARFI. That is, the more severe the liver fibrosis, the faster the shear wave propagates. The diagnostic value of AFRI in assessing liver fibrosis is similar to FibroScan, and ARFI shows promising accuracy in the quantitative assessment of liver fibrosis, especially for grading S2 and worst fibrosis.

However, the elastic values for each liver fibrosis stages as determined by ARFI, the cutoff values for grading liver fibrosis, and the diagnostic efficacy for liver fibrosis vary significantly among different studies. Zhang et al. [23] performed ARFI and FibroScan in 180 patients. The speed of the shear waves in liver fibrosis stages S0/S1, S2, S3, and S4 was 1.24 ± 0.20 m/s, 1.40 ± 0.38 m/s, 1.93 ± 0.70 m/s, and 2.19 ± 0.66 m/s, respectively. The elasticity values of distinct stages of liver fibrosis were significantly different, showing a prominent correlation to histological grades, with a correlation coefficient of 0.599. The AUROCs of ARFI for diagnosing liver fibrosis grades ≥S2, ≥S3, and S4 were 0.764, 0.852, and 0.825, respectively. This previous study indicated that ARFI had better performance in diagnosing liver cirrhosis than did FibroScan. However, both techniques possessed a

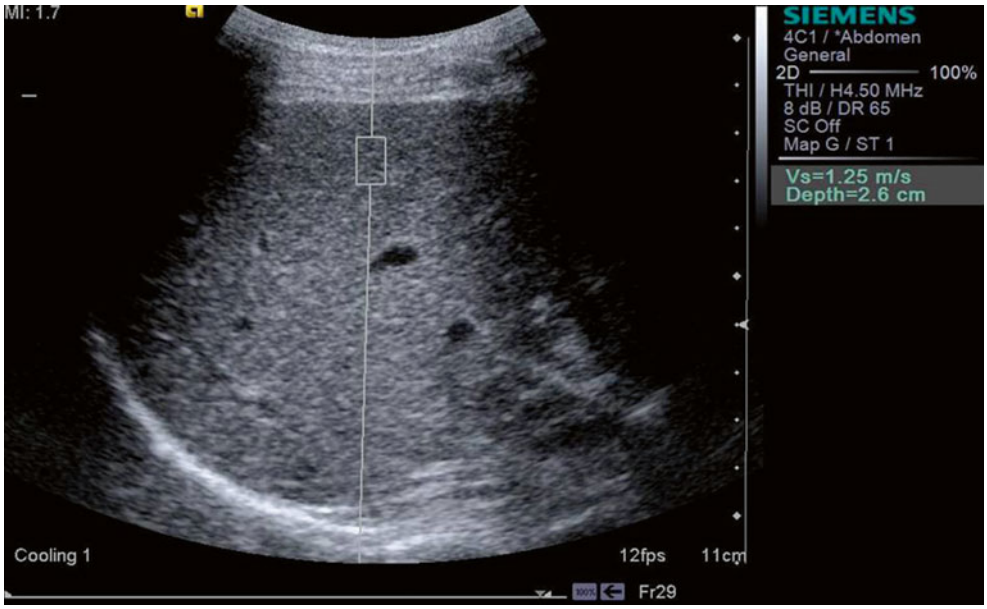

Fig. 6.1 Imaging of a normal liver using ARFI; the sonogram shows the velocity of shear waves and the depth of the ROI

similar diagnostic ability for liver fibrosis. A study of 349 various types of chronic liver disease patients conducted by Cassinotto et al. [24] compared ARFI, SSI, and FibroScan for the diagnosis and grading of liver fibrosis. The results indicated that the speeds of the shear waves propagating in S0 to S4 liver fibrosis were, respectively, 1.16 ± 0.60 m/s, 1.28 ± 0.42 m/s, 1.51 ± 0.70 m/s, 1.77 ± 0.54 m/s, and 2.24 ± 0.69 m/s. Using ≥1.35 m/s as the cutoff value for liver fibrosis ≥S1, the AUROC was 0.81, the sensitivity was 61 %, the specificity was 96 %, and the accuracy was 65 %. When using ≥1.38 m/s to diagnose liver fibrosis ≥S2, the AUROC was 0.81, and the sensitivity, specificity, and accuracy were 72 %, 81 %, and 75 %, respectively. Using ≥1.50 m/s as the cutoff value for ≥S3, the AUROC was 0.85, the sensitivity was 79 %, the specificity was 81 %, and the accuracy was 80 %. When using ≥1.61 m/s to determine S4, the AUROC was 0.84, and the sensitivity, specificity, and accuracy were 81 %, 77 %, and 78 %, respectively. The above study suggested that ARFI can differentiate between different grades of liver fibrosis; moreover, it had better diagnostic value and accuracy in severe liver fibrosis and cirrhosis. However, the diagnostic value and accuracy for grading liver fibrosis of ARFI were lower than for SSI. A meta-analysis of eight studies that included 518 cases of all types of liver fibrosis cases performed by Friedrich-Rust et al. [25] indicated that the AUROCs of ARFI in grading ≥S2, ≥S3, and S4 were 0.87, 0.91, and 0.93, respectively, and the cutoffs were 1.34 m/s, 1.55 m/s, and 1.80 m/s, respectively, with acceptable sensitivity and specificity. Generally speaking, ARFI can be used for measuring and differentiating distinct liver fibrosis stages.

Results have varied widely in studies applying ARFI for the measurement of liver fibrosis. Here, we list some possible explanations. First, different etiologies result in natural pathological diversity along liver fibrosis course. Second, diversity exists in liver stiffness in the context of liver fibrosis among different races. Bota et al. [26] studied 5 countries, 2 areas, and 1242 patients with variable etiologies, concluding that different reference values of liver stiffness for liver fibrosis should be adopted for the European and Asian populations. These authors also reported that stiffness as measured by ARFI could be affected by ALT levels. For European HCV patients with normal or mild elevated ALT, the respective diagnosing values for fibrosis ≥S2 and S4 were 1.20 m/s and 1.75 m/s, while the values for HBV patients were 1.35 and 1.55 m/s, and the values for Asian hepatitis patients with normal ALT levels were 1.30 and 1.55 m/s. Third, there was no unified standard for measuring liver fibrosis by ARFI, and the cutoff values for grading liver fibrosis differed. All of the above factors may explain the variable results to a certain degree.

Instead of an external mechanical low-frequency vibrator, ARFI uses a regular-sized ultrasound probe and can be applied in patients with the narrow intercostal spaces or ascites. This vibrator is mounted to regular ultrasound, allowing real-time observation of the ROI with guidance by gray-scale sonogram to directly avoid intrahepatic blood vessels and occupational lesions. However, Bota et al. [27] also studied the factors that influence liver fibrosis measurements made with ARFI. The results indicated that obesity, old age, and male sex had adverse effect on the success rate and accuracy of ARFI. In addition, intra-abdominal gas, large arterial pulses, and respiratory movements could interfere with the measurement. Moreover, the ARFI measurement might fail and return an invalid value of "X.XX" when the stiffness of the ROI is too high or too low. With a fixed sampling frame,

the maximal depth of ARFI measurement is 8 cm, confining its measurement range. Owing to the advantages and disadvantages of ARFI mentioned above, the diagnostic standard and process still need to be optimized.

6.2.3 Application of ElastPQ for Grading Liver Fibrosis

ElastPQ is a novel ultrasound elastosonography technique that uses a shear wave-based technology. An ultrasonic radiation force impulse generates shear waves directly in the tissue, and pulse-echo technology is used to measure the shear wave propagation speed. From this value, the vibrating phase of the shear waves of different frequencies can be estimated, and the tissue elasticity coefficient can be calculated. Then, using the tissue elasticity distribution obtained by a mutual correlation elasticity reconstruction algorithm, tissue elasticity is calculated [28]. Using a standard ultrasonic transducer, and the data being added to a two-dimensional ultrasonogram, ElastPQ represents tissue stiffness (kPa) directly on the sonogram. Recently, the iU22 ultrasound diagnosis system with ElastPQ technology developed by Philips has been applied in practice. However, studies on this technology are limited owing to its short appearance. Some researchers have already applied it for the quantification of liver fibrosis grades, and some have used it for differentiating benign or malignant liver tumors. All of the above studies showed its potential in measuring tissue stiffness and quantification of liver fibrosis grades.

Numerous efforts have been made by our department to apply ElastPQ in grading liver fibrosis. We performed ElastPQ on 278 HBV patients undergoing hepatectomy due to liver cancer from 2011 to 2013. The ROI was liver parenchyma more than 2 cm away from the liver tumors, the area of sampling was 15 × 10 mm, and the elasticity value was displayed directly on a two-dimensional sonogram. The surgical samples we used provided us with more representative histological results than did the liver biopsy. Our study indicated a significant positive correlation between ElastPQ values and liver fibrosis grades, with correlation coefficients of 0.704 (95 % CI: 0.639–0.759). For detailed ElastPQ values for different liver fibrosis grades, see Table 6.1. Figures 6.2 and 6.3 illustrate the corresponding sonogram and histological images. Moreover, we analyzed the diagnostic value and accuracy of ElastPQ in diagnosing liver fibrosis grades. Using 5.8 kPa as the cutoff for fibrosis ≥S1, the AUROC was 0.959, and the sensitivity, specificity, and accuracy were 88.4 %, 100 %, and 89.9 %, respectively. The AUROC was 0.943 when using 6.9 kPa to determine liver fibrosis ≥S2, and the corresponding sensitivity, specificity, and accuracy were 81.6 %, 97.4 %, and 84.2 %, respectively. Using 9.1 kPa as cutoff value for fibrosis ≥S3 showed an AUROC of 0.887, a sensitivity of 67.6 %, a specificity of 93.5 %, and an accuracy of 75.5 %. When applying 10.4 kPa for diagnosing S4, the AUROC was 0.855 (sensitivity 62.2 %, specificity 87.4 %, and accuracy 75.9 %). ElastPQ appeared to have a similar diagnostic value for liver cirrhosis compared with other ultrasonic elastography methods based on shear wave technology, such as FibroScan and ARFI. Similarly, this technique showed diagnostic accuracy for no/mild or significant fibrosis (≥S2) and cirrhosis (S4) in chronic HBV patients. Furthermore, we analyzed the influence of necroinflammation degrees and copies of HBV-DNA and ALT on liver stiffness. The results indicated a slight correlation between necroinflammation and liver stiffness ($r = 0.393$), which was in accordance with Ma et al.'s [29] study. Additionally, ElastPQ might overestimate liver fibrosis in patients with elevated ALT levels or high copy numbers of HBV-DNA. Ma et al.'s [29] study of 291 HBV patients noted that S3 and S4 liver stiffness measured by ElastPQ were 8.71 ± 3.14 kPa and 10.87 ± 5.25 kPa, which is significantly lower than those in our study. However, their values for S0-S2 liver fibrosis were similar to ours. These differences may be due to different proportions of liver fibrosis patients in these studies. We included a patient population undergoing surgery with a potentially larger proportion of S3 and S4 fibrosis compared with the patients undergoing liver biopsies in Ma et al.'s study with a potentially smaller proportion of S4 fibrosis.

Moreover, we explored factors that influenced the stiffness measurements of ElastPQ [30]. The results revealed differences between ElastPQ values in different liver segments. The value and consistency of the right lobe of the liver, especially the right anterior inferior segment, were significantly higher than those of the left lobe. The respiratory phase might influence measured liver stiffness. In our study, liver stiffness at the end-expiratory phase was higher than that at the end-inspiratory phase. However, age, direction of the probe, and body mass index (BMI) showed no significant effect on the measured liver stiffness. The influence of different genders on liver stiffness remains controversial. Similar to ARFI, with a fixed sampling frame, the maximal depth of ElastPQ measurements is 8 cm, confining its measurement range. As a result, standardization of the measurement process with ElastPQ is needed.

Table 6.1 Liver stiffness values for different fibrosis stages

Fibrosis stage	Mean (kPa)	Range (kPa)	SD
S0	4.6	3.4–5.8	0.8
S1	5.5	3.4–7.9	1.2
S2	7.5	3.9–11.3	1.8
S3	9.4	5.6–17.8	3.1
S4	13.0	4.8–38.3	5.3

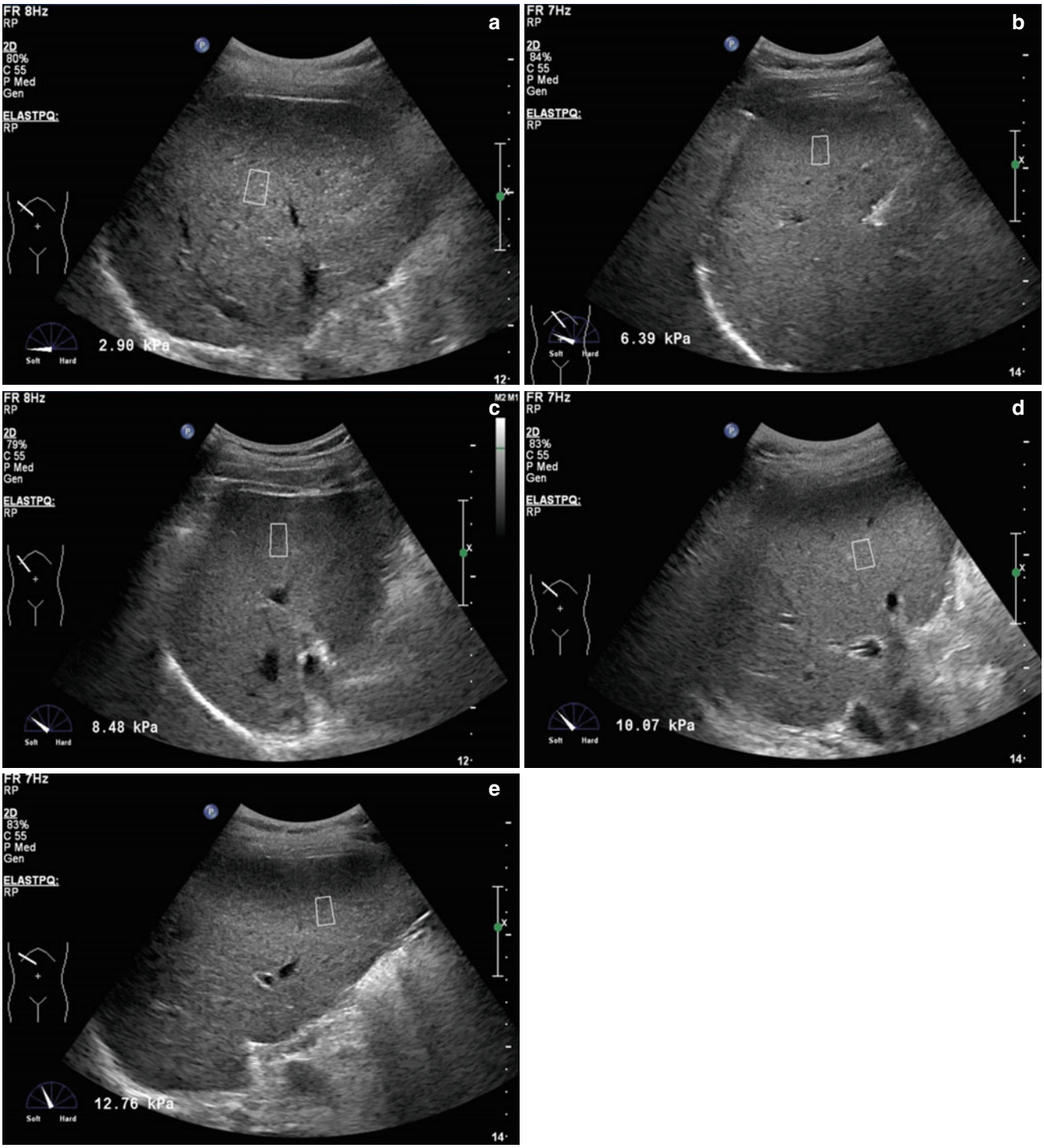

Fig. 6.2 (**a**) ElastPQ sonogram of liver fibrosis S0. (**b**) ElastPQ sonogram of liver fibrosis S1. (**c**) ElastPQ sonogram of liver fibrosis S2. (**d**) ElastPQ sonogram of liver fibrosis S3. (**e**) ElastPQ sonogram of liver fibrosis S4

6.2.4 Application of SSI for Grading Liver Fibrosis

Super-speed acoustic radiation force impulses emitted by medical-frequency ultrasound probe focus consecutively along the acoustic axis at different depths of the tissue, causing simultaneous dislocation of the tissue along the acoustic axis, forming a conical shear wave front is formed, an effect also known as Mach cone effect. Based on this effect, SSI not only improves the propagation efficiency of the shear

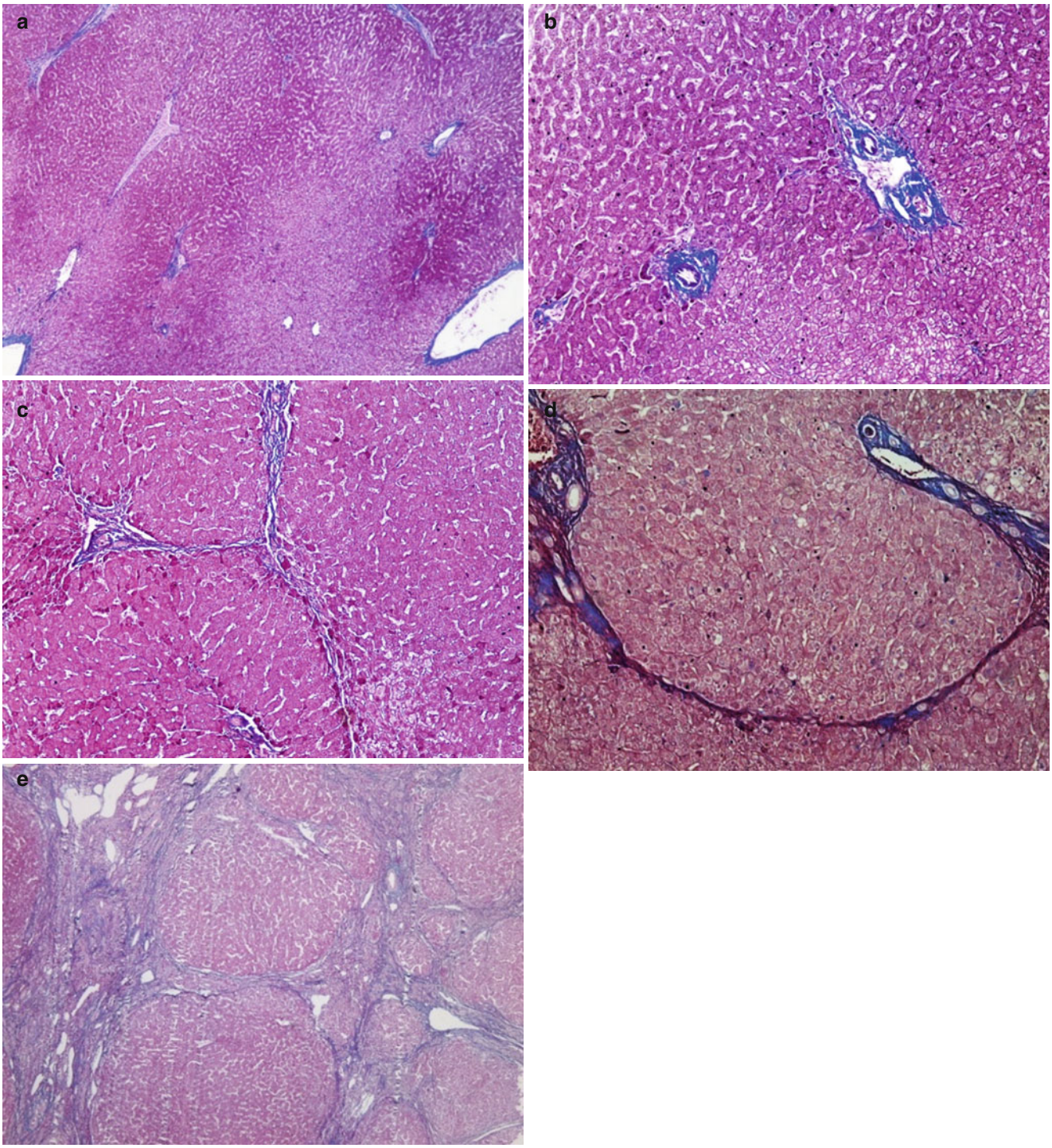

Fig. 6.3 (**a**) Histological image for S0 (Masson staining, 4×). (**b**) Histological image for S1 (Masson staining, 10×). (**c**) Histological image for S2 (Masson staining, 4×). (**d**) Histological image for S3 (Masson staining, 4×). (**e**) Histological image for S4 (Masson staining, 4×)

wave but also avoids adverse bio-effects due to continuous focus on the same site. In addition, adopting a super-speed video mapping technique to trace and detect the real-time propagation velocity of the shear wave and to perform video mapping provides a real-time shear wave elasticity image with ultrahigh time resolution and tissue stiffness values [31, 32]. The SSI technology that is currently used in practice is Aixplorer ShearWave™, a real-time ultrasonic shear wave elastography system developed by the French company SuperSonic Imagine. In ShearWave™ elastography, ultrafast imaging is performed at 20,000 frames/s, which allows for real-time acquisition and tracing of the shear wave. With the

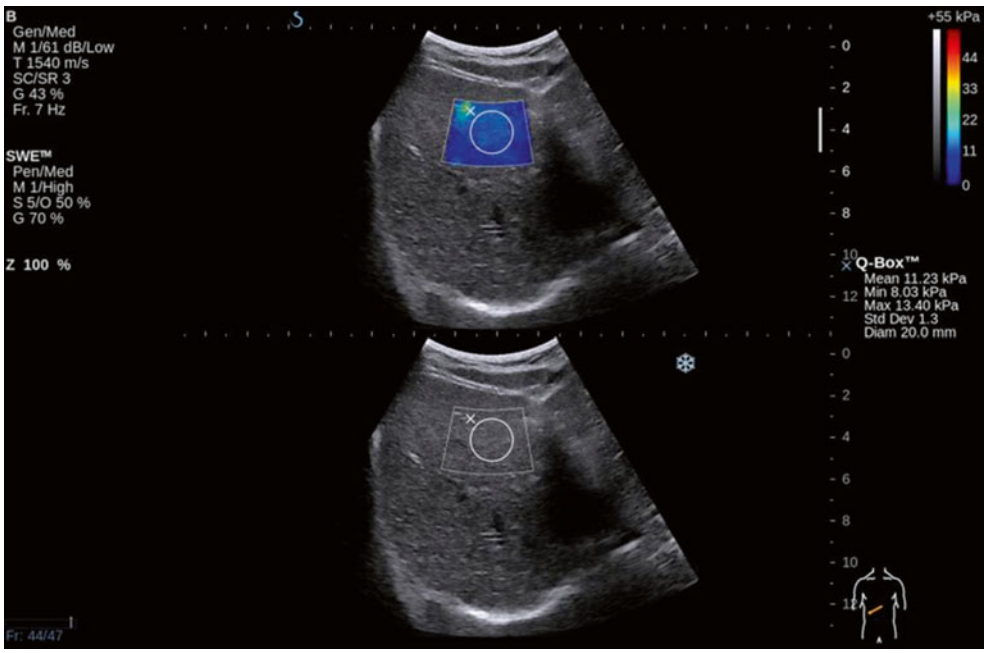

Fig. 6.4 Liver stiffness of S4 measured by SSI

real-time elasticity image of the shear wave, the Young modulus of the tissue is acquired, meaning that the stiffness of the ROI is directly acquired. These data are representing on the elasticity image using a color-coded technique (see Fig. 6.4, expressed as kPa). The SSI value increases with tissue stiffness.

SSI is widely applied in practice and in the noninvasive quantitative evaluation of liver fibrosis in research. Because of the short-time clinical application, studies have shown differences in the diagnostic efficiency of SSI for liver fibrosis; however, the results suggest that it has great value in grading liver fibrosis. Jeong et al. [33] studied SSI on 70 chronic liver disease patients with various causes. The liver stiffness was positively correlated with the liver fibrosis grade, with a correlation coefficient of 0.774. The stiffness values for fibrosis S0-1, S2, S3, and S4 were 6.77 ± 1.72 kPa, 9.98 ± 3.99 kPa, 15.80 ± 7.73 kPa, and 22.09 ± 10.09 kPa, respectively. When defining 8.6 kPa as the cutoff for fibrosis ≥S2, the AUROC was 0.915, the sensitivity was 78.20 %, and the specificity was 93.30 %. When using 10.46 kPa to diagnose fibrosis ≥S3, the AUROC, sensitivity, and specificity were 0.913, 88.60 %, and 80.00 %, respectively. Using 14.00 kPa as the cutoff for fibrosis S4 showed an AUROC of 0.878, a sensitivity of 77.30 %, and a specificity of 85.40 %. In this study, we noted that the diagnostic ability of SSI for S4 was slightly lower than that for ≥S2 and ≥S3, which is inconsistent with several other studies. Jeong et al. attributed this difference to insufficient sample size. A study of SSI applied in 206 HBV patients performed by Zeng et al. [34] indicated that liver stiffness values for S0, S1, S2, S3, and S4 were 5.7 kPa, 6.3 kPa, 8.2 kPa, 11.3 kPa, and 18.1 kPa, respectively. The AUROC values were 0.917, 0.945, and 0.945, respectively, when using 7.2 kPa, 9.1 kPa, and 11.7 kPa for diagnosing cutoffs of ≥S2, ≥S3, and S4. This study showed a high diagnostic value of SSI for diagnosing HBV-related liver fibrosis, especially severe liver fibrosis and cirrhosis. Moreover, a significant correlation existed between liver stiffness and both γ-glutamyltranspeptidase and serum albumin. Ferraioli et al. [35] compared SSI and FibroScan applied on 121 chronic HCV patients. The results showed a positive correlation between liver fibrosis grades and liver stiffness as measured by both SSI and FibroScan, with correlation coefficients of 0.83 and 0.74, respectively. Liver stiffness values for S0-1, S2, S3, and S4 were 6.2 kPa, 7.6 kPa, 10.0 kPa, and 15.6 kPa, respectively. SSI showed better diagnostic ability for fibrosis ≥S2 than did FibroScan (AUROC 0.92 vs. 0.84, respectively). Both SSI and FibroScan showed a similar ability in diagnosing ≥S3 and S4 fibrosis (AUROC 0.96 and 0.98 vs. 0.96 and 0.98, respectively). However, Cassinotto et al. [24] compared SSI, ARFI, and FibroScan for grading liver fibrosis in 349 various types of chronic liver disease patients. The results indicated that SSI had better diagnostic ability for ≥S2 fibrosis than did ARFI, but the diagnostic ability was similar to that of FibroScan. The AUROCs of SSI, ARFI, and FibroScan were 0.88, 0.81, and 0.84, respectively. SSI performed better in diagnosing fibrosis ≥S3 than did ARFI and FibroScan, with AUROC values of 0.93, 0.89, and 0.87, respectively. However, the three techniques showed no difference in differentiating S4, with AUROC values of 0.93, 0.90, and 0.90, respectively. In contrast to the results mentioned above, the study conducted by Deffieux et al. [36] of 120 chronic liver disease patients using SSI and FibroScan showed no difference in diagnostic ability for all liver fibrosis grades.

The diagnostic value of SSI for liver fibrosis grading is widely accepted by clinicians; however, results have varied among studies. These differences may be caused by numerous factors, such as various etiologies, diverse races, different proportions of patients with different grades of liver fibrosis, and various measuring methods. Huang et al. [37] performed a multivariable analysis on SSI for measuring liver stiffness. The results showed differences between liver segments. Similar to our study using ElastPQ, the right anterior inferior segment exhibited the most stable measurement values. Body position might influence SSI results. Liver stiffness measured in the right lateral position was higher than that measured in the supine position, which might be the result of gravity. The depth of the ROI had a significant influence on SSI measurement. A study showed that liver stiffness measured at depths of 3–5 cm below the body surface and 1–2 cm inferior to the liver capsule was the most stable and reliable value [38]. Sampling area, age, and BMI had no remarkable effect on SSI measurement. However, the liver stiffness of men measured by SSI was higher than that of women; whether sex influences liver stiffness remains controversial. Although the application of SSI in practice is still an area of exploration, and the results are susceptible to multiple factors, SSI exhibits potential in noninvasive diagnosis for fibrosis for its stability, reproducibility, massive sampling area, and high safety performance. However, considering the short time that SSI has been used, the lack of both clinical experience and uniform measurement standards, and uncertainty of influencing factors, further research of SSI is required.

6.2.5 Application of RTE for Grading Liver Fibrosis

RTE indirectly measures tissue strain. A longitudinal or axial displacement occurs after an external force or alternating vibration compresses the tissue. After the collection of reflex-echo signals before and after compression, this displacement is measured using a combined autocorrelation method. With RTE, the relative tissue strain is displayed on conventional B-mode images in gray-scale or color-coded imaging. Areas with higher strain (relatively hard tissue) and those with lower strain (relatively soft tissue) in the ROI are displayed in red and blue, and tissue of medium stiffness is displayed in green. Studies have shown its significant value in diagnosing superficial organs lesions, such as mammary gland diseases, due to its manual compression approach [39]. Some studies [40, 41] reported RTE's potential in quantitative assessment for liver fibrosis; however, the results were rather subjective because they were semiquantitative and based on elasticity score. The new generation of RTE tissue dispersion quantitative technology developed by the Japanese company Hitachi measures tissue displacement caused by the compression of the abdominal cardiovascular beat, which not only enhances the sensitivity of signal collecting but also makes liver stiffness measurement possible. This technique is loaded on the Hitachi-HIVISION Preirus color Doppler ultrasound, and 11 feature values for assessing liver fibrosis are obtained by histogram analysis of the ROI using diffuse quantitative analyze software. These values include the mean relative strain values (MEAN), the standard deviation of relative strain values (SD), the percentage of low strain area (percentage of blue color area, %AREA), the complexity of the low strain area (COMP), kurtosis (KURT) and skewness (SKEW) of the histogram, the contrast ratio (CONT), the homogeneity (entropy, or ENT), the complexity (inverse differential moment, or IDM), the uniformity (angular second moment, or ASM) of texture, and the correlation ratio (CORR). The liver fibrosis index (LFI) is calculated based on multiple regression analysis using the above 11 parameters as variables. LFI and the 11 parameters are displayed directly on a two-dimensional ultrasound elastogram, avoiding subjective bias. Although researchers have used different parameters obtained by RTE for the quantitative assessment of liver fibrosis (most using LFI, with only a few using the 11 feature values), the results all suggested that RTE can quantitatively assess liver fibrosis.

We performed RTE on 112 chronic HBV patients, and the LFIs for liver fibrosis grades S0, S1, S2, S3, and S4 were 2.36 ± 0.46, 2.38 ± 0.45, 2.84 ± 0.54, 3.16 ± 0.59, and 3.69 ± 0.55, respectively. When using 2.83 and 3.69 as cutoffs for $\geq$S2 and S4, the AUROC values were 0.78 and 0.80, respectively. RTE elasticity images for each grade of liver fibrosis are shown in Fig. 6.5. A multicenter study on 747 HBV patients performed by Wu et al. [42] indicated a positive correlation between LFI and fibrosis grades. Defining 2.099 as cutoff for $\geq$S2 showed an AUROC of 0.858, a sensitivity of 77.0 %, a specificity of 76.8 %, and an accuracy of 76.9 %. Using 2.511 to differentiate S4 fibrosis gave an AUROC of 0.862, a sensitivity of 74.3 %, a specificity of 79.8 %, and an accuracy of 79.3 %. The results were significantly different from our study, which may be due to the different sample numbers and distributions of each fibrosis grade. Morishita et al. [43] used the ratio of subcutaneous adipose tissue strain and the liver parenchyma strain for liver fibrosis assessment; the results showed a significant correlation between this ratio and fibrosis grades, with a correlation coefficient of 0.797. In addition, the AUC, sensitivity, and specificity for diagnosing liver fibrosis were 0.913, 96.0, and 88.9 %, which are significantly better than those for serum markers. Wang et al. [44] studied the application of RTE for HBV-related fibrosis assessment and concluded that the elasticity index was significantly correlated to liver fibrosis grades (correlation coefficient of 0.81). Zeng et al. [45] indicated that among all 11 feature values, %AREA was the most critical indicator for

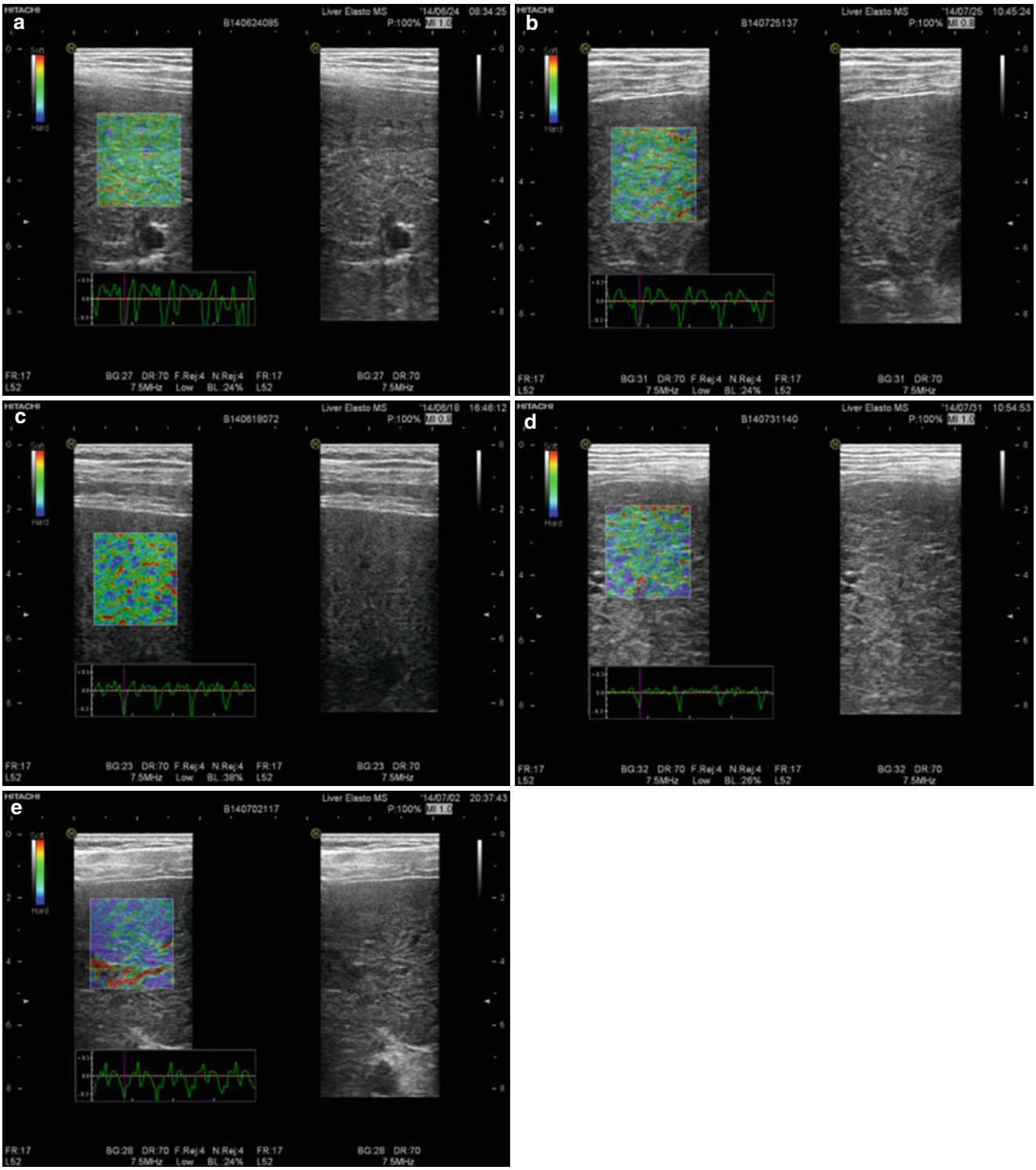

Fig. 6.5 (**a**) RTE elasticity image for S0. (**b**) RTE elasticity image for S1. (**c**) RTE elasticity image for S2. (**d**) RTE elasticity image for S3. (**e**) RTE elasticity image for S4

assessing fibrosis, with a correlation coefficient of 15.467. Morikawa et al. [46] reported that the MEAN, SD, %AREA, and COMP had greater diagnostic ability for fibrosis than the other feature parameters, with AUC values of 0.91, 0.84, 0.91, and 0.93, respectively. In general, RTE can provide vital information for liver fibrosis assessment.

The ROI that RTE can analyze is bigger than those of ARFI, FibroScan, and ElastPQ, and its adjustable ROI size

allows for more tissue information. In addition, 11 feature parameters are obtained through histogram analysis, and auto-analysis of indexes for liver fibrosis grades, such as the elasticity index or the ratio of subcutaneous adipose tissue strain to liver parenchyma strain, is performed. These indexes somewhat directly reflect liver stiffness and provide more accurate and objective data. However, RTE for ROI can be affected by large vascular pulsation and gastrointestinal movements. In our study, the left lobe of the liver was more likely to be influenced by large vascular pulsation, thus having a lower success rate and stability than did the right lobe. RTE's performance was susceptible to a variety of factors, such as respiratory movements, obesity, and ascites. However, the influence of age and sex on RTE measurement remains controversial.

6.3 Prospects

As a novel imaging technique, ultrasound elastography can directly or indirectly reflect tissue elasticity, a biomechanical property of the tissue. This technique not only enriches diagnostic information of conventional ultrasound but also functions as a brand new real-time effective tool for the noninvasive assessment of liver fibrosis. With evolving advances in elastography, liver stiffness measurements can be performed simultaneously with routine ultrasound examination, providing an accurate assessment of liver fibrosis and integrating conventional ultrasound examination with the real-time assessment of liver fibrosis.

However, differences in cases of liver fibrosis with different causes and disease states are likely to affect the elasticity measurement values. Additionally, cutoff values for liver fibrosis are different due to variable causes. Moreover, units of elasticity and cutoff values for diagnosis also differ when using different elastography principles. Therefore, in clinical practice, reasonable elastography technique and diagnostic standard should be carefully selected depending on the actual situation. The application of elastography is currently influenced by a variety of factors, such as measuring conditions and examiner proficiency. As a result, the measuring process of the various types of elastography must be standardized. Moreover, further studies of elastography in clinical practice, especially cooperative research among multiple centers with large sample sizes and various disease entities, are necessary to provide more evidence for the future clinical application of ultrasound elastography.

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Techniques of Vascular Inflow Occlusion and Liver Parenchymal Transection

7

L.N. Yan and Zhenni Liu

Liver resection has experienced more than 100 years of development as the primary treatment for HCC. To the end of the nineteenth century, the animal experiment research had shown that liver parenchyma incision is feasible. When the liver had been cut off three quarters, the animal was still alive. In 1888, Langenbuch, a German surgeon, successfully resected a tumor on the edge of the liver in a woman patient. Therefore, he was regarded as the first person who succeeded in resecting liver tumors. William Keen (1899) was considered as the first American surgeon in liver resection; he reported three successful surgical cases. However, the perioperative mortality (70–90 %) of liver resection was very high during that period [1]. One of the main reasons was that the blood loss in the surgery could not be effectively controlled. The control of hemorrhage during liver resection is very important for HCC patients, especially with cirrhosis, because the amount of blood loss and transfusion in the operation have been shown to correlate with morbidity, mortality, and long-term survival after operation [2–4].

The Pringle maneuver, a technique of transient hepatic vascular inflow occlusion, was described by Pringle a British surgeon in 1908 [5]. It could reduce blood loss in liver surgery by total clamping the hepatoduodenal ligament. The validity of it in reducing hemorrhage in liver resection had been proved by Man et al. [6]. However, the Pringle maneuver can induce ischemia-reperfusion injury to the rest of the liver [7, 8]. In addition, some surgeons even claimed that the Pringle maneuver should be avoided in partial hepatectomy, because of its induction of tumor recurrence and worse prognosis [9, 10].

To avoid ischemia-reperfusion injury to the remnant liver, hemihepatic vascular inflow occlusion has been suggested by Makuuchi et al. in 1987 [11]. This technique can only occlude the blood supply of the hemi-liver where liver resection is carried out; the remnant liver has normal blood inflow. Therefore, there is no ischemia-reperfusion injury to the rest of the liver and it can maintain the stability of hemodynamics.

However, for hemihepatic vascular inflow occlusion, a special technique called lowering the liver plate by lifting up the segment 4b of the liver and incising Glisson's sheath at its base is necessary, and the hepatic portal structure would be exposed clearly. This technique had a potential risk to injure the bile ducts and vessels.

In our center, a new technique called "simple hemi-occlusion" was created by Yan [12, 13] in 1994 and now is routinely used in our center.

Certainly, there are other techniques of vascular occlusion, but the Pringle maneuver and hemihepatic vascular occlusion are most commonly used in the clinical setting. However, which method of vascular occlusion should be chosen during liver resection is still a controversial issue.

When cavitron ultrasonic surgical aspirator (CUSA) or water jet was used for liver parenchymal transection, it was always combined with no vascular occlusion or hemi-occlusion, because much more time was needed for major resection. But when the "hooking with ligation" was used [12, 13] for parenchymal transection, a short time was needed (always less than 30 min), so we always used total hepatic occlusion or sometimes hemi-occlusion.

7.1 Pringle Maneuver

A rubber catheter bypassed the whole hepatoduodenal ligament. Tightening or loosening the catheter will result in blocking or without blocking the vascular inflow to the liver.

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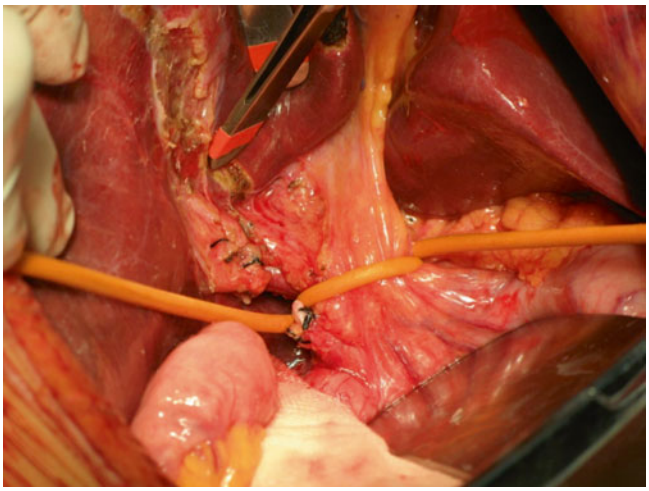


Fig. 7.1 Pringle maneuver

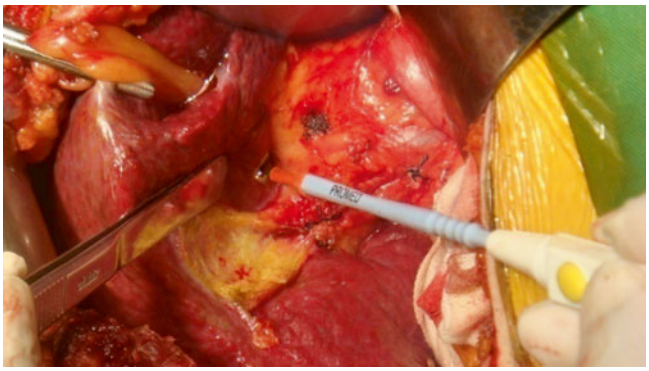


Fig. 7.2 On the visceral envelope overlying the confluence, a small hole was made using a sharp blade

In this method, intermittent vascular occlusion was applied (Fig. 7.1). The circulation of blocking and without blocking vascular inflow was 15/5 min.

"Simple hemi-occlusion" was created by Yan [12, 13] in 1994 and now is routinely used in our center.

The general steps are as described below:

We did not dissect hepatoduodenal ligament. Following the direction of the common hepatic duct, the confluence of the right and left portal pedicles would be found. After that an incision would be drawn on the liver capsule overlying the confluence using electrocautery (Fig. 7.2).

Then we inserted a right-angle pliers in the incision to gently mobilize the liver substance outside Glisson's sheath. The right-angle pliers should mobilize in the liver parenchyma toward the liver caudate lobe and there is no resistance (Fig. 7.3).

Finally the sharp end of the right-angle pliers would come out from the junction of portal vein and liver caudate lobe (Fig. 7.4).

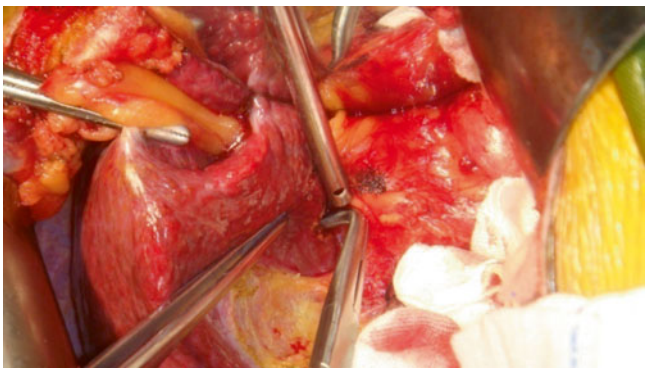


Fig. 7.3 A right-angle forceps was inserted to gently mobilize the liver parenchyma outside Glisson's sheath

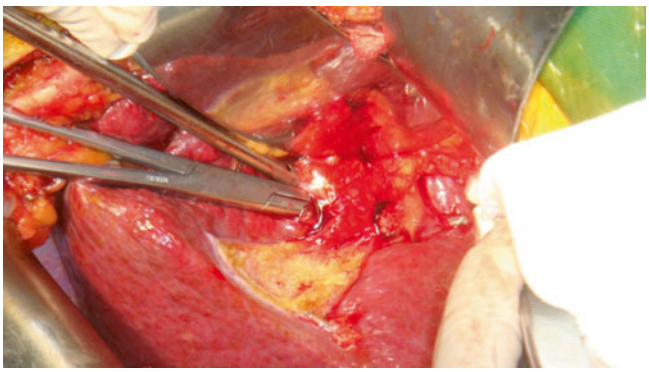


Fig. 7.4 The right-angle forceps should mobilize in the liver parenchyma toward the caudate lobe

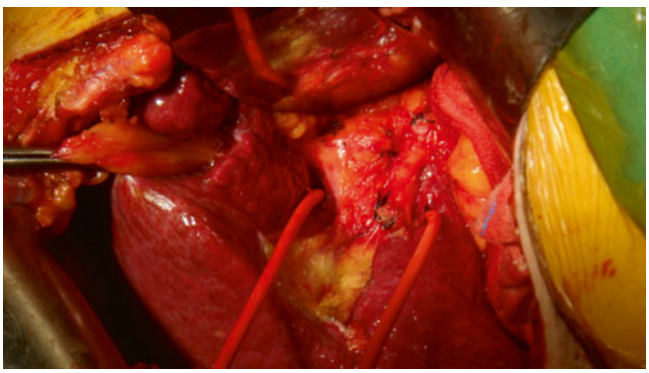


Fig. 7.5 A catheter was introduced

In the meanwhile, a catheter was then wrapped around the right side branch of the portal pedicle through the incision (Fig. 7.5).

Tightening the catheter, the right hemihepatic vascular inflow would be occluded (Fig. 7.6) and the color in the hepatic surface is changed (Fig. 7.7).

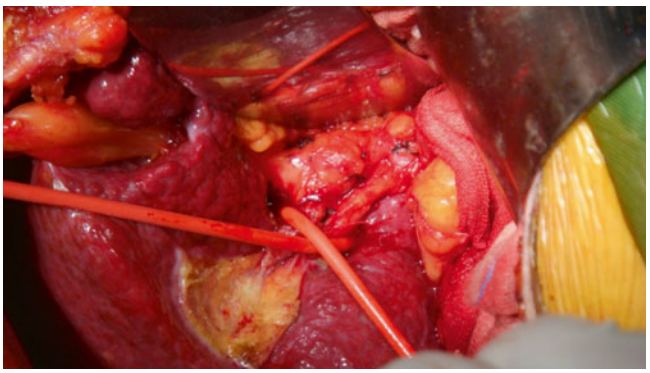


Fig. 7.6 Tightening the catheter

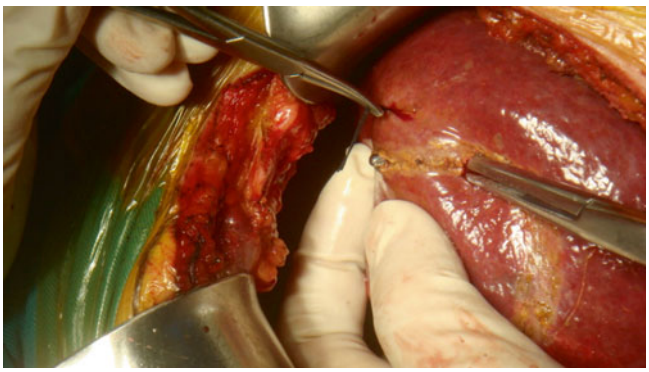


Fig. 7.9 Right-angle forceps hooking the hepatic tissue

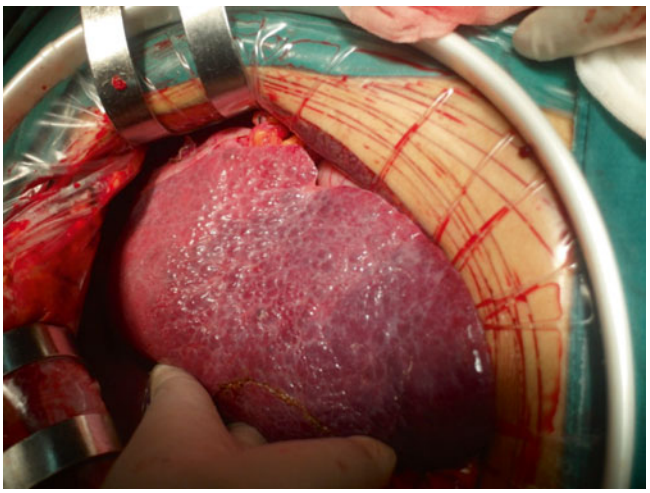


Fig. 7.7 The color in hepatic surface is changed

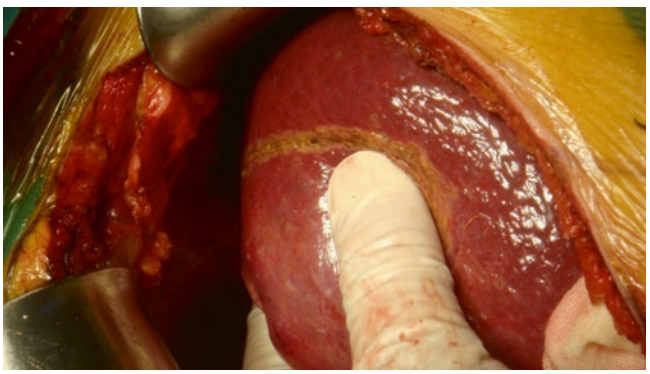
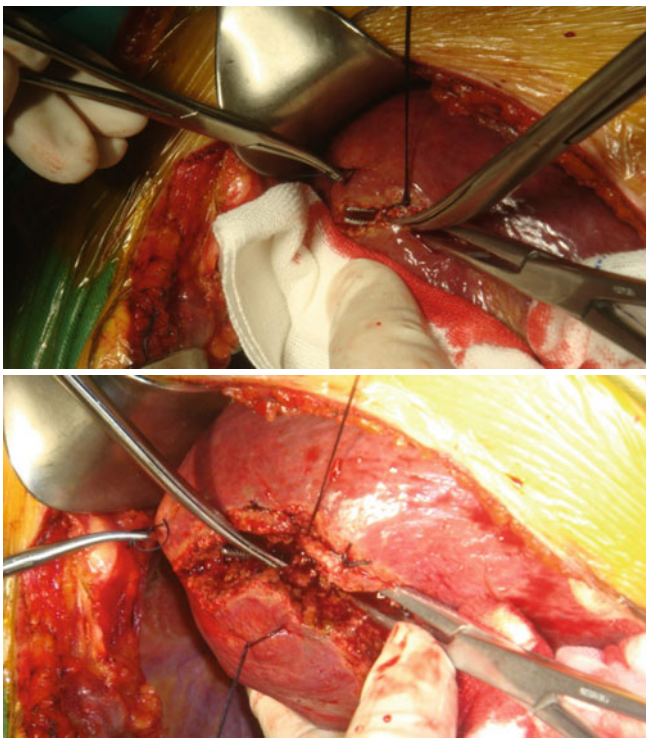


Fig. 7.8 The resection line was marked by electrocautery on the hepatic surface



Figs. 7.10 and 7.11 Cannular structures were ligated and cut

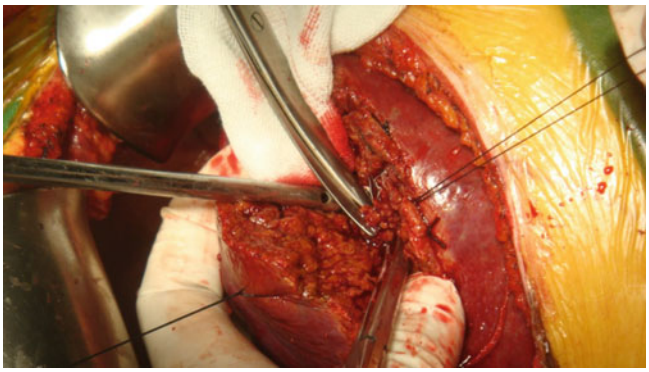
When put on one side of the catheter through the foramen of Winslow and then come out from the ligamentum hepatogastricum, tightening the catheter would result in occluding the left hemihepatic vascular inflow. In this method, intermittent vascular occlusion was not applied (Fig. 7.7).

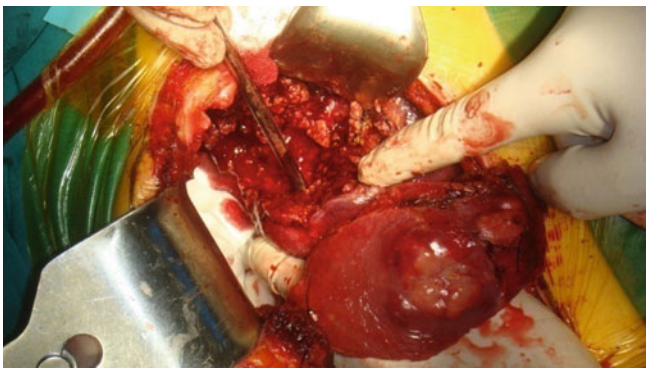
"Hooking with ligation" is a simple and effective technique for liver resection created by Yan in 1994 [12, 13] and now is routing used in our center.

The surgical procedure is described below:

The resection line was marked by electrocautery on the hepatic surface before hepatectomy (Fig. 7.8).

The liver was dissected by right-angle forceps hooking the hepatic tissue, and cannular structures were ligated one by one (Figs. 7.9, 7.10, 7.11, 7.12, and 7.13).





Figs. 7.12 and 7.13 Right-angle forceps hooking the hepatic tissue forward one by one

If the main branches of hepatic vessels came forth, the rupture should be continuously sutured with 4-0 or 5-0 prolene. After the occlusion of hemihepatic vascular inflow was relaxed, the hepatic transaction was sutured and ligated for hemostasis. Drains were usually left in the peritoneal cavity.

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Hepatic Parenchyma Transection Using Modern Instruments

8

Xiao Xu

8.1 Introduction

The parenchymal transection is considered the critical step during hepatectomy, and has the direct impact on excessive bleeding as well as the postoperative complications [1]. The history of development of surgical techniques of liver resection is largely a struggle against massive bleeding and the consequent blurred operative visual field. Thus, the hepatectomy was limited until the 20th century. With the increasing knowledge of the liver anatomy and surgical strategies, as well as the development of various transection instruments, hepatectomy has developed into the current standard procedure. Nowadays, hemorrhage is no longer the major concern after hepatectomy. A novel strategy, "precise hepatectomy," originating from minimally invasive surgery, has been advocated to minimize insult on livers, maximally preserve remnant hepatic function, and as much as possible improve the outcome of hepatectomy.

In 1974, Lin [2] firstly introduced the clamp-crush technique in hepatectomy, which is a simplification of their earlier reported finger fracture technique [3]. The clamp-crush technique subsequently gained wide acceptance as a standard method of parenchymal transection. Since then, device development has been of particular interest with the development of various instruments aimed to improve operative blood loss, operative speed, and resection margins. The following conventional or low-tech methods for parenchymal dissection, which do not require special instruments, have been proposed to reduce blood loss during liver resection: the finger fracture technique, the crush clamp method, or simply blunt dissection. Several new techniques, such as dissection with a cavitron ultrasonic surgical aspirator, water jet dissection (also known as hydrojet), ultrasound scalpel, radiofrequency devices [4], or vascular stapling devices [5], have also been established. These new instruments not only contribute to the precise resection but also effectively control blood loss and reduce liver damage without hepatic vascular occlusion technology [6]. Due to improvements in technology, morbidity and mortality rates in hepatectomy have decreased dramatically over the last two decades [7]. Perioperative mortality rates are reported with less than 5 % [8], and morbidity rates vary between 20 and 40 % [9, 10]. The selection of the resection technique and device mainly depends on the extent of the resection and also on the liver disease, costs, surgeon experiences, and preferences. This chapter discusses the advantages and drawbacks of instructions for the surgeon to choose during parenchymal transection according to actual individuals.

8.2 Parenchyma Structure and Technology Basis

Liver macroscopic and microscopic anatomy serves as the important basis which is put into the practice of liver transection. The former, such as Couinaud's hepatic segment classification based upon the portal venous system [11] and 3D imaging of liver structures [12], laid the foundation for the anatomic hepatectomy. Various anatomic variations should be handled with flexibility for liver surgeons. The latter refers to the liver parenchyma structure and is the base of new instrument development. Liver parenchyma is a highly vascular tissue containing hepatocytes and non-parenchymal cells suspended in a collagen-based extracellular matrix through which runs a network of vessels and biliary structures. This structure allows the development of new instruments and devices able to selectively divide parenchyma from duct and vessel systems according to their different mechanical resistances (in which hepatocytes contain less collagen and elastin than the duct and vessel, thus offering less resistance to crush-

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ing during parenchymal division). The bile ducts are more resistant in their structure compared to arteries, portal vein branches, and hepatic veins. Depending on the structure of parenchyma, various instruments including clamp-crush technique, ultrasound, microwaves, and staplers have been developed to dissect the parenchyma with the vascular tissues left ligatured using titanium clip or sealed by electrocautery.

Precise hepatectomy is proposed under the high precision demand, for comprehensive optimization of a series of scientific theory, traditional surgical techniques and proper employment of surgical instruments in the hepatic surgery. The fundamental principles of precise hepatectomy are: (1) accurate preoperative evaluation of lesion location and the individual variation of vessel branches by comprehensive application of modern technologies; (2) maximal protection of liver structure and remnant functional volume; (3) minimal intraoperative bleeding and invasion and best rehabilitation.

8.3 Preoperative Virtual Hepatectomy Simulation and Intraoperative Real-Time Navigation in Precise Hepatectomy

Three-dimensional (3D) simulation softwares can construct 3D images from the enormous imaging datasets of CT and MRI, and represent the complex architecture of intrahepatic vessels and allow the evaluation of the volume and the territory supplied by any selected vessel at any angles and in different direction [13]. Take of these advantages, we can create virtual hepatectomy and display the different segments with different colors, providing critical preoperative proposal for surgoens. Intraoperative real-time navigation can present the real-time motion and deformation of the liver, the inferior vena cava, the intrahepatic vessels, and lesion locations [14]. Additionally, the tracer (eg. indigo carmine dye) can also be used to identify the demarcation line inside the liver for intropeative assistance [15]. These methods enable the surgoen to depict the intrahepatic resectional plane, injury to the hepatic vein and Glissonean branch on the preserved side is readily avoided [16]. With the development of modern virtual hepatectomy simulation and intraoperative real-time navigation technologies, the precise hepatectomy for liver functional volume protection and anatomical resection can be perfectly accomplished.

8.4 The Techniques of Parenchyma Transection

8.4.1 Clamp-Crush Technique

In 1958, finger fracture, first introduced by Lin, refers to insertion of the fingers to effectively compress the liver parenchyma and release allowing better identification of vascular structures during transection to be ligated. The finger fracture was demonstrated to improve operative blood loss and mortality [3, 17]. However, this technique, even in combination with pedicle clamping, could not completely prevent excessive blood loss, which still remained the obstacle of hepatic surgery. The finger fracture technique was not selective for the tiny vessels responsible of the weak but continuous bleeding during hepatic division. Besides, the finger fracture can cause damage to the liver parenchyma. Therefore, the adoption of the finger fracture method was also slow over the world.

In 1974, Lin further simplified the finger fracture technique to use the instruments instead of fingers to compress liver parenchyma along the transection line during the crush and release phase, called the clamp-crush technique. In his retrospective analysis, Lin demonstrated the clamp crush allowed a more selective hemostasis, further reducing blood loss [2]. However, in the only one study, Smyrniotis et al. [18] found no significant difference in blood loss or transfusion requirement as well as morbidity or operative time when using the clamp-crush technique compared to sharp transection. Actually, according to the results of the present RCTs and meta-analysis, none of the current devices provided a marked benefit with regard to patients' outcome, blood loss, duration of surgery, and hospital stay compared with the clamp-crush technique [19, 20]. This method also enables surgeons to perform hepatic parenchymal transection without vascular inflow occlusion. Besides, application of the clamp-crush technique is associated with little cost for maintenance and disposal of material; the cost-effective advantage of the clamp-crush technique is obvious. The clamp crush remains the reference technique for liver parenchyma transection. Nowadays the clamp-crush technique is still one of the routine techniques of liver surgeons. However, in certain cases, such as living donor and complex central liver resections, more accurate tools (e.g., cavitron ultrasonic surgical aspirator) might be better.

8.4.2 Cavitron Ultrasonic Surgical Aspirator

In the 1980s, the cavitron ultrasonic surgical aspirator (CUSA) was introduced for liver transection. It allows liver parenchymal fragmentation in diameter of about 1–2 mm by ultrasonic energy and aspiration (Fig. 8.1). The blood vessels and bile structures are exposed and can be subsequently clipped or ligated. Inflow occlusion (anatomic vascular occlusion or Pringle maneuver) has to be applied occasionally, only in the presence of significant hemorrhage that prevents selective coagulation or ligation of smaller structures. The CUSA is a popular technique and preferred for liver parenchymal transection by nearly half of the surgeons in UK national survey in 2013 [21]. Despite the absence of enough evidences to support that CUSA is the best technique for liver

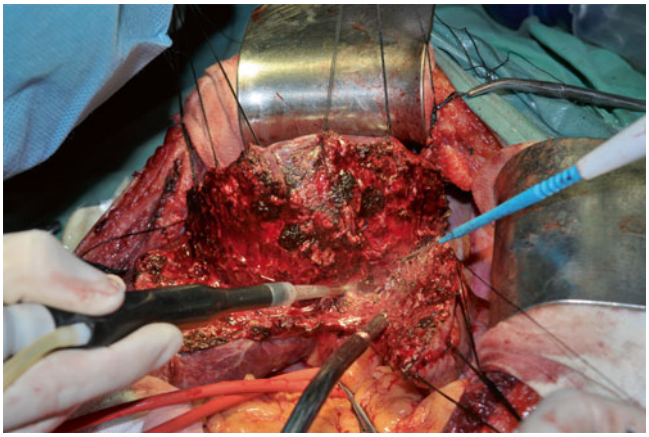

Fig. 8.1 Liver parenchyma using cavitron ultrasonic surgical aspirator (CUSA). The liver parenchyma is fragmented by ultrasonic energy and simultaneously aspirated, leaving the vascular and ductal structures to be ligated or sealed by electrocautery

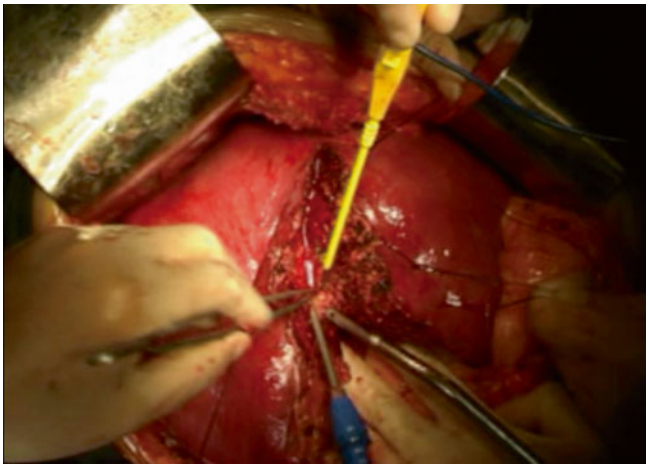

Fig. 8.2 Transection of the liver parenchyma with water jet dissector to fragment the liver parenchyma tissue and leave the vascular and ductal structures for subsequent treatment

transection, the CUSA has for many years been accepted as the standard technology for dividing the parenchyma. Therefore, the CUSA is generally thought to allow the hepatic surgeon to complete and master difficult, meticulous dissections, particularly along the hepatic pedicles and major vessels [22]. Negative aspects of the CUSA are that it is time consuming and sometimes difficult to master.

8.4.3 The Water Jet Dissectors

In the 1980s, the water jet (hydrojet) dissectors appeared for liver resection. The technique was first reported to be applied in 45 lobectomies in dogs and in 4 liver resections in humans [23]. The water jet dissector employs a pressurized jet of water to fragment the liver parenchyma tissue and leave the vascular and ductal structures visible and easily controlled during dissection (Fig. 8.2). Rau and colleagues refined this technique in in vitro and in vivo trials and introduced it into clinical routine in liver surgery [24]. Rau et al. found that a pressure of 30–40 bar and a nozzle diameter of 0.1 mm are very effective to dissect normal liver tissue, and the pressure needed for dissection is 10 bar higher in case of cirrhotic liver parenchyma. However, one disadvantage of water jet and CUSA in liver transection is the long transection time because of the need for ligation or clipping of individual vessels. There are also concerns of increased risk of venous air embolism with water jet technique, although this appears to be a clinically rare problem [25, 26]. In the practice, the water jet should be used in the cirrhotic liver with more experienced, a higher jet pressure is needed to cut the fibrotic hepatic parenchyma. The higher pressure leads to more vessel injuries without coagulation function, especially of the hepatic veins, which corresponds to a higher blood loss. Although the new water jet is added with electoral cautery for hemostasis, it does not work simultaneously.

8.4.4 Radiofrequency (RF)-Assisted Devices

In the 2000s, the RF-assisted device has been used for hepatic parenchyma transection by creating thermal coagulative necrosis along the transection plane, followed by transection of the coagulated liver using a simple scalpel [27, 28]. This method used an RF needle originally designed for ablation of liver tumors, rather than for liver transection [29], and has been reported to be a useful technique for hepatic resection. This early RF-assisted device is monopolar probe. However, this technique was found to be time consuming, produced uncontrolled amount of energy and excessive amount of dead tissue, and also carried the risk of skin burns from the grounding pad [30].

To address these problems, Habib's group designed and developed a bipolar RF device, the Habib 4X [31]. The probes are introduced into the liver along the transection plane. The generator is programmed to produce thermal coagulation. This allows a small, less than 10 mm, margin of coagulated liver parenchyma to remain behind ensuring sealed vessels and bile ducts. The probes are introduced again adjacent to the last coagulated area, in a serial fashion, until the area to be transected is ablated. The surgeon can either apply energy to the whole resection margin and then cut or apply energy to a partial section and then cut that section and repeat it (Fig. 8.3). RF-assisted liver resection has been shown to be effective in reducing intraoperative blood loss [31–34]. Moreover, RF-assisted liver resection potentially increases the margin of clearance, thus providing an oncological advantage [35]. However, this technique has the limitation of potential damage to the major intrahepatic bile duct or vessels because there is a risk of the needle being inserted into or near a major intrahepatic segmental bile duct or vessel. Thus its application close to the hilum and the inferior vena cava requires experience and dissection of the hepatic hilum and the hepatic veins before applying this

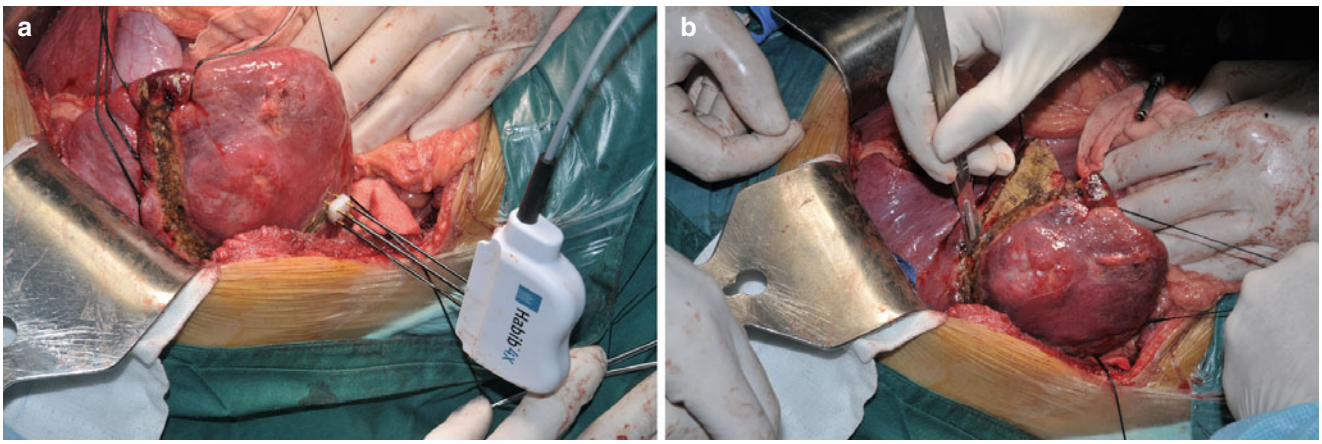

Fig. 8.3 Liver resection with bipolar radiofrequency device: Habib 4X. The probe is introduced into the transection line to cause the coagulative necrosis (**a**), and then cut that section (**b**)

device close to these structures. Left lateral lobectomy needs exposure of biliary duct before application of this device. Besides, the amount of tissue necrosis in the remnant liver is substantial, especially when the transection area is large. This is a major concern when patients with cirrhosis and limited liver function reserve require major hepatic resection [35]. In addition, some researchers reported that RF-assisted liver resection caused a higher rate of both bile leak and abdominal abscess formation and needed a longer operation time compared with clamp crush [36].

8.4.5 Harmonic Scalpel

Harmonic scalpel, firstly introduced in the 1990s, is an ultrasonic surgical device that simultaneously cuts and coagulates. During liver transection, this technology uses ultrasonically activated shears to seal small vessels between the vibrating blades (Fig. 8.4). The blade's longitudinal vibration can dissect liver parenchyma easily, creating heat and thereby denaturing protein to form coagulum. Vessels up to 2–3 mm in diameter are coagulated on contact with the vibrating blade. The tissue-cutting effect derives from a saw mechanism in the direction of the vibrating blade [37]. Additionally, the temperature of the harmonic scalpel is less than 80 °C when dissecting, far lower than that of the electrome (150 °C) and thus far less damage to the surrounding tissues. Precise dissection around the important tissues could be performed by harmonic scalpel.

But it is reported that harmonic scalpel was associated with a significantly increased rate of postoperative bile leakage, raising the concern that harmonic scalpel may not be effective in sealing bile ducts [38]. This remains to be proven by a randomized trial, which is not available in the literature yet. The instrument may also be limited to dissect the liver parenchyma around the main trunk of hepatic veins, since it is difficult to achieve sufficient control of bleeding from large vessels using the harmonic scalpel alone [39].

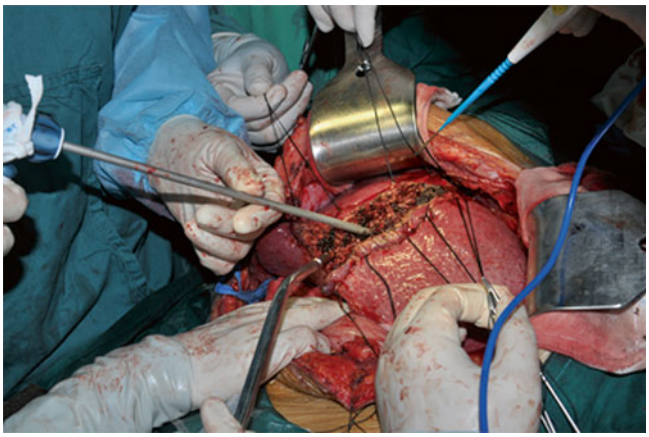

Fig. 8.4 Use of harmonic scalpel in open liver resection, the liver parenchyma is coagulated and divided by the coagulating shears

Although the benefit of the use of harmonic scalpel in open liver resection remains uncertain, harmonic scalpel with the longer arm is commonly used in laparoscopic liver resection and could achieve excellent results, especially for resection of peripheral lesions. The harmonic scalpel may also be useful in transection of cirrhotic liver, for which the clamp crush and water jet may not be very effective [37].

8.4.6 The LigaSure Vessel Sealing System

The LigaSure vessel sealing system (LVSS) was introduced into clinical practice for liver resection in the 2000s and developed for transection and hemostasis, rather than a standard hemostasis technique [40, 41]. Its wide use in hemorrhoidectomies, neck operations, and pulmonary resections has been well reported [42–44]. The device uses compres-

sion pressure and powerful bipolar radiofrequency energy; it causes shrinkage of collagen and elastin between opposing walls of small- and medium-sized blood vessels as well as bile vessels. It can seal effectively and create a permanent seal of arteries up to 7 mm and veins up to 12 mm in a wide variety of clinical applications [45]. It is more efficient than ultrasonic shears for hepatic resection in a porcine model [46].

The LVSS can be used alone for liver transection or in combination with clamp crushing to seal vessels [47]. The use of LVSS improves surgical results via reducing blood loss and transfusion and postoperative complications such as bile leakage and intra-abdominal abscess [45, 48–50]. Similar to the harmonic scalpel, LVSS is a useful instrument for liver transection in the setting of laparoscopic resection of peripheral liver lesions. In one study, LVSS is shown to be effective for liver transection in normal or near-normal liver but to fail to achieve hemostasis in three patients with cirrhotic liver [51]. Nevertheless, the usefulness of LVSS has been highlighted.

8.4.7 Vascular Stapling Devices

Vascular stapling devices have been suggested as alternative instruments for parenchymal transection [52, 53]. Stapler hepatectomy in patients with a diseased liver may, moreover, be supported by the ability to perform resections without routine use of inflow occlusion. The technique is simple and easy to learn and master. Advantages of the stapler technique include a fast transection with potentially reduced intraoperative hemorrhage and postoperative bile leakage due to a highly standardized closure of vascular and biliary structures. Another point that must be taken into account is that dividing the portal branches and the hepatic vein using the stapler is already a central part of many hepatic procedures. The use of endoscopic vascular staplers is a feasible, safe, attractive approach for dividing liver parenchyma during routine hepatic surgery. The results are comparable to those obtained using the CUSA without additional cost. However, the use of a stapler for transection of the liver parenchyma may be applicable in minor wedge resection or left lateral segmentectomy when the liver tissue is not too bulky [37].

8.5 Comparison of Different Liver Transection Techniques

Liver resection comes along with risks, and the rate of complications remains high. Therefore, the need to reduce such complications has led to the development of various innovative methods of liver resection. During the past decade there has been a significant increase in the number of liver resections and various new device applications [54]. However, sufficient evidence has still not been accumulated to establish the most effective method, and liver surgeons still select the method of liver transection according to their own preferences.

8.5.1 Modern Instructions Versus Clamp Crush in Liver Transection

Clamp crush has been generally considered to be the standard method for liver parenchymal transection over the past decades [55]. Even in the well-equipped center, the liver surgeons should have this basic ability. Of four meta-analyses comparing the technology-assisted versus clamp-crush liver resection, the results are shown in Table 8.1. The latest outcomes by Alexiou including all RCTs or non-RCTs may be relatively best evidenced. According to Table 8.1, the current evidence-based medicine demonstrates that: of the alternative methods used in liver resection (LVSS, CUSA, hydrojet, harmonic scalpel, and RFDS), only LVSS appeared to offer significant benefit over standard clamp crush regarding blood loss, postoperative bile leak, and hospital stay. Clamp crush is quicker than CUSA, hydrojet, and RFDS and cheaper than the other methods. RFDS could reduce the blood loss but is associated with a higher rate of intra-abdominal abscess than the clamp-crush method. Nevertheless, further well-designed trials are required to warranty the usefulness of LVSS and RFDS. LVSS has been successfully used in many surgical subspecialties [43] but has only recently been introduced in liver surgery, and the experience of most surgeons is rather limited. Thus, they may be reluctant to change their standard practice.

The stapler technique is the relative novel modality used in liver resection. Thus far, there is only one RCT for the stapler technique versus clamp crush [19]. A total of 130 patients were enrolled in this study; there was no difference between groups in total intraoperative blood loss. But blood loss during parenchymal transection was significantly lower in the stapler transection group that is due to the shorter of parenchymal transection time in the stapler group. There were no significant differences in postoperative morbidity or mortality between groups.

8.5.2 Comparison Among Modern Instructions

There have been several studies to date, including randomized controlled trials, comparing the clinical benefits of different methods of liver transection. However, few if any data have been presented to suggest that one transection technique has advantages over another [22, 59–62].

Table 8.1 Meta-analysis comparing the modern instructions versus clamp crush in liver transection

Study	Comparison with clamp crush	Results
Gurusamy et al. (2009) [56]	CUSA (2 RCTs), RFDS (2 RCTs), hydrojet (1 RCT), sharp dissection (1 RCT)	Infective complications and transection blood loss were greater in the RFDS than in clamp crush Clamp crush is quicker than CUSA, hydrojet, and RFDS and cheaper than the other methods No significant differences in the mortality, morbidity, or hospital stay in the other comparisons
Rahbari et al. (2009) [55]	CUSA (3 RCTs), LVSS (1 RCT), hydrojet (1 RCT), sharp dissection (1 RCT)	No difference between alternative transection method and clamp crush in terms of blood loss, transection time, morbidity, biliary leakage, and hospital stay
Alexiou et al. (2013) [57]	LVSS (3 RCTs and 3 non-RCTs), CUSA (4 RCTs and 1 non-RCT), RFDS (3 RCTs and 3 non-RCTs)	LVSS has lower blood loss, lower risk for bile leak, and shorter hospital stay and similar parenchyma transection time and mortality compared with clamp crush No difference was observed between CUSA or RFDS and clamp crush for any of the abovementioned outcomes
Xiao et al. (2014) [58]	RFDS (4 RCTs and 5 non-RCTs)	Total intraoperative blood loss and blood loss during liver transection were lower in RFDS RFDS is associated with a higher rate of intra-abdominal abscess than the clamp-crush method No significant difference was observed between both the groups for the incidence of both blood transfusion and bile leak

Presently, it can be concluded that no specific tool and/or approach has been found superior to the other when it comes to the liver parenchyma transection. This was also the conclusion of a recent systematic review of the literature [55, 56]. In fact, even today the standard of method in hepatic surgery is to divide the tissue by use of simple devices such as Kelly clamp technique. Despite these conclusions, reached from an evidence-based platform, it is clear that many expert centers across the world also prefer to use the CUSA to divide the parenchyma. A generally advocated opinion is that the CUSA allows the hepatic surgeon to complete and master more difficult and meticulous dissections, particularly along the hepatic pedicles and major vessels.

The choice of transection techniques is currently a matter of preference of surgeons, as there are few obvious evidences that suggest one transection technique has advantages over another. Probably the best option should be a combined approach, making full use of each advantage.

8.6 Complications and Treatment

With the arrival of the precise hepatectomy age, the overall complication rate has often been reported to be markedly decreased, but hemorrhage and bile leakage remain major complications after liver parenchyma transection. Hemorrhage is one of the most serious complications, and re-laparotomy is frequently required to control active hemorrhage. Bile leakage and biloma formation present major obstacles for an uneventful recovery after liver resection [63].

8.6.1 Hemorrhage

The incidence of hemorrhage usually occurs within 48 h with about 10 % [64, 65]. The incidence of life-threatening hemorrhage requiring re-laparotomy varies from 1 to 8 % [66, 67]. Three common reasons for hemorrhage are: (1) bleeding from the transection surfaces, which may be a consequence of arterial branch truncation or congestion of the hepatic vein due to stenosis or ligation; (2) incomplete intraoperative hemostasis, such as inappropriate manipulation of the hepatic vein root or trauma to the diaphragm, and increased vena cava pressure; and (3) vascular sutures loosened or fallen off, an event which usually is ascribed to elevated pressure in the vena cava from patients' body movement, such as turning over or coughing severely [68]. Thorough intraoperative hemostasis is critical and must be ascertained before the operation is concluded. When the root of the hepatic vein is suspected to be injured intraoperatively, hemorrhage from the vein or the inferior vena cava should be carefully sought by increasing the intrathoracic pressure artificially. Mattress sutures with hepatic needles should be used for the hemostasis, and the traumatized surface can be covered with gelatin sponge, biological glue, or omentum as means of achieving additional hemostasis. Close monitoring of vital signs and transfusion of whole blood, platelets, and plasma are usually recommended to ensure the patient's blood pressure and pulse remain stable. Otherwise, re-laparotomy should be considered.

Indications for re-laparotomy after hepatectomy were hemorrhage resulting in serious hypovolemic shock intractable to fluid resuscitation and/or blood transfusion, such as persistent low blood pressure (systolic pressure < 60 mmHg

or pulse pressure < 20 mmHg), more than 200 ml of blood from an abdominal drain in 10 min, and a drop of >3 g/dl of hemoglobin within 1 h despite ongoing blood transfusion. At re-laparotomy, the abdominal cavity was explored to look for any active bleeding site, which was then managed by ligation, suturing, or repair of the vessel wall. Pringle maneuver should be avoided to prevent further ischemia–reperfusion injury to the liver, unless the bleeding from the surface was so massive that the surgical field was obscured. When no definite bleeding site was identified and only extensive oozing was observed, the raw wounds were treated with argon beam coagulation. If oozing continued, gauze compression packing was used for hemostasis. In summary, careful manipulation during operation and thorough hemostasis and drainage are critical for success in attaining hemostasis.

8.6.2 Bile Leakage

The incidence of bile leakage ranges from 6 % to 17 % [69–71]. Common causes of postoperative bile leakage are: truncation of the distal bile duct in the residual liver, the most common cause, and injury of the bile duct from inappropriate surgical technique. Traumatized liver surface area, intraoperative blood loss, and operative time were reported as the independent risk factors for bile leakage after hepatectomy [72, 73]. During surgery, the residual liver can be covered with wet gauze, in which the presence of minimal bile seepage may predict postoperative bile leakage. To avoid postoperative bile leakage, biological glue can be applied to the surface of the residual liver [74]. Postoperative monitoring should include observing for abdominal pain, rebound tenderness, muscle tension, and bile leakage from the drainage tube. In addition, CT or MRCP can be used to determine if the bile duct is occluded and, if so, where the occlusion is located. The bile leakage may resolve spontaneously within two months. However, if peritonitis develops, open surgery should be performed as soon as possible for thorough cleaning of the abdominal cavity and repair of the damaged bile duct. In general, nonoperative treatment was sufficient if the results of MRCP and CT were negative for bile leakage, but operative intervention was needed if conservative therapy failed. Moreover, we recommend the reoperation of patients who present significant bile leakage during the first 24 h after the operation.

8.6.3 Liver Failure

Liver failure is a severe postoperative complication of hepatectomy, even liver transplantation is required to save lives. It is closely associated with active hepatitis, cirrhosis, small residual liver volume, the duration of hepatic portal vein occlusion, and even the perioperative medication used. An incidence of liver failure after hepatectomy of about 8 %-10 % has been reported [75, 76]. Some common preventive measures are more important: carefully assess the liver's functional reserve and reduce intraoperative bleeding, especially for patients with liver cirrhosis. After hepatectomy, the patient should be closely monitored, with particular attention to abnormalities in levels of consciousness, liver function, the volume and character of drainage fluid, and serum lactic acid levels. Acidosis is very common in liver failure, so the level of serum lactic acid should be carefully monitored. Serum bilirubin level should rapidly decrease. If the level increases abruptly after the second postoperative day, the risk of hepatic failure increases. Comprehensive therapy for liver failure includes postoperative supplementation with albumin, fibrinogen, or prothrombin complex and transfusion of fresh blood.

8.6.4 Abdominal Ascites

Abdominal ascites are common after hepatectomy. Accumulation of much ascites may result in imbalance of water and electrolytes. Excessive ascitic fluid should drain from the drainage tube timely. Administration of diuretics and albumin is preferred. However, if the ascites is suspected of being infected and the source of fever, diagnostic paracentesis under ultrasonic guidance and routine drainage examination or biochemical analysis should be performed. If abdominal abscess is found, effective drainage and sensitive antibiotics are necessary.

8.6.5 Fever and Infections

Infections may occur after hepatectomy and include incisional infection, subphrenic infection, pulmonary infection, and urinary tract infection. In addition to anti-inflammatory therapy, the treatment varies across different infections. The sutures and necrotic tissue should be removed and adequate drainage established for incisional infection. Subphrenic fluid collections should be aspirated under ultrasonic guidance, and thorough drainage of the fluid is critical.

8.7 Summary

As the clear evidences for the best liver transection techniques are lacking, currently the choice of technique is often based on the individual surgeon's experience and preference. Certain general recommendations can be made based on existing data and the author's experience. Clamp crushing is a low-cost technique but it requires substantial experience to

be used effectively for the cirrhotic liver. CUSA is currently the standard liver transection technique in many centers and associated with low blood loss and has a well-established safety record, with low risk of bile leak. Several alternative methods have been proposed, such as LVSS, but the advantages of them over the others need further RCTs to confirm. The result with each transection instrument is significantly affected by the individual surgeon's experience. The devices should be used within the limits of each instrument, with the goal of minimal injury and excellent curative effect as well as reducing cost. With availability of the new technology, we should neither court nor reject blindly, but have a selective try. To learn from the experiences of others and combine self-feelings, the instrument, just right for you, should be determined after repeated comparisons and then would be used with great facility.

The instruments currently available for liver resection have the advantages of fine dissection, hemostasis, and no blocking blood flow and can also do precise anatomic resection, and the damage to remnant liver is minimized, which is consistent with today's concept of precise hepatectomy. However, these instruments also have weaknesses such as slow operation, complicated steps, and needing other technical assistance and cannot completely replace the traditional operation method. Pursuing the precise hepatectomy as the goal, with the further development of the instruments, a novel instrument with fast transection speed, reliable pipeline-closed effect, and less damage to the liver will appear. Relying on discipline-virtual visualization technology, a platform for interactive virtual surgery would be established; surgeons in the preoperative simulation compare the different surgical planning and choose the optimized surgical approach for patients. The future liver visualization model is not only a simple morphological basis but also a combination of form and function which would contribute greatly to the development of precise hepatectomy.

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The Key Points of Postoperative Monitoring and Nursing Care

9

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9.1 Preoperative Nursing Care

9.1.1 Preoperative Workup

1. History
   1. Background: age, sex, marital status, and occupation
   2. Etiology and predisposing factors: hepatitis, cirrhosis, diet and lifestyle habits such as intake of aflatoxin-containing food or exposure to carcinogenic nitrosamines, and liver cancer or other malignancies in family members
   3. Past history and comorbidities: history of surgeries, medications, allergies, neoplasms involving other sites, and miscellaneous comorbidities
2. Assessment of symptoms and signs [1]
   1. Pain: pain in the region of the liver is the most common symptom (inquiry about the timing, location, predisposing factors, level, and other characteristics of the pain as well as any associated symptoms). Attention should be paid when acute excruciating epigastric pain occurs, as this symptom is likely to indicate intra-abdominal hemorrhage due to rupture of a hepatic carcinoma.
   2. GI symptoms: poor appetite, abdominal distention, nausea, vomiting, diarrhea, etc.
   3. Systemic symptoms: weakness, progressive weight loss, continued low-grade fever, or intermittent fever of unknown causes.
   4. Other symptoms: anemia, jaundice, ascites, edema of the lower extremities, subcutaneous hemorrhage, etc.
3. Laboratory and radiologic findings
   1. Laboratory results: AFP, ferritin, CEA, CA19-9, serum enzymology indicators, liver function tests, hepatitis virus markers, and HBV DNA copies
   2. Radiologic findings: abdominal Doppler, CT, and MRI
4. Psychological and social well-being
   1. Do patients and their family adequately understand the nature of the planned procedure? Do they adequately understand possible consequences of the disease and how to recover promptly from surgery?
   2. Are the patients and their family afraid or worried about the procedure and the potential bad outcomes and complications that may occur during and after the operation? Can they face these possibilities?
   3. Is the treatment financially affordable for the patients?

9.1.2 Preoperative Nursing Care

1. Psychological: Anxiety, depression, loneliness, anger, sadness, and helplessness are the commonest psychological problems occurring in patients after hepatectomy. We should carefully evaluate the mental well-being and family/social background of the patients and then offer tailored psychological nursing care, such as confidence therapy, comfort therapy, etc. Strengthening exchanges with patients are also important. In this way, patients can acquire information about the hepatectomy, build up self-confidence, and maintain optimism.
2. Improve the function of critical organs: Assist patients in completing the preoperative examination in order to gather information about the condition of critical organs like the heart, lung, brain, and kidney. Measures should be taken to treat underlying comorbidities in order to avoid perioperative complications. In the case of preoperative respiratory infections, surgery can be considered only after the infection is treated with antibiotics and nebulized medications.

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3. Correct coagulation disorders: Cirrhotic patients are susceptible to hemorrhage because of inadequate synthesis of coagulation factors by the liver or thrombocytopenia due to splenomegaly. To lower the risk of massive perioperative hemorrhage, administration of intravenous or intramuscular vitamin K prior to the operation can be considered in specific cases, based on the procoagulation time, prothrombin time, and blood platelet count.
4. Hepatic support therapy: This should be individualized. Liver-protective drugs should be given to patients with deteriorating liver function, and albumin should be given to patients with hypoalbuminemia. For patients with impaired liver function and ascites, the intake of water and sodium should be strictly controlled; the 24-h intake and output volumes of liquid, body weight, and abdominal circumference should be closely monitored and accurately recorded on a daily basis.
5. Improve nutritional condition: An easily digested diet rich in protein, calorie, and fiber, with low fat and low residue, is encouraged preoperatively. To improve patients' nutritional condition and tolerance of the operation, patients should be encouraged to eat independently and given parenteral nutritional support when they are unable to eat.
6. Routine preoperative preparation
    1. Respiratory preparation: Smoking cessation should be encouraged, and patients should be instructed to perform deep breathing exercises and to cough.
    2. Bowel preparation: Conventionally, patients are required to fast for 8 h before surgery and are given non-retention enema once on the night before the operation. Conventional methods of bowel preparation have been greatly changed since the concept of accelerated surgical rehabilitation was widespread in recent years. A great deal of research has demonstrated that carbohydrate intake 2 h before surgery can make patients more comfortable and reduce the incidence of hypoglycemia and postoperative insulin resistance. Additionally, routine bowel preparation before surgery has been abandoned in order to reduce perioperative stress.
    3. Skin preparation: Patients are advised to shower the day before the surgery and to dress in clean clothes. Hair growing between the xiphoid process and the pubic area should be shaved 2 h prior to the operation, and skin in this region should be cleaned.
    4. Preparation of intraoperative medication: Antibiotics and blood products (e.g., erythrocyte suspension) should be prepared.
    5. Gastrointestinal decompression and indwelling urinary catheters should be placed prior to the operation based on the medical orders.

9.2 Postoperative Nursing Care

1. Postoperative positioning: Before fully awakening from anesthesia, the patient should remain supine, without a pillow, with the head turned to one side; this position can prevent aspiration from vomiting. The patient should be in the half-lying position while awake, which can relieve tension on the incision and benefit respiration and drainage.
2. Postoperative observation and management:
    1. Neurologic system: Closely monitor the patient's level of consciousness, pupil dilation, light reflex, and muscle strength before recovery from anesthesia. Record the time when the patient awakens and provide restraints in irritable patients in order to prevent accidental injury. Check his/her consciousness level and mental status every half hour or hour immediately after the patient awakening from anesthesia and every 4–6 h when the patient is in stable condition.
    2. Respiratory system: After hepatectomy, extubation should be performed as soon as the patient regains consciousness, normal neuromuscular reflexes, and hemodynamic stability. At this time, the patient should be kept in the half-lying position and given low-flow oxygen. The frequency and depth of breathing and the oxygen saturation should be closely monitored, and the patient should be protected from airway obstruction. Patients should be guided to practice deep breathing and to cough at least three times per day from the first postoperative day. Lethargic patients who are unable to expectorate should be encouraged to turn over; lung physiotherapy (e.g., vibrated expectoration facilitated by a physical therapy device) and patting the back should be performed frequently, which can help remove airway secretions. Additionally, early ambulation and maintenance of oral hygiene with care solution rinses should be advocated to prevent lung infection, atelectasis, and other pulmonary complications.
    3. Circulatory system: Vital signs, including pulse rate and blood pressure, should be closely monitored every half hour or every hour and every 4–6 h once the patient's hemodynamic status is stable. The 24-h urine volume should also be monitored. The composition, volume, and speed of fluid infusions can be adjusted based on the above data.
    4. Digestive system: The color, character, and volume of gastric juice should be closely observed in patients who have gastric decompression. The nasogastric tube should be withdrawn as soon as postoperative complications such as GI bleeding, gastric retention, and intestinal obstruction are not present. Patients should gradually be transitioned to a normal diet after tolerating liquid and

semiliquid diets. Bowel sounds and peristalsis should also be monitored. The time that flatus and defecation occur should be recorded, and the color and character of the stool should be observed.

5. Abdominal examination and incision care: Abdominal tenderness, rebound tenderness, and rigidity, as well as redness, drainage, and pus at the incision site, should all be evaluated. To keep the dressing over the incision clean and dry after hepatectomy, dressings should be changed every 3 days or whenever the dressing falls off or becomes contaminated. Stitches can be removed 10–14 days after the hepatectomy once the incision has healed.
6. Abdominal drainage: Indwelling abdominal drainage after hepatectomy is not routinely placed. If such a drain is present, it should be fixed firmly in position to avoid compression, kinking, or folding and ensure unobstructed drainage. The drainage bag should be changed once or twice per week. The color, volume, and pattern of intra-abdominal collections in the drain should be carefully observed and recorded. The drain should be discontinued once the drainage volume has decreased and the color appears normal.

3. Pain management: Patients are usually unable to effectively cough or to breathe deeply because of postoperative pain. Effective postoperative analgesia can mitigate diaphragmatic restriction and perioperative stress as well as improve tidal volume and vital capacity. The patient should be queried about pain using a pain scale; patients with pain can be offered oral or intramuscular pain medications or patient-controlled epidural analgesia, which can make patients feel more comfortable.
4. Postoperative complications:
   1. Intra-abdominal hemorrhage [2, 3]: This is one of the major complications of hepatectomy and usually occurs 24–48 h after surgery. Therefore, vital signs, hemoglobin levels, and drainage amounts should all be closely observed in case of hemorrhage. It is normal for approximately 100–300 ml of pale pink fluid to drain from around the liver on the day of hepatectomy; however, we should be alert if the drainage fluid increases in quantity or becomes darker. If hemorrhage is caused by a coagulation disorder, prothrombin complex concentrate, vitamin K, hemostatic drugs, or even fresh blood product transfusions can be used to correct the problem. Reoperation should be considered when a great deal of blood consistently drains in a short time or in cases where bleeding does not stop and vital signs remain unstable even after transfusion and adequate fluid infusion.
   2. Liver failure [3]: Patients in whom more than half of the liver is removed and those who undergo hepatectomy for primary liver cancer that is associated with severe cirrhosis or portal hypertension are at risk of liver failure. The etiology of liver failure after hepatectomy can be multifactorial. Reasons for postoperative liver failure include the following: there is inadequate functioning liver tissue left after hepatectomy; there is intraoperative damage to hepatocytes due to hepatic ischemia and hypoxia following prolonged occlusion of the hepatic blood supply or massive bleeding; anesthetic drugs can be toxic to the liver; total parental nutrition or postoperative medications can also cause damage. Patients with liver failure can present with massive ascites, elevated transaminase levels, coagulation disorders, jaundice, and even hepatic encephalopathy. Therefore, patients who are going to undergo hepatectomy, especially those who have severe cirrhosis and portal hypertension, should be carefully evaluated with combined methods like Child-Pugh grading, indocyanine green (ICG) excretion test, etc. for liver reserve. The volume of liver tissue to be removed can also be estimated using CT in order to preserve sufficient functioning liver tissue. Additionally, liver failure can be prevented by intraoperatively maximizing blood flow to the liver and minimizing bleeding as well as postoperatively continuing low-flow oxygen inhalation and rational medication regimens. Measures should be taken to eliminate predisposing factors and to support liver function to avoid hepatic encephalopathy if liver failure occurs.
   3. Hepatic encephalopathy [3]: We should be alert to any early symptoms of hepatic encephalopathy such as change in personality and behavior, emotionlessness, or flapping tremor, and the patient's physician should be alerted. In patients suffering from hepatic encephalopathy, we should avoid triggering factors and lower blood ammonia levels. Predisposing factors include upper gastrointestinal bleeding, high-protein diets, infection, constipation, and the use of drugs such as narcotics, sedative-hypnotics, etc. Blood ammonia levels can be controlled in the following ways: reducing ammonia production by lowering the intestinal pH, using techniques such as a retention enema with a weakly acidic solution instead of soapsuds (e.g., vinegar 1–2 ml plus normal saline 100 ml or oral lactulose), using arginine to lower blood ammonia or infusion of branched-chain amino acid to correct the disproportion of branched amino acid and aromatic amino acid, and decreasing source of blood ammonia by controlling protein intake.
   4. Infection:
      1. Subphrenic collection and abscess [2, 3]: This is a severe complication of hepatectomy. Fluid and blood accumulate because of poor drainage or early

drainage withdrawal after hepatectomy. Necrotic tissue and bile from the cutting face of the liver can accumulate, creating subphrenic collections that can turn into an abscess if it becomes infected. Subphrenic collections and abscess commonly occur 1 week after hepatectomy and should be suspected in patients with relapsing fever or a consistently elevated temperature that is accompanied by epigastric or right upper quadrant pain, hiccuping, tachycardia, and elevated white blood cell counts with a neutrophil percentage of over 90 %. Using Doppler ultrasound guidance, we can assist doctors to perform needle puncture aspiration and insert an external catheter to drain pus. The abscess cavity can be flushed through the inserted catheter, while intensive care and appropriate antibiotic therapy should not be neglected.

2. Pulmonary infections and pleural effusions: Airway secretions should be sampled in order to identify the pathogen and choose the appropriate antiseptic therapy in patients with pulmonary infections after hepatectomy. Postoperative pleural effusions can be complicated by either pulmonary infections or the hypoalbuminemia that results from postoperative hydrothorax and ascites and insufficient production of albumin by the remnant liver. Postoperative hypoalbuminemia can in turn exacerbate hydrothorax and ascites. This is a vicious cycle. Patients should be encouraged to maintain a half-lying position. Nebulizer treatments should be given, and patients should be instructed to breathe deeply and cough after surgery. Respirations, oxygen saturation levels, and body temperature should also be observed closely. Thoracentesis and drainage guided by ultrasound can be performed in patients with large pleural effusions. It is of great importance to maintain catheter patency and to accurately record the color, texture, and volume of the drainage fluid.

5. Bile leak [2]: Fluid that drains after hepatectomy is normally light red or yellow. Bile leakage should be suspected when the drainage is yellow or green similar to the color of bile. Bile leak after hepatectomy usually comes from the cut face of the liver and is related to the condition of the bile ducts of the cut face, tissue healing, and postoperative nutrition. Patients should be closely observed for abdominal signs such as peritoneal irritation, and drains should be kept open. A small bile leak from the cut face can stop spontaneously and heal uneventfully with unobstructed drainage, while a fistula can be cured by antisepsis and nutritional support.
6. Other: Hypercapnia due to prolonged artificial pneumoperitoneum should be suspected in patients who have undergone laparoscopic hepatectomy and have shallow and slow breathing, high CO_2 pressure, and decreased pH values. Symptoms disappear soon after the administration of inhaled oxygen and alkaline medications (which are dosed according to arterial blood gas results). Subcutaneous emphysema presents as focal crepitation but is unusual after laparoscopic hepatectomy. Subcutaneous emphysema should be monitored and can spread to a patient's neck, resulting in considerable swelling. In certain circumstances, tracheotomy may be indicated if dyspnea occurs.

4. Health guide:
   1. Activity: Patients can perform some movements in bed after hepatectomy, such as turning over, lifting the hip, and moving the lower extremities, in order to prevent bed sores and deep vein thrombosis. Patients who are in stable condition can ambulate early after the operation; however, overactivity should be avoided in case bleeding from the cut face is present.
   2. Diet: Patients can gradually be transitioned to a normal diet if liquid and semiliquid diets are tolerated and no GI complications are present postoperatively. Enteral nutritional preparations or a light diet of easily digested foods that is rich in protein and fiber, such as eggs, fish, meat, fresh vegetables, and fruits, is recommended. The salt intake should be limited in patients with massive ascites and edema, and protein intake should be limited in patients with symptoms predictive of hepatic encephalopathy.
   3. Inform patients of the need for adequate rest and sleep in order to prevent fatigue.
   4. Help patients and their family build the confidence needed to withstand treatment and fight the disease.
   5. Notify patients about the treatment of hepatitis and the need for regular follow-up to detect recurrent malignancy as soon as possible, when early treatment is warranted.

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Short-Term Outcomes of Liver Resection

10

Haiqing Wang and Lunan Yan

10.1 Introduction

Liver surgery has always been challenging, with high mortality and morbidity rates that are due to the complicated anatomy and the risks of massive hemorrhage and liver failure. The first liver resection was reported by Langenbuch in 1888 [1]. Even in the 1970s, only slight improvements were made, and perioperative mortality rate remained as high as 20–28 % [2, 3]. A retrospective study conducted by Foster and Berman [3] in 1977 included 621 liver resections and found that the postoperative mortality rate was 20 % and was as high as 58 % for cirrhosis patients. In the past three decades, refinements in liver surgery have included improvements in surgical techniques, anesthetic techniques, patient selection, and perioperative management, allowing liver resection to become a safe procedure with markedly decreased postoperative morbidity and mortality rates. Recent large studies have suggested that the mortality rates of liver resection have decreased from 20–30 % to 1–4 % [4–8]. It is also encouraging that several large studies have even reported no deaths after liver resections [2, 9]. Fan reported a reduction in the hospital mortality rate from 28 % in 1989 to 0 % in 1996 and 1997 at Queen Mary Hospital, Hong Kong [2], with a corresponding reduction in the postoperative complication rate from 48 to 35 %. Advances in perioperative outcomes are related to the following aspects of care [10]. (1) Accurate patient selection using tests such the Child-Pugh (CTP) score, the Model for End-Stage Liver Disease (MELD) score, and indocyanine green (ICG)-15 has helped to reduce the rates of liver failure, comorbidity, and mortality. (2) Improved understanding of the anatomy of the liver reduces the risk of bile duct and vessel injury and reduces operative times. (3) Hepatic blood flow occlusion during hepatectomy, using approaches such as the Pringer technique, reduces intraoperative hemorrhage. (4) Liver parenchymal transection techniques, such as ultrasonic dissection and LigaSure (Valleylab, Boulder, Colorado, USA), make liver resection more precise and can help to reduce injuries. (5) Operative skills and perioperative management techniques are constantly improving. (6) Many other procedures, including percutaneous radiofrequency ablation, microwave ablation, percutaneous alcohol injection, and laparoscopic hepatectomy, have been introduced to hepatic surgery. These new procedures have ushered the era of minimally invasive surgery into liver resections and have reduced mortality and morbidity. Safety improvements also have allowed surgeons to develop increasingly complicated liver resection procedures. At the same time, surgical indications have expanded constantly; portal hypertension, comorbidities, advanced age, and major liver resection are no longer considered contraindications. In addition, some other therapeutic methods, including portal vein embolization, downstaging treatments for hepatocellular carcinoma (HCC), and radiofrequency ablation, have allowed some advanced-stage patients to undergo radical resection. These patients also have satisfactory postoperative results and long-term survival.

However, liver resection continues to have high morbidity rates, especially in patients with HCC and hilar cholangiocarcinoma. It is well known that 80–90 % of HCC patients have hepatitis B virus (HBV) infection, and their liver parenchyma always has underlying damage, such as cirrhosis and fibrosis [5]. For these patients, liver reserve function is decreased, portal venous pressure is higher, liver regeneration is limited, and coagulation function is impaired, increasing mortality and morbidity. High morbidity rates not only increase medical costs but also affect long-term survival because of surgery-related systemic inflammatory reactions and immunosuppression.

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10.2 Mortality and Morbidity after Liver Resection

Most large studies have reported mortality rate of less than 5 %, but the reported morbidity rate for liver resection varied considerably at different medical centers, ranging from 14.5 to 42 % [4, 7, 8, 11–14]. A study including 5270 patients showed a postoperative mortality rate of 2.6 % and a morbidity rate of 14.5 % [14]. Ramacciato [4] conducted a meta-analysis that included 148 papers published between January 2000 and April 2008 with a total of 36,629 patients and found that the overall morbidity and mortality rates after liver surgery were 29.32 and 3.15 % (4.01 % for HCC patients and 2.34 % for non-HCC patients), respectively. The most frequent causes of death were liver failure (30 %), ascites (15.6 %), sepsis (12.6 %), bleeding (10.2 %), and cardiovascular complications (10 %) (Table 10.1). The most frequent complications were pulmonary complications (27.8 %), liver failure (14.1 %), bile leakage (11.6 %), intra-abdominal abscess (11.3 %), sepsis (8.8 %), and bleeding (6.1 %) (Table 10.2). Investigators at West China Hospital of Sichuan University [5] have studied 1543 HCC liver resections from 2009 to 2013 and reported a postoperative mortality of 1.5 % and a morbidity rate of 30.1 %, with a severe complication rate of 8.1 % (Clavien-Dindo grading III–V).

Table 10.1 Causes of death after liver resection [4]

Cause of death	Percentage (%)
Liver failure	30.0
Ascites	15.6
Sepsis	12.6
Bleeding	10.2
Cardiovascular	10.0
Gastrointestinal bleeding	4.4
Pulmonary complications	4.1
Bile leakage	2.4
Intra-abdominal abscess	0.9
Others	9.8

Table 10.2 The most frequent complications after liver resection [4]

Complications	Percentage (%)
Pulmonary complications	27.8
Liver failure	14.1
Bile leakage	11.6
Intra-abdominal abscess	11.3
Sepsis	8.8
Bleeding	6.1
Cardiovascular	4.1
Ascites	1.9
Gastrointestinal bleeding	1.2
Others	13.1

In the past decades, not only has the technique of open hepatectomy been refined, but also the other therapeutic methods have been developed. These techniques include radiofrequency ablation, microwave ablation, alcohol injection, and cryotherapy. The development of these technologies has enriched the treatment of liver cancer and reduced postoperative complications; for some patients with unresectable liver tumors, these techniques provide a selective method of treatment. However, mortality and morbidity rates differ depending on the surgical procedure. (1) Radiofrequency ablation techniques (including percutaneous, laparoscopic, and open surgical approaches), microwave ablation, and cryotherapy are rapidly gaining acceptance in the radiologic and surgical communities, particularly for patients who have inoperable tumors. These techniques are generally regarded as safe, effective, and minimally invasive; these procedures are also associated with less bleeding and have significantly lower morbidity and mortality rates than open surgical procedures [14–18]. A retrospective study in Japan [14] of 11688 radiofrequency ablations found that the mortality rate was 0.25 % and the morbidity rate was 4.5 %. After cryotherapy, the mortality and morbidity rates were 0.9–1.5 % and 6–29 %, respectively. (2) Living-donor liver resection is a special type of liver resection that is performed in healthy persons with normal liver parenchyma and function. The risk of postoperative morbidity is reduced, and mortality is rare. A study of 3565 cases of living-donor liver resection showed that the complication rate was only 8.4 % and the mortality rate was less than 0.1 % [19]. (3) Laparoscopic liver resection is becoming an attractive option for patients with liver disease and is considered to be a safe alternative to open surgical intervention. The complication rate was 10.5 %, and the mortality was 0.3 % in a meta-analysis that included 2804 patients [20]. However, most laparoscopic liver resections have been limited to tumors in the anterolateral segments. (4) Patients with hilar cholangiocarcinoma always have poor liver function, and the mortality and morbidity rates after major surgery are relatively high, ranging from 5.9 to 7.6 % and 22 to 77 %, respectively [21, 22]. The mortality and morbidity rates for different types of liver resection are displayed in Table 10.3.

10.3 The Clavien-Dindo Classification of Surgical Complications

Although high-volume studies of liver resection are frequently reported worldwide, the reported rate of complications is highly variable, ranging from 14.5 to 42 %. One important cause of this variation is the absence of standard definitions and a widely accepted ranking system to classify surgical complications, which has hampered the interpretation of surgical outcome data and comparisons between different medical centers. In 2004, Clavien [23, 24] proposed a

Table 10.3 Short-term outcomes of liver resections

Surgical procedures	Morbidity (%)	Mortality (%)
Radiofrequency ablation	4.5–8.9	0.09–0.5
Open surgical	9.9	0.5
Laparoscopic	9.5	0.5
Percutaneous	2.2–7.2	0.3
Microwave ablation	7–14.2	0.7–2.3
Cryotherapy	6–29	0.9–1.5
Laparoscopic liver resection	10.5–21.7	0.3
Living-donor hepatectomy	8.4–28	<0.1
Hilar cholangiocarcinoma	22–77	5.9–7.6

Table 10.4 The Clavien-Dindo classification of surgical complications [24]

Classification	Definition
I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, or radiological interventions. Allowed therapeutic regimens are drugs such as antiemetics, antipyretics, analgesics, diuretics, and electrolytes, as well as physiotherapy. This grade also includes wound infections that are opened at the bedside
II	Requiring pharmacological treatment with drugs other than those allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included
III	Requiring surgical, endoscopic, or radiological intervention
IIIa	Intervention not under general anesthesia
IIIb	Intervention under general anesthesia
IV	Life-threatening complication (including CNS complications) requiring IC/ICU management
IVa	Single organ dysfunction (including dialysis)
IVb	Multi-organ dysfunction
V	Death of a patient

classification system for complications that is known as the Clavien-Dindo classification and is based on the therapy used to treat the complication (Table 10.4). This system is an important tool for quality assessment in surgery worldwide. Research from West China Hospital of Sichuan University [5] has summarized complications of liver resection, based on the Clavien-Dindo classification, in an analysis of 1543 cases of HCC liver resection; the results are displayed in Table 10.5.

10.4 Risk Factors for Short-Term Outcomes after Liver Resection

Many factors contribute to the development of complications and mortality, including the extent of liver damage, the general condition of the patient, comorbidities, and surgical factors. However, the influence of any single factor (such as the Child-Pugh score, the MELD score, the ICG-15 results, etc.) on adverse events is limited, although these factors have been identified as predictors of outcomes. Scoring systems have been proposed recently by many medical centers, but these systems have low sensitivity and specificity and have not been verified by other centers. Even for scoring systems that integrate important risk factors, the predictive ability for complications remains unsatisfactory [4, 8].

Table 10.5 The Clavien-Dindo classification of complications in HCC patients undergoing hepatectomy [5]

Complication grade	Cases (incidence)
Grade I	146 (9.5 %)
Grade II	193 (12.5 %)
Grade IIIa	58 (3.8 %)
Grade IIIb	13 (0.8 %)
Grade IV	31 (2 %)
Grade V	23 (1.5 %)

10.4.1 Liver-Related Risk Factors

10.4.1.1 Liver Function

The most frequently used indices for accessing liver function are the Child-Pugh score, the MELD score, and ICG-15. To prevent liver failure, liver resection is permitted when the Child-Pugh score is A. The risk of liver failure is associated with the MELD score. When the MELD score is <9, 9–10, or >10, the corresponding postoperative liver failure rates are 0.4, 3.8, and 20.3 % [25]. The use of ICG-15 is popular in Japan and Asia. Generally, liver resection of four segments is permitted when ICG-15 < 10 %, the resection of two to three segments is permitted when the ICG-15 is between 10 and 19 %, and the resection of one segment can be performed in patients whose ICG-15 is between 20 and 29 %.

10.4.1.2 Cirrhosis and Fibrosis

The cirrhotic liver tolerates acute tissue loss poorly, given its impaired function and decreased ability to regenerate. Fibrosis also affects the liver's functional reserve and increases the risk of liver failure. Furthermore, patients with cirrhotic or fibrotic livers always have poor liver function, portal hypertension, ascites, and poor coagulation ability [10].

10.4.1.3 Steatohepatitis and Steatosis

Steatosis of the liver is another common condition and is usually related to obesity, diabetes mellitus, metabolic disorders, chemotherapy, and alcohol consumption [10]. Steatohepatitis is also the most frequent pathologic change in the liver parenchyma, with an incidence of 30 % in the western population. Among patients undergoing liver

surgery, approximately 20 % of liver resection patients have steatosis, and this rate approaches to 25 % for living donors. Liver steatosis affects liver function and liver regeneration and commonly is considered to be a significant risk factor for liver failure after hepatic surgery [26]. One meta-analysis that included 1000 liver resections revealed a significant association between the degree of steatosis and an increased risk of postoperative complications and mortality [27]. Patients with at least 30 % steatosis had a significantly higher risk of postoperative complications (with a RR of 2.01) than patients without steatosis [27].

10.4.1.4 Portal Hypertension

Patients with portal hypertension always have accompanying poor liver function and cirrhosis, which contraindicate liver resection because of the higher risk of complications. However, recent studies have revealed that liver resection can be performed safely in patients with portal hypertension, with acceptably higher rates of liver failure and complications [28].

10.4.1.5 Tumor

Tumor size, tumor location, and the presence of vascular invasion are all associated with surgical injury and blood loss. In addition, the location of the tumor also affects the surgical plan and the postoperative blood supply and outflow. Tumors located in special segments such as the caudate lobe or segments VII and VIII are associated with increased operative difficulty and blood loss.

10.4.2 Patient-Related Risk Factors

10.4.2.1 Age

Elderly patients always have other diseases such as hypertension, diabetes mellitus, chronic obstructive pulmonary disease, etc. These comorbidities and poor physical condition can reduce the tolerance of elderly patients to surgery and increase the operative risk. Many studies have also suggested that patients over 65 or 70 years of age have higher morbidity and mortality rates after liver resection than younger patients [29, 30].

10.4.2.2 Body Mass Index (BMI)

With the prevalence of obesity continuously increasing worldwide, obesity and overweight have become increasing public health problems. In China, 36.2 % of adults were obese or overweight, while in the USA, this rate is as high as 66.2 % [31]. Obesity and overweight are not only associated with an increasing incidence of a number of conditions, including diabetes mellitus, cardiovascular disease, and nonalcoholic fatty liver disease, but also increase operative difficulty and operative time. A retrospective study that included 3960 liver resections found that obese patients seemed to have worse perioperative outcomes with higher rates of complications and mortality [32]. Data from our center indicate that although BMI did not increase the total complications, postoperative wound complications were more common in overweight and obese patients [33].

10.4.2.3 Comorbidities

The most common comorbidities in patients undergoing liver resection are chronic hepatitis B, hypertension, diabetes, chronic obstructive pulmonary disease, and cardiovascular disease. The Charlson comorbidity index is an effective method of integrating and assessing comorbidities that affect the vital organs. Higher Charlson index scores are associated with higher complication rates [34].

10.4.2.4 American Society of Anesthesiologists (ASA) Index

The ASA index is another method of assessing the degree of tolerance for surgery. Higher ASA scores are associated with higher surgical risks. Studies have suggested that patients with an ASA grade of III–VI have a 1.5- to twofold elevated risk for postoperative complications than patients with an ASA grade of I–II [5, 13].

10.4.3 Surgery-Related Risk Factors

10.4.3.1 Blood Loss

Blood loss during surgery plays a crucial role in postoperative short-term outcomes and is associated with mortality and morbidity. Many studies have shown that bleeding and subsequent blood transfusions are independent risk factors for complications [35]. Transfusions also contribute to immunosuppression, organ injury, and postoperative infection [36].

10.4.3.2 Occlusion of Blood Flow and Methods of Liver Resection

Occlusion of blood flow, especially the Pringer procedure, is the most important method of controlling bleeding during surgery. Although blood flow occlusion often results in gastrointestinal tract congestion, liver ischemia, and reperfusion injury, blood flow occlusion still can reduce postoperative morbidity and mortality. We conducted a study of 574 patients with hepatitis B-related HCC who underwent major hepatectomy and found that the amount of intraoperative blood loss in the no-occlusion group was greater than in the Pringer and the hemihepatic occlusion groups [37]. Presently, hemorrhage during liver resection can be well controlled, even without blood occlusion, with the use of equipment such as the Cavitron Ultrasonic Surgical Aspirator (Valleylab, Boulder, Colorado, USA), the water jet, and LigaSure.

10.4.3.3 Extent of Liver Resection

The extent of the liver resection affects blood loss and the risk of liver failure. Schindl's study [38] identified a relative residual liver volume of 26.6 % as the cutoff value for severe hepatic dysfunction. However, the relative residual liver volume should be increased appropriately for patients with conditions such as

cirrhosis that impair liver function. Suda [39] performed a study in patients with obstructive jaundice and suggested that the relative residual liver volume should be as high as 40 % to prevent liver failure. For patients with cirrhosis, a residual liver volume of 40–50 % is necessary [39]. In our study, we found that liver resection of more than three segments was associated with a 3.15-fold increased risk of complications, compared with resections of less than three segments [5].

10.4.3.4 Extrahepatic Procedures

Extrahepatic procedures, such as bowel resection, adrenalectomy, diaphragmatic resection, biliary tract exploration, and adhesion separation due to a prior operation, increase the risk of complications [13].

10.4.4 Other Risk Factors

Other factors, such as operative time, reoperation, and so on, have been identified as risk factors.

10.5 Bile Leakage

Bile leakage is one of the most frequent complications of liver resection, with an incidence of between 5.3 and 33 %. Bile leakage can result in peritonitis, liver abscess, and sepsis if prompt and reasonable treatment is not given [40]. Mild bile leaks can resolve on their own with sufficient peritoneal drainage; however, severe bile leakage always requires surgical intervention.

10.5.1 Definition and Grade

According to the International Study Group of Hepatobiliary and Pancreatic Surgeons [41], bile leakage is defined as a bilirubin concentration in the drain of at least three times the serum bilirubin concentration on or after postoperative day 3 or as the need for radiologic or operative intervention to treat biliary collections or bile peritonitis. Using this criterion, the severity of bile leakage was classified according to its effects on the clinical management of patients. Grade A bile leakage requires no change in clinical management. Grade B bile leakage requires active therapeutic intervention but is manageable without repeat laparotomy; in Grade C, repeat laparotomy is required to treat bile leakage.

10.5.2 Risk Factors for Bile Leakage

10.5.2.1 Bile Duct Injury

Bile duct injury often occurs at the time of hepatic inflow occlusion and liver resection. Bile leakage can happen when a bile duct injury is not detected or sufficiently repaired.

10.5.2.2 Insufficient Blood Supply to the Bile Duct

Excessive separation of the tissue around the biliary tree may injure the vascular supply to the bile duct. Insufficient blood supply after surgery can cause bile leakage, especially at the common bile duct and the common hepatic duct.

Inadequate suturing and repair of the liver section may omit small bile ducts, which is the most common cause of bile leakage. Another cause is partial necrosis and shedding of liver tissue, exposing the bile duct.

10.5.2.3 Postoperative Biliary Obstruction

Biliary obstruction can increase the bile duct pressure and cause bile leakage.

10.5.3 Clinical Manifestations

Bile leakage mainly presents clinically with persistent abdominal drainage of bile, with 100–300 mL of drainage every day. The presentation may be nonspecific when abdominal drainage remains unobstructed. Patients without peritoneal drainage tubes can present with distension, abdominal pain, or peritonitis (with abdominal tenderness and rebound tenderness). In addition, fever and elevated white blood cell counts are common. Severe cases present with sepsis. Identifying bile during a diagnostic puncture or laparotomy is diagnostic for bile leakage.

10.5.4 Treatment

The principle for treating bile leakage is to maintain the patency of bile drainage, prevent infection, and promote healing of the fistula.

10.5.4.1 Conservative Treatment

Conservative treatment is suitable for bile leakage without associated peritonitis. Treatment includes maintaining the patency of bile drainage, anti-infective treatments, nutritional support, and maintaining appropriate fluid and electrolyte balance. Most patients are cured after 2 weeks to 3 months of such treatment.

10.5.4.2 Percutaneous Puncture Drainage of the Abdominal Cavity [42]

For patients with biliary peritoneal effusions, percutaneous puncture drainage of the abdominal cavity should be performed with ultrasound or CT guidance.

10.5.4.3 Endoscopic Treatment

Endoscopic treatment includes endoscopic retrograde cholangiography (ERCP), endoscopic nasobiliary drainage (ENBD), and biliary stent placement [43]. ERCP and ENBD can reduce bile duct pressure and promote healing of the

fistula. Many studies have shown that endoscopic treatments are minimally invasive, simple, and effective.

10.5.4.4 Abdominal Laparotomy

For patients with diffuse peritonitis, abdominal laparotomy should be performed in a timely fashion.

10.5.5 Prevention

10.5.5.1 Suturing the Liver Section

The main way to prevent bile leakage after liver resection is to suture the liver section and suture the transection of the bile duct; sometimes, repeated checking is necessary.

10.5.5.2 Bile Leakage Test

The bile leakage test is a common approach to reduce the risk of postoperative bile leakage. With this technique, after cholecystectomy and liver resection, a catheter is inserted through the cystic duct into the common bile duct, and the distal common bile duct is occluded. A solution is slowly injected into the biliary tree, and a clinical judgment is then made as to whether a bile leak is present on the transected surface of the liver. If so, the bile leak site will be closed steadily beforehand to avoid bile leakage. The solution used for the bile leakage test includes isotonic sodium, fat emulsion, indocyanine green, and methylene blue. A meta-analysis has found that the bile leakage test reduces the risk of postoperative bile leakage and does not increase the incidence of complications. Fat emulsion is the best choice of solution for the test [44].

10.5.5.3 Intraoperative Cholangiography

Intraoperative cholangiography can help to identify bile duct injury or stenosis and bile leakage.

10.6 Liver Failure

Liver failure is the most severe complication of liver resection. Although the reported incidence is only 2.6–14.1 % [4, 45, 46], this complication always has a poor prognosis and a high mortality rate of more than 50 % [46].

10.6.1 Definition and Grading

Liver failure is defined as damage to liver function with impairment of synthesis, biliary secretion, and detoxification. The main manifestations are coagulopathies, hyperbilirubinemia, ascites, and hepatic encephalopathy. The reported criteria for liver failure [45] are varied, and there is no uniform standard. However, two definitions are widely accepted at present.

10.6.1.1 "50-50 Criteria" [46]

The "50-50" criteria are the findings of prothrombin time <50 % and serum bilirubin >50 umol/L on postoperative day 5. The finding of positive 50–50 criteria on postoperative day 5 is an accurate and early indicator of liver failure, predicting 50 % mortality after liver resection.

10.6.1.2 International Study Group of Liver Surgery (ISGLS) Criteria [46]

Postoperative deterioration in the ability of the liver (in patients with normal and abnormal liver function) to maintain its synthetic, excretory, and detoxifying functions is characterized by an increased INR (or the need for clotting factors to maintain a normal INR) and hyperbilirubinemia (according to institutional upper limits of normal) on or after postoperative day 5. If the INR or serum bilirubin concentration is increased preoperatively, liver failure is defined by an increasing INR (decreasing prothrombin time) and increasing serum bilirubin concentration on or after postoperative day 5 (compared with the values of the previous day). Other obvious causes for the observed biochemical and clinical alterations, such as biliary obstruction, should be excluded.

Grading:

A. Liver failure resulting in abnormal laboratory parameters but requiring no change in the clinical management of the patient
B. Liver failure resulting in a deviation from the regular clinical management but manageable without invasive treatment
C. Liver failure resulting in a deviation from the regular clinical management and requiring invasive treatment

According to these criteria, the mortality rates for liver failure of grades A, B, and C are 0 %, 12 %, and 54 % [45], respectively.

10.6.2 Risk Factors

Many factors may contribute to liver failure, including the patient's preoperative condition, as well as operative and perioperative management. However, the extent of the liver resection and the quality of the liver are the most important factors.

10.6.2.1 Liver Quality

The quality of the normal liver is crucial for maintaining the liver's functions of synthesis, biliary secretion, and detoxification. It is also associated with liver regeneration. Cirrhosis and steatohepatitis are the two most common causes of liver damage; in these conditions, the liver cells are injured, and the regenerative capacity is poor.

10.6.2.2 Residual Liver Volume

The extent of liver resection affects the risk of liver failure. The relative residual liver volume should be at least 25 %. For patients with normal liver parenchyma, a relative residual liver volume of more than 25–30 % is necessary to prevent liver failure. For patients with underlying liver diseases, such as cirrhosis or steatohepatitis, a relative residual liver volume of more than 40 % is necessary [47].

10.6.2.3 Blood Loss and Transfusion

Intraoperative blood loss and blood transfusions often lead to excessive fluid loss, bacterial translocation, systemic inflammation, and coagulation disorders. These factors can contribute to liver failure.

10.6.2.4 Other Risk Factors

The other risk factors for liver failure include age, comorbidities, nutritional status, hepatitis, blood occlusion, infection, and the use of perioperative medications such as anesthetics.

10.6.3 Clinical Manifestations

Liver failure is mainly characterized by jaundice, hypoalbuminemia, coagulopathies, intractable ascites, and fluid/electrolyte imbalances. Severe cases can have oliguria, hepatopulmonary syndrome, diffuse peritonitis, hepatorenal syndrome, and even hepatic coma.

10.6.4 Treatment

Although there has been obvious progress in surgical techniques and perioperative management for patients undergoing liver resection, the treatment of liver failure remains very difficult. The usual methods of treatment are as follows.

10.6.4.1 Etiological Treatment

This includes anti-infective measures and the correction of fluid and electrolyte imbalance, avoiding the using of drugs that can impair liver function.

10.6.4.2 Nutritional Support

For patients with liver failure, adequate energy balance should be maintained. The best choice is to provide a large amount of glucose, which can reduce the breakdown of tissue protein and help reduce blood ammonia levels.

Correct hypoalbuminemia, coagulation abnormalities, and renal function; provide supportive therapy for other organs.

Employ exogenous liver replacement therapies such as extracorporeal membrane oxygenation (ECMO) therapy.

Liver transplantation: Liver transplantation is the most effective treatment for liver failure.

10.6.5 Prevention

Prevention is better than treatment for liver failure [48].

10.6.5.1 Improve the Patient's General Condition

This includes improving liver function and providing nutritional support, blood glucose control, and so on.

10.6.5.2 Adequate Residual Liver Volume

For patients with relatively small residual liver volumes, preoperative portal vein thrombosis should be considered to promote contralateral liver regeneration and prevent small-for-size syndrome. In addition, combining liver partitioning and portal vein ligation for a staged hepatectomy can also be considered.

Controlling intraoperative blood loss, reducing the need for blood flow occlusion.

10.7 Post-hepatectomy Hemorrhage

Post-hepatectomy hemorrhage is a severe complication of liver resection, usually resulting in hemorrhagic shock and death. With developments in liver surgery and anesthetic management, blood loss and post-hepatectomy hemorrhage rates have decreased; however, the reported post-hepatectomy hemorrhage rate remains 1–8 % [49]. The reported mortality rate of post-hepatectomy hemorrhage is up to 16.7–25 % [50], accounting for 10 % of all deaths [4].

10.7.1 Definition and Grading

The definition of post-hepatectomy hemorrhage varies considerably within the hepatic surgery literature. The International Study Group of Liver Surgery defines post-hepatectomy hemorrhage as follows [49]: (1) a postoperative drop in hemoglobin level of >3 g/dl compared with the postoperative baseline level, (2) any need for the postoperative transfusion of packed red blood cells for a falling hemoglobin level, and (3) the need for radiological intervention (such as embolization) and/or repeat laparotomy to stop bleeding. Post-hepatectomy hemorrhage can also be graded according to transfusion requirements. Transfusion of up to two units of PRBCs is considered Grade A. Grade B requires transfusion of more than two units of PRBCs, and the need for invasive interventions such as embolization and/or repeat laparotomy defines Grade C. The mortality rates for the above three grades are 0 %, 17 %, and 50 %, respectively [49].

10.7.2 Risk Factors

10.7.2.1 Incomplete Hemostasis

Incomplete intraoperative hemostasis is the main cause of post-hepatectomy hemorrhage; the most frequent locations are the liver section, the hepatic vein, and the end of the hepatic artery.

10.7.2.2 Liver Necrosis

Liver tissue can become necrotic due to ischemia of the liver parenchyma. The necrotic tissue contributes to subdiaphragmatic abscess and bleeding.

10.7.2.3 Coagulation Disorders

Coagulation disorders usually occur on postoperative days 3–5 and can appear in patients with cirrhosis, extensive blood loss, postoperative infections, small residual liver volumes, and after major surgery.

Other risk factors include reoperation, portal hypertension, and so on [50–52].

10.7.3 Clinical Presentation

The timing of post-hepatectomy hemorrhage varies depending on the cause. Approximately 50 % of bleeding episodes occurred in the 8 h after surgery [51]. Approximately 80 % of bleeding episodes occurred within 24 h of surgery. Vascular hemorrhage usually occurs on postoperative day 1, but hemorrhage due to coagulopathy usually occurs on postoperative days 3–5. Also, hemorrhage due to intraperitoneal infection usually occurs on postoperative days 7–10. Patients with minimal bleeding can be asymptomatic or may have drainage of bright red blood from the abdominal cavity or abdominal distension. Patients with moderate bleeding can develop hypotension, tachycardia, anemia, oliguria, and other symptoms. Massive hemorrhage can lead to shock and multiple organ failure.

10.7.4 Treatments

The principle of treating intraperitoneal hemorrhage is to add volume, administer blood transfusions, and perform surgery to stop the bleeding.

10.7.4.1 Fluid Resuscitation

Fluid resuscitation is the first step in treatment. The goals of resuscitation in the face of hemorrhagic shock are to restore end-organ perfusion and maintain tissue oxygenation. Ideal resuscitation fluids include colloid and crystalloid solutions. Blood transfusion is necessary when the hemoglobin concentration declines.

Correct coagulopathies with treatments including plasma transfusion, drug therapy, and anti-infective measures.

10.7.4.2 Laparotomy

When patients present with hypotension, tachycardia, and shock, massive hemorrhage should be considered, and invasive interventions and laparotomy should be performed as soon as possible.

10.8 Ascites

Ascites is a common complication of liver resection, especially for patients with cirrhosis. Without a uniform criterion for the diagnosis of ascites, the reported incidence varies and ranges from 1.9 to 25.5 % [4, 53, 54]. Ascites is generally regarded as the result of liver cirrhosis and portal hypertension and is often associated with hepatic insufficiency or cirrhosis. Ascites often leads to fluid/electrolyte disorders and hypoalbuminemia.

Liver resection in patients with cirrhosis may result in damage to the liver function and increase the portal venous pressure. Also, liver resection can damage the intrahepatic lymphatic circulation, further aggravating portal hypertension and leading to refractory ascites. The presence of ascites does not only increase the complication and mortality rates; it also affects the long-term survival rate in patients with HCC. In addition, massive ascites is associated with liver failure.

10.8.1 Definition and Grading

The International Ascites Club defines ascites as follows [55]: Uncomplicated ascites is not infected and is not associated with hepatorenal syndrome. Grade 1 ascites is mild and is only detectable by ultrasound examination. Grade 2 ascites or moderate ascites is manifested by moderate symmetrical distension of the abdomen. Grade 3 ascites is large or gross ascites with marked abdominal distension. The International Ascites Club has defined “refractory ascites” as ascites that cannot be mobilized or whose early recurrence cannot be satisfactorily prevented by medical therapy.

However, these definitions are not suitable for patients with indwelling peritoneal drains. Chan [54] defined ascites in patients who have undergone resection as ascitic drainage of greater than 500 mL per day.

10.8.2 Risk Factors

10.8.2.1 Portal Hypertension

Portal hypertension is the underlying cause of ascites. For patients with cirrhosis, liver resection can increase the portal pressure and aggravate ascites. First, portal hypertension can trigger massive ascites by stimulating the neurohormonal systems to promote renal water and sodium resorption [54]. Second, portal pressure can be elevated after liver resection

because of shrinkage of the hepatic vascular bed. Third, a large amount of blood loss may also increase postoperative water and sodium retention, as a decrease in effective arterial blood volume has been considered the major factor that promotes renal dysfunction in patients with portal hypertension [54].

10.8.2.2 Cirrhosis

Ascites is the most common complication of cirrhosis. Approximately 85 % of patients with ascites in the USA have cirrhosis. Liver resection in the setting of cirrhosis increases the risk of ascites [53, 54]. Moreover, the ability of the liver to repair itself by regenerating functional hepatocytes is strongly associated with the degree of liver cirrhosis.

10.8.2.3 Increased Vascular Permeability

Increased vascular permeability often occurs in patients with tumors, as tumor cells can secrete vascular endothelial growth factor, which increases vascular permeability, allowing large quantities of plasma and protein to exude into the abdominal cavity. After liver resection, massive ascites will develop.

10.8.2.4 The Ratio of the Remnant Liver Volume to the Whole Liver Volume

Many studies [56, 54] have indicated that the ratio of the remnant liver volume to the whole liver volume is an independent risk factor for postoperative ascites. This phenomenon may be associated with the fact that smaller remnant liver volumes are associated with higher portal pressures.

Other risk factors include operative time, blood flow occlusion, and portal vein stenosis.

10.8.3 Treatment

Current treatment paradigms for ascites have improved significantly. The management of ascites includes sodium restriction, diuretics, and intermittent paracentesis, based on the extent of the ascites [57].

10.8.3.1 Sodium Restriction

A negative sodium balance can be achieved by dietary salt restriction or by increasing renal sodium excretion. With dietary salt restriction, ascites decrease in 10–15 % of patients [55].

10.8.3.2 Diuretics

The initial episode of moderate ascites should be treated with an aldosterone antagonist such as spironolactone alone, starting at 100 mg/day and increasing stepwise every 7 days (in 100-mg steps) to a maximum of 400 mg/day if there is no response. In patients who do not respond to aldosterone antagonists (as defined by a reduction of body weight of less than 2 kg/week), or in patients who develop hyperkalemia, furosemide should be added at an increasing stepwise dose from 40 mg/day to a maximum of 160 mg/day (in 40-mg steps). Patients should undergo frequent clinical and biochemical monitoring, particularly during the first month of treatment [54, 57].

10.8.4 Albumin Infusion

10.8.4.1 Paracentesis

Serial therapeutic paracentesis is a treatment option for patients with refractory ascites. Repeated large-volume paracentesis plus albumin (8 g/L of ascites removed) is the first line of treatment for refractory ascites.

10.8.4.2 Other Treatment Measures

Infection should be prevented; TIPS and liver transplantation can also be performed when indicated.

10.9 Surgical Site Infection

Surgical site infection (SSI) is the most frequent nosocomial infection suffered by surgical patients. Surgical site infection is defined as an infection of the surgical site that develops within 30 days after surgery and includes both superficial and deep site infections, as well as organ/space infections. A study of 2332 liver resections from 173 hospitals in the USA reported that the incidence of SSI ranged from 9.7 to 18.3 %. Another study [7] of 5651 liver resections reported an SSI rate of 12.2 %, including a 4.8 % rate of superficial surgical site infection, a 1 % rate of deep surgical site infection, and a 6.4 % rate of organ space infection.

10.9.1 Definition

SSI after liver resection [58] includes superficial and deep surgical site infections and organ space infections. Superficial incisional SSI is defined as an infection occurring at the incision site within 30 days postoperatively that involves only the skin and subcutaneous tissue. Organ/space SSI is defined as an intra-abdominal abscess without clinical evidence of anastomotic leakage.

SSI must meet at least one of the following criteria: there is purulent drainage from the incision; an organism is isolated by culture of fluid from the incision; and evidence of infection is found by CT, physical examination, or laparotomy. Subdiaphragmatic abscess is the most common organ/space SSI after liver resection. Intra-abdominal abscesses and superficial incisional infections are very common in patients with hepatoliths who undergo liver resection. The

most common SSI pathogens are *Staphylococcus aureus*, *E. coli*, and *Enterococcus* [58].

10.9.2 Risk Factors

Patient characteristics, as well as factors related to the operation and operative environment, are likely to affect the incidence of SSI.

10.9.2.1 Patient Characteristics

Diabetes, smoking, nutritional status, prolonged hospital stay, obesity, steroid use, hypoalbuminemia, and fatty liver disease all can contribute to the occurrence of SSI.

10.9.2.2 Factors Related to the Operation

The most common cause of intra-abdominal abscess after hepatectomy is drain obstruction, which can lead to subphrenic liquid collection and infection. Other risk factors include infectious surgery, tissue ischemia, stitches, prolonged operative time, transfusion, and antimicrobial prophylaxis. In addition, many studies [59] have shown that reoperation and bile leakage are risk factors for SSI.

10.9.2.3 Clinical Presentation

Superficial incision infections or deep tissue infections often present with incisional pain, redness, tenderness, and induration. Some patients have systemic infectious symptoms such as fever and elevated white blood cell counts. Patients with intra-abdominal abscesses often have abdominal pain, chills, fever, upper abdominal tenderness, muscle tension, and even shock. Patients with diaphragmatic abscesses or effusions can also present with intractable hiccups.

10.9.3 Treatments

Superficial incisional SSI and deep site infections should be treated with dressing and adequate drainage.

10.9.3.1 Percutaneous Drainage

Percutaneous drainage with CT or ultrasound guidance should be performed in patients with abscesses. It is important to prevent obstruction of the drain.

10.9.3.2 Laparotomy

For patients with peritonitis or failure of percutaneous drainage, laparotomy should be performed as soon as possible.

10.9.3.3 Antibiotics

Empiric antibiotic treatment should be considered as soon as possible. The antibiotic regimen must be adjusted based on the results of drug sensitivity testing.

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Long-Term Outcomes of Liver Resection

11

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Common diseases that require liver resection include hepatocellular carcinoma (HCC), metastatic liver cancer, gallbladder carcinoma, hilar cholangiocarcinoma, hepatolithiasis, hepatic hydatid, etc. Long-term outcomes depend on the characteristics of the primary disease. In this chapter, we introduce the long-term outcomes of HCC-performed liver resection.

HCC is the third most common malignancy around the world and has a poor prognosis, with an overall 5-year survival of 15.6 % [1]. For patients with unresectable HCC, survival is poorer, with a median survival time of 4 months. For patients with resectable HCC, if no radical treatments have been performed, the median survival time is also less than 1 year [2]. Liver resection can improve the long-term outcomes; however, only approximately 20 % of all HCCs can undergo radical resection when the tumor is diagnosed. Most patients cannot undergo resection because of advanced tumor or inadequate liver reserve. In the past decades, great progress has been made in terms of clinical management, screening, surveillance, and prevention. The overall survival of HCC has doubled during the past two decades [2]. However, HCCs continue to have a poor prognosis. For patients who are candidates for surgical resection, most studies have found that the 5-year survival ranges from 40 to 70 %, and the 5-year disease-free survival is 30 %, depending on the stage of disease [2]. The reported 10-year survival ranges from 22 to 35 % [3]. The 3-year recurrence rate after liver resection is greater than 50 % and the 5-year recurrence rate greater than 70 % [4]. Many factors have been shown to contribute to the recurrence and survival of HCCs after liver resection. Early tumor recurrence within the 2–3 years after surgery is primarily related to local invasion and intrahepatic metastasis and is associated with tumor biology. Conversely, late recurrence occurring beyond 2–3 years after surgery is primarily related to de novo tumor formation, coded in the surrounding cirrhotic non-tumor tissue due to the carcinogenic field effect [5–6]. The prognosis of HCC is very complicated and differs from other malignant tumors. Most HCC occurrence is based on original liver cirrhosis, and thus, the damage of liver function significantly influences prognosis.

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11.1 Risk Factors for Survival and Recurrence

Many risk factors have been associated with the prognosis of HCCs, primarily involving the tumor characteristics and underlying liver diseases. Among the several risk factors for HCC, the most common is cirrhosis because of chronic hepatitis B virus or hepatitis C virus infection, alcohol consumption, obesity, diabetes, and tumor stage.

11.1.1 Tumor Characteristics

11.1.1.1 Characteristics of Pathology

The pathology characteristics of HCC, such as capsule presence, microscopic vascular invasion, histological grading, and daughter invasion, have been demonstrated to influence recurrence after surgery [7–12]. Microscopic vascular invasion is a crucial risk factor for HCC recurrence because of the development of micrometastasis-based vascular invasion. Many studies have also suggested that poor HCC differentiation grade is associated with presence of microvascular invasion. However, these factors are strictly related to the pathological features of the tumor that are only assessable after surgery and therefore primarily contribute to prognosis but are of little assistance in selecting the best treatment.

11.1.1.2 Tumor Size and Number

Tumor size and number have significant prognostic influence on HCC with radical resection. For patients with bigger and

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multinodular tumors, the tumor has greater possibility of invasion ability, poorly differentiated grade, microscopic vascular invasion, and an ultimately poorer prognosis. In the Barcelona Clinic Liver Cancer (BCLC) stage, only a tumor less than 2 cm in diameter is recommend for resection, and this tumor size is associated with a good 5-year survival of 70 % [6]. However, many patients are out of BCLC criterion for liver resection when diagnosed and other studies have confirmed that these patients still have a relatively good prognosis after liver resection. Whether resection should be performed on patients with tumors larger than 5 cm remains controversial. Studies have found that hepatic resection can be safely performed in patients with large or multinodular HCC, with an overall 5-year survival rate of 39 %. However, patients with a tumor less than 5 cm in size have significantly better 5-year survival than patients with tumors larger than 5 cm [13]. Many large-volume centers perform liver resection not only for patients with tumors larger than 5 cm but also for patients with tumors larger than 10 cm. These studies have shown that resection achieves relative good overall survival and recurrence-free survival in selected patients with tumors larger than 10 cm, with a median survival time of 10–32 months and 5-year survival of 21–33 %. However, the prognosis remains poorer than patients with tumors smaller than 10 cm [14–16].

11.1.1.3 Vascular Invasion

Portal vein and hepatic venous tumors are the most common vascular invasions in HCC patients. Visible vein tumors are the relative contraindication of liver resection. However, satisfactory survival results have still been achieved in patients with a portal vein tumor. A portal vein tumor is the most important biological characteristic of HCC with invasiveness and influences the recurrence and metastasis of HCC. The reported incidence of portal vein tumors ranges from 20 to 70 % [17]. HCC patients with portal vein tumors have poorer survival and earlier tumor recurrence than patients without portal vein tumors [12, 18–19]. For patients with portal vein tumor, the location of portal vein tumor also influences the prognosis of HCC. Ikai [20] divided portal vein tumors into five categories: Vp0, no portal vein tumor; Vp1, tumor above the portal vein secondary branches; Vp2, tumor includes the portal vein secondary branches; Vp3, tumor includes the left and right branch of the portal vein; and Vp4, tumor includes the main portal vein. After radical liver resection, the corresponding 5-year survivals were 50 %, 31 %, 26 %, 12 %, and 7 %, respectively.

11.1.2 Risk Factors Related to the Liver

11.1.2.1 Cirrhosis

Cirrhotic patients with chronic HBV infection carry the highest annual incidence for the development of HCC, ranging from 2 to 6 %. In the cirrhotic liver, long-term survival after HCC resection is likely related to cirrhosis because cirrhosis is not only related to late tumor recurrence but also influences long-term survival because of damaged liver function [19, 21–23]. In addition, liver fibrosis with varying degrees has also been identified as a risk factor for tumor recurrence. One study has indicated that the survival of patients with liver cirrhosis was significantly impaired compared with patients with normal liver status and that the prognosis for patients with liver fibrosis was better than those with cirrhosis [19, 21, 24].

11.1.2.2 Liver Function

Patients with poor liver function always have cirrhosis, steatohepatitis, and portal hypertension. These factors could influence the postoperative complications and survival of patients with underlying liver diseases. Child score, MELD score, and ICG-15, which are designed to assess liver function, have been identified as independent risk factors for long-term outcome in patients after liver resection [6, 25–26].

11.1.2.3 Portal Hypertension

Portal hypertension is ever a contraindication to liver resection because such patients have damaged liver function, with a Child score of B or C, or esophageal varices. That is because portal hypertension is an independent risk factor for morbidity and long-term survival [27]. In spite of lower survival, patients with portal hypertension still have satisfactory and acceptable survival after liver resection [28–30]. Hidaka [30] indicated that the 5-year survival and disease-free survival for patients with portal hypertension were 31 % and 12 %, respectively, which is lower than patients without portal hypertension, who had a 5-year survival of 63.7 % and disease-free survival of 52.5 %.

11.1.2.4 Hepatitis and Antiviral Treatment

The common hepatitis-related HCCs involve hepatitis B (HBV) and hepatitis C (HCV). Chronic active hepatitis is a risk factor for recurrence, including multicentric carcinogenesis, and the recurrence rate after the resection of HCV-related hepatocellular carcinoma is higher in patients with HCV viremia than those without viremia. In addition, postoperative antiviral treatment could also decrease the recurrence and prolong the survival after HCC resection. One randomized controlled trial (RCT) [31] suggested that postoperative interferon-a therapy appears to decrease recurrence after resection of hepatitis C virus-related HCC. One meta-analysis including 13 RCTs [32] also confirmed that adjuvant interferon reduced the recurrence of HCC after curative therapies. In Asia, especially in China, 85 % of HCC derives from HBV infection. The HBV-DNA level is not only associated with HCC development but also with the recurrence of HCC. After liver resection, the immune system is suppressed, and

19–28 % of HBV is activated, which is higher in patients without antiviral therapy [33]. Antiviral therapy after liver resection can suppress the replication of HBV and inflammation reaction and prevent HCC recurrence. Huang [34] conducted a retrospective study and found that HBV reactivation was common after partial hepatectomy and that the 3-year disease-free survival rate and overall survival rate after resection in patients with HBV reactivation were significantly lower than those without reactivation. A meta-analysis [35] including nine studies also indicated that antiviral therapy has potential beneficial effects after the curative treatment of HBV-related HCC in terms of tumor recurrence and can reduce recurrence by 41 %.

11.1.3 Risk Factors Related to Surgery

11.1.3.1 Anatomical Hepatectomy

Previous studies have shown that HCC recurrence is divided into early recurrence and late recurrence, and the primary manner of recurrence is early recurrence, in which the tumor derives from the primary lesion. Early recurrence often starts from the liver incisal margin, which has subclinical metastases. These subclinical metastases derive from the primary lesion through the portal vein branch of the hepatic segment or direct invasion [6]. Therefore, eradication of intrahepatic metastasis is the most crucial consideration for improving the surgical outcome in HCC. Anatomical hepatectomy, also called segmentectomy or subsegmentectomy, is a systematic removal of a hepatic segment confined by tumor-bearing portal tributaries that reduces HCC recurrence. A study including 543 HCC patients with cirrhosis found that anatomical hepatectomy conferred better overall and recurrence-free survival than non-anatomical hepatectomy and suffered from significantly less hepatic dysfunction. After 1-to-1 match, the advantage of anatomical hepatectomy was limited to reduced early recurrence (<2 years) of poorly differentiated tumors and tumors with microvascular invasion [36]. Another retrospective study including 2267 anatomical hepatectomies and 3514 non-anatomical hepatectomies found that anatomical hepatectomy had better recurrence-free survival, especially for patients with tumors 2–5 cm in diameter [37]. Many studies and meta-analyses [38–41] have also reached the same conclusion that anatomical hepatectomy has better survival and recurrence-free survival; however, this advantage was limited to tumors with a diameter of 2–5 cm and for preventing early recurrence.

11.1.3.2 Blood Loss and Transfusion

The transfusion rate after liver resection is approximately 20 % [42]. Massive blood loss and subsequent transfusion can promote HCC recurrence by suppressing the immune system. A previous study showed that the lymphocyte population in the peripheral blood declines after transfusion and that the function of NK and cytotoxic T cells is restrained, suppressing the immune system and promoting infection and HCC recurrence [43]. One systematic review [42] including 22 studies and 5635 HCC with resection showed that the 1-, 3-, and 5-year tumor recurrence rates in patients with transfusion were 1.7-, 1.22-, and 1.16-fold higher compared with patients without transfusion. In addition, transfusion also influences overall survival.

11.1.3.3 Surgical Margin

Deciding the surgical margin, especially for patients with cirrhosis, is difficult. Theoretically, to prevent tumor recurrence, wide hepatectomy should be performed, or some daughter nodule could be left. However, wide hepatectomy may result in inadequate liver tissue and causes liver failure. One RCT [44] on single HCC found that a wide resection margin of 2 cm and narrow resection margin of 1 cm had similar morbidity and mortality, but the wide resection margin group had better 1-, 2-, 3-, and 5-year survival (96.5 %, 91.8 %, 86.9 %, 74.9 % vs 92.9 %, 83.3 %, 70.9 %, 49.1 %, respectively). In addition, all recurrences at the margins of liver resection were observed in the narrow margin group, and multiple tumor recurrence was also significantly higher in the narrow margin group than the wide margin group. However, a meta-analysis including four non-RCTs suggested that [45] the patients with a resection margin greater than 1 cm had similar 1-, 3-, and 5-year survival compared with patients with a resection margin less than 1 cm; a further study found that most of the included patients had HCC more than 2 cm. Another study found that a resection margin greater than 1 cm had better survival than a resection margin less than 1 cm for patients with a tumor less than 2 cm in diameter; however, for patients with tumors larger than 2 cm in diameter, resection margin did not influence survival [46]. Similarly, several studies [47–48] have demonstrated that R1/R2 resection had worse survival than R0 resection. Lang [49] found that patients with R0 resection had a 3- and 5-year survival of 54 % and 39 %, respectively, but for patients with R1/R2 resection, these rates were 23 % and 0 %, respectively.

11.1.4 Alpha Fetoprotein (AFP)

AFP has been used worldwide as a standard for diagnosing HCC compared with other serum markers, although this method has unstable sensitivity and specificity. In addition, the serum AFP level also plays an important role in the surveillance of HCC recurrences. AFP ≥200 ng/mL combined with the imaging examination of liver lesions could be diagnosed as HCC [6]. We [50] conducted a retrospective cohort study of 2304 HCC patients and found that 73.6 % of all the patients were with AFP ≥20 ng/mL. HCC differentiation, size, and

vascular invasion have strong relationships with AFP, and poor differentiation and HCC size ≥10 cm are independent predictors of elevated AFP. Many studies have shown that AFP level is associated with HCC recurrence and overall survival. Ma [51] divided AFP levels into three groups (AFP ≤20 ng/mL, AFP 20–400 ng/mL, AFP ≥400 ng/mL) and found that patients with AFP ≤20 ng/mL had a lower 2-year recurrence rate and higher 2-year survival. Another study also found that preoperative AFP mRNA level was associated with recurrence and metastasis [52]. Increased AFP levels after operation were considered a marker for HCC recurrence [53].

11.1.5 Molecular Markers

Although many risk factors have been identified to be associated with HCC recurrence, the stage systems and prediction tools cannot completely predict HCC recurrence and survival. A complex interplay of unknown host- and tumor-related factors is associated with aggressive tumor biology. A large number of tissue and serum markers associated with invasiveness, metastasis, recurrence, and potential prognostic significance have been identified; however, specific markers and their reliability are currently lacking [54]. Nevertheless, there are many markers related to HCC survival. P53 mutation has been shown to be associated with HCC oncogenesis and recurrence, with a higher percentage of 10–60 %. One meta-analysis including 37 studies showed that patients with P53 mutations had worse overall and disease-free survival than patients without P53 mutations [1]. Other identified molecular markers include a five-gene model [5], G1–G6 classification, miRNA21, etc. [55]

Other risk factors, such as age, gender, preoperative TACE, chemotherapy, and lymph node metastasis, are associated with HCC recurrence and survival.

11.2 Stage System for HCC

Distinct from other malignancies, survival in patients with HCC depends on both the pathologic stage of the disease and the severity of underlying liver dysfunction. Therefore, an ideal staging system should consider both of these factors [2]. In addition, a good staging system also includes the following characteristics: (1) simplicity and convenience, (2) good repeatability, (3) reflecting the natural history of disease, and (4) subgroup analysis. Several staging systems are used for patient stratification. Common grading systems include the tumor-node-metastasis (TNM) classification system, the BCLC staging system, the Japan Integrated Staging (JIS) score, the Cancer of the Liver Italian Program (CLIP) score, the model for the Chinese University Prognostic Index (CUPI) grade, and the Okuda staging system. Each system has unique advantages and disadvantages; thus, there is no completely accepted staging system for guiding the management of HCC. The most widely used stage systems are the BCLC staging system and the TNM staging system proposed by the American Joint Committee on Cancer (AJCC).

11.2.1 BCLC Staging System

The BCLC staging system [56] includes variables related to tumor stage, liver functional status, physical status, and portal hypertension. It divides patients into five grades (stage 0, A, B, C, D; Table 11.1) and gives appropriate treatment for each grade. The American Association for the Study of Liver Diseases (AASLD) [6] recommends the BCLC staging system as the guideline for treatment. It identifies patients with early HCC (stage 0-A) who may benefit from curative therapies (such as liver resection, liver transplantation, or radio frequency), those at an intermediate disease stage who may benefit from palliative treatments of TACE, those at an advanced disease stage who may benefit from sorafenib, and those at terminal stage with symptomatic treatment [6]. The BCLC staging classification has been externally validated worldwide. According to the BCLC stating system, the patients with stage A have a 5-year survival of 50–70 % after radical resection. The West China Hospital of Sichuan University [57] had 774 cases of HCC from 2007 to 2009, and the 1-, 3-, and 5-year survival rates were 95.8 %, 72.8 %, and 44.6 %, respectively, for patients with stage A and 78.2 %, 41.3 %, and 22.9 %, respectively, for patients with stage B. For stage C patients, the 1- and 3-year survivals

Table 11.1 The BCLC staging system for HCC

BCLC staging	PS	Tumor stage	Child-Pugh	PH	Treatment
Stage 0: very early	0	Sing <2 cm	A	No	Resection
Stage A: early	0	Sing or three nodules <3 cm	A–B	PH or no	Resection, transplantation, or RAF
Stage B: intermediate	0	Multinodular	A–B	Any	TACE
Stage C: advanced	1–2	Portal invasion	A–B	Any	Sorafenib
Stage D: terminal	>2	Any	C	Any	Symptomatic treatment

PH portal hypertension, *RAF* radio-frequency ablation, *PS* physical status

were 50 % and 8.1 %, respectively. The BCLC staging system was developed based on a retrospective analysis of various studies of HCC patients. Thus, this grading system is suitable for most HCC patients. However, this system has some limitations. First, it was proposed based on a review of the used staging systems and a discussion of the natural history and prognosis of different tumor stages. Thus, the rationality of the statistics is relatively poor. Second, some parameters are subjective, and thus, accuracy may be influenced, such as with the Child and physical status (PS) scores. Third, the BCLC staging system was established using a large proportion of unresectable HCC patients. However, the BCLC has demonstrated better survival stratification and prognosis prediction than other staging systems, such as the Okuda, CLIP, CUPI, TNM, and JIS classifications, and has been proposed as the best available prognostic system.

11.2.2 TNM Staging System

Similar to the staging systems of other neoplasms, the TNM staging system [58] for HCC also includes tumor size, number, vascular invasion, lymphatic metastasis, and metastasis (Table 11.2). The TNM staging system emphasizes the characteristics of the tumor, which comprehensively and accurately describe the developmental history of HCC. Many studies have identified that the seventh edition of the AJCC TNM staging system is able to adequately stratify patients, and this system is one of the most widely accepted staging systems for HCC. The major modification from the sixth to the seventh edition was the separation of the T3 stage into T3a and T3b; this change indicates major vascular invasion of portal or hepatic veins as an important predictive factor for prognosis. AJCC recommends the TNM staging system for HCC patient staging. The West China Hospital of Sichuan University examined 774 cases of HCC from 2007 to 2009 according to the TNM staging system. The respective 1-, 3-, and 5-year survival rates were 89, 65.1, and 41.1 % for patients with stage I HCC; 78.5, 32.2, and 15.1 % for stage II HCC; 55.3, 13.4, and 10.1 % for stage III HCC; and 44.4, 5.6, and 0 % for stage IV [57]. However, there are several limitations of the TNM staging system, and the TNM system has limited stratification ability. (1) The TNM staging system only includes tumor-related morphology but not liver performance-related parameters, such as liver function and portal hypertension. (2) The TNM staging system is based on postoperative pathology results; therefore, its application has been limited because most patients with HCC are at an advanced stage that is surgically unresectable at the time of diagnosis. (3) The TNM staging system considers tumor size, number, and vascular invasion with equivalent prediction value for survival. This classification would underestimate the prognosis of patients with large, solitary tumors without vascular invasion and fail to adequately stratify patients.

Table 11.2 The seventh AJCC/TNM staging system for HCC

TNM staging			
Tumor (T)			
Tx: no tumor			
T1: single tumor without vascular invasion			
T2: single tumor with vascular invasion or multiple tumors, none >5.0 cm			
T3a: multiple tumors, any of which are >5.0 cm T3b: involving a major branch of the portal or hepatic vein			
T4: with direct invasion of an adjacent organ other than the gallbladder or with perforation of the visceral peritoneum			
Node (N)		Metastasis (M)	
Nx: lymph node metastasis is not unclear		Mx: distant metastasis is not unclear	
N0: no regional lymph node metastasis		M0: no distant metastasis	
N1: regional lymph node metastasis		M1: distant metastasis	
Staging	T	N	M
I	T1	N0	M0
II	T2	N0	M0
IIIa	T3a	N0	M0
IIIb	T3b	N0	M0
IIIc	T4	N0	M0
IVa	Any T	N1	M0
IVb	Any T	Any N	M1

11.2.3 Okuda Staging System

The Okuda staging system was proposed by Okuda and is the first staging system to combine liver function and tumor characteristics (Table 11.3) [59]. This system is based on 850 cases of HCC patients with liver resection. At that time, early HCC diagnosis was relatively rare, and the staging system was therefore based on data from patients with advanced disease [60]. Thus, the median survival time for the 850 HCC cases was 4.1 months. This staging system includes an index for tumor characteristics (tumor size) and three indexes for liver function (ascites, albumin, and bilirubin). Many other HCC staging systems are based on the

Table 11.3 Okuda system for staging of HCC

	Score	
Parameters	0	1
Tumor	≤50 % liver	>50 % liver
Ascites	No	Yes
Albumin (g/L)	≥30	<30
Bilirubin (mg/dl)	<3	≥3

Score 0, stage I; score 1–2, stage II; score 3–4, stage III

Okuda system and have been constantly improved. The Okuda system is primarily suitable for advanced patients, and several limitations also exist. First, the Okuda system is inadequate for contemporary HCC cases, particularly those that are diagnosed early. Thus, it has limited ability to stratify patients with early HCC. Second, this system did not consider several other tumor characteristics, such as single and multifocal tumors, AFP levels, vascular invasion, and metastasis. In addition, the stratification of tumor size is also very difficult. Third, the cutoff value of bilirubin is high and suitable for patients with severe liver function damage. Fourth, some subjective indices remain, such as ascites and liver size.

11.2.4 CLIP Staging System

The system proposed by the Cancer of the Liver Italian Program (CLIP) in 1998 was based on a retrospective study with 435 patients in Italy and was subsequently prospectively validated [60]. The CLIP system has been widely demonstrated to be a more appropriate prognostic model for the late-stage HCC population and has been validated in case series from various parts of the world [61–62]. This system was proposed to overcome the disadvantage of the TNM staging system and is superior to the Okuda system. This system includes four indexes: Child-Pugh grade, tumor morphology, AFP, and portal vein thrombosis (Table 11.4). However, this system included a small number of advanced cases and many radically treated patients in their original studies. The main limitations are as follows. First, approximately 70–80 % of all patients have a CLIP score of 0–2. The CLIP score can discriminate patient populations with scores of 0–3, but it is not able to discriminate score between scores of 4–6. Second, the definition of tumor morphology in the best prognostic group is too advanced [63]. Third, other indexes for tumor characteristics are not included in this system, such as lymph node invasion and metastasis. Therefore, this system cannot identify the groups who would most benefit from curative and aggressive treatment.

Table 11.4 CLIP system for grading of HCC

	Score		
Parameters	0	1	2
Child-Pugh	A	B	C
Tumor morphology	Uninodular and ≤50 %	Multinodular and ≤50 %	Massive or >50 %
AFP (ng/ml)	<400	≥400	
Portal vein thrombosis	No	Yes	

Score 0, early HCC; score 1–3, intermediate HCC; score 4–6, advanced HCC

11.2.5 JIS Staging System

The JIS staging system combines Child-Pugh grade and the TNM staging system based on the LCSGJ criteria [63]. It was proposed in Japan in 2003 (Table 11.5) based on 722 HCCs and is believed to have greater stratification ability than the CLIP scoring system and perform better than the CLIP scoring system in selecting the best prognostic patient group. Each patient with a Child-Pugh classification of A, B, or C was allocated scores of 0, 1, and 2, respectively. Based on the TNM staging of the LCSGJ, stage I (fulfilling the following three conditions: solitary, <2 cm, no vessel invasion), stage II (fulfilling two of the three conditions), stage III (fulfilling one of the three conditions), and stage IV (fulfilling none of the three conditions) were allocated scores of 0, 1, 2, and 3, respectively. The summation of the tumor staging score and the Child-Pugh classification score was defined as the JIS score [63].

This system is suitable for most HCC patients, especially for patients with good prognosis. However, the JIS system may be limited in its ability to stratify patients with advanced scores because it uniformly assigns tumor stage and liver function.

11.2.6 CUPI Staging System

The CUPI score was the only system widely used for Chinese HCC patients with HBV infection. This system was based on a study cohort of 926 Chinese patients with primarily hepatitis B-associated HCCs in 2002 by Leung [64]. The CUPI score includes the conventional TNM system, a number of other liver functional factors, AFP level, and performance status (Table 11.6) [65]. The CUPI was more discriminant than the TNM staging system, Okuda staging systems, and

Table 11.5 (A) The JIS system for HCC grading. (B) The JIS scoring system

Tumor stage	Single, size <2 cm, no vessel invasion
T1	Fulfilling three factors
T2	Fulfilling two factors
T3	Fulfilling one factor
T4	Fulfilling zero factor
Stage I	T1N0M0
Stage II	T2N0M0
Stage III	T3N0M0
Stage IVa	T4N0M0 or any TN1M0
Stage IVb	T1–T4, N0 or N1, M+

	Score			
Parameters	0	1	2	3
Child-Pugh grade	A	B	C	-
TNM stage	I	II	III	IV

Table 11.6 CUPI system for staging of HCC

Parameters	Weight (CUPI score)
TNM staging	
I, II	−3
IIIa, IIIb	−1
Iva, IVb	0
Asymptomatic disease on presentation	−4
Ascites	3
AFP ≥500 ng/ml	2
Bilirubin (μmol/L)	
<34	0
34–51	3
≥52	4
AKP ≥200 IU/L	3

CUPI scores: summation of the weights of TNM staging + asymptomatic disease on presentation + ascites + AFP+ bilirubin + AKP (low-risk group, CUPI score ≤l; intermediate-risk group, CUPI score = 2–7; high-risk group, CUPI score ≥8)

CLIP prognostic score in classifying patients into different risk groups and was better at predicting survival. This system is primarily suitable for patients with HBV-related HCC, especially in China. The limitations are as follows. First, it is unclear whether this system can be used in other western counties. Second, this system includes an objective index. Third, most patients in the CUPI study were advanced patients. Therefore, the application for radical liver resection is limited.

11.2.7 Comparing the Staging Systems

Any staging system should classify patients into subgroups with significantly different outcomes and should simultaneously help to direct therapy. Clinical staging for cancers provides guidance for predicting survival outcome and deciding optimal treatment strategies. Although several staging systems have been proposed over the past several decades, there is no ideal staging system for patient stratification and survival prediction. Generally, the Okuda staging system, CLIP staging system, CUPI staging system, and JIS staging system are more appropriate for assessing advanced HCC patients without operation, with an overall median survival time of 4–5 months. The TNM system and BCLC system are suitable for patients with liver resection. Currently, most studies have acknowledged that the TNM, CLIP, and BCLC systems are better for patient stratification and survival prediction, especially the BCLC system. Several studies [60, 66–68] have suggested that the BCLC system is better than the Okuda, CLIP, CUPI, JIS, and TNM staging systems for predicting survival. The CLIP system is superior to the Okuda system [60], and JIS is superior to CUPI [68].

More clinical investigations should be performed to confirm these staging systems or propose new systems. The conventional staging systems have the disadvantage of including objective indexes and pathology results. Many parameters reflecting tumor characteristics are morphological, which is not an index that could reflect the nature of HCC. Therefore, new parameters, such as genes, miRNAs, and proteinogram, should be considered for constructing novel staging systems.

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Glisson's Pedicle Approach and Liver Round Ligament Approach in Anatomical Hepatectomy

12

Hong Wu, Kunlin Xie, and Ming Li

12.1 Glisson's Pedicle Approach in Liver Resection

12.1.1 Anatomy

The hepatic artery, portal vein, and bile ducts (the portal triad) in the ligamentum hepatoduodenale are encased in a membrane and branch, and they constitute Glisson's system. This system consists of extrahepatic and intrahepatic portions. The portal triad encased in the connective tissue and peritoneum, up to the porta hepatis, constitutes the extrahepatic portion of Glisson's system, whereas the portion that extends into the liver is considered intrahepatic. The ligamentum hepatoduodenale is the main stem of Glisson's system and gives rise to two primary branches at the porta hepatis. The left primary branch of Glisson's pedicle (including the left branch of the portal vein, the left hepatic artery, and the left hepatic duct) runs in the left hilar plate and turns upward in the fissure toward the ligamentum teres hepatis after giving rise to branches leading to the II segment at the left-most part of the left hilar plate. The left primary branch of Glisson's pedicle gives off branches to the III segment at the left side of the base of the fissure for the ligamentum teres hepatis and branches to the IV segment at the right side of the base of the fissure for the ligamentum teres hepatis; it then continues with the ligamentum teres hepatis. The main stem of the right primary branch of the Glisson's pedicle is short and occasionally even absent, and it quickly divides into two secondary branches (Fig. 12.1). Based on this anatomical foundation, Professor Takasaki (Tokyo Women Medical University) divided the liver into three sections: the right segment, middle segment, and left segment, which correspond, respectively, to the right posterior lobe, right anterior lobe, and left lobe in Couinaud's hepatic segments [1]. By extrahepatic dissection of Glisson's pedicle, we can address the structure in Glisson's pedicle without opening Glisson's sheath, thus avoiding complex operations and potential damage to the hepatic portal. This procedure is called Glisson's pedicle transection hepatectomy. After development and promotion by Machado and others, this technology has been available for hepatic segmentectomy, hepatic lobectomy, hemihepatectomy, and extensive hepatectomy and shows its unique advantages [2, 3].

Advantages This technique addresses hepatic ducts without opening Glisson's sheath, saves time, and avoids potential damage to the hepatic portal.

Disadvantage This technique requires adept operative skills and solid hepatic anatomy, and it may cause duct injury when there is variation in the hepatic portal.

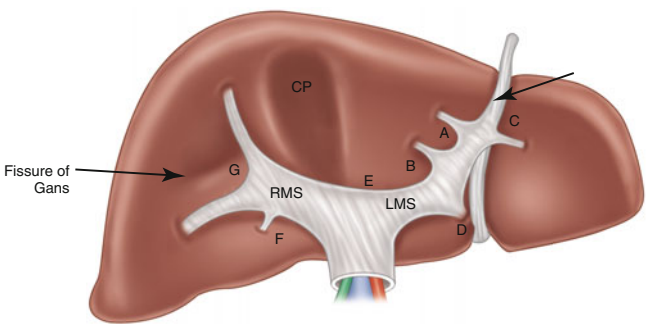

Fig. 12.1 Blocking the inflow of the corresponding hepatic lobes or hepatic segments. *A*: The basis of the round ligament, right side; *B*: inferior margin of the quadrate lobe, near the left end of the hilar plate; *C*: the basis of the round ligament, left side; *D*: superior margin of the quadrate lobe, near the left end of the hilar plate; *E*: inferior margin of the quadrate lobe, near the capsule bed; *F*: inferior margin of Glisson's pedicle near the portal vein branches, *right side*; *G*: fissure of Ganz. *LMS* left branch of Glisson's pedicle, *RMS* right branches of Glisson's pedicle, *CP* cystic plate, the *arrows* indicate the round ligament

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12.1.2 Techniques

Take the right costal margin incision along the midline directly up to the xiphoid. Confirm that there are no intrahepatic metastases or intra-abdominal metastases. Cut the falciform ligament and the round ligament, and reserve the stump of the round ligament for traction. Dissect the coronary ligament until the conjunctive region of the suprahepatic inferior vena cava, hepatic vein, and inferior vena cava is exposed. Cut off the left side of the deltoid ligament and completely dissociate the left liver. Locate the tumor and confirm the relationship between the cancer and the intrahepatic ducts with intraoperative ultrasound.

12.1.2.1 Hepatic Left Lateral Lobectomy

Control the Inflow of Left Lateral Lobe Blood into the left lateral lobe (including the S2 and S3) is supported by the left Glisson's pedicle branches along the left side of the fissure of the round ligament. A small incision on the left side is the basis for the fissure of the round ligament (Fig. 12.1); then, make an incision on the front of the left venous ligament and left Glisson's pedicle branch confluence (Fig. 12.1). Use long curved forceps for blunt dissection from site C to site D until the curved forceps pierce site D. Then, a tourniquet can surround the left Glisson's pedicle branches with the curved forceps traction until the branches are broken off.

Parenchymal Transection Resect the liver at the diaphragmatic surface along the left border of the falciform ligament, at the visceral surface along the left border of the round ligament, and toward the Arantius ligament follows an order of a superior-inferior movement and then an inferior-superior movement. Because the inflow of the left lateral lobe and bile duct has been amputated, the hepatectomy can be performed more quickly. After exposing the left hepatic vein trunk, amputate it, and reinforce the stump with 5/0 polydioxanone suture (PDS) wire. Remove the entire specimen, staunch the bleeding, place the drainage tube, and close the abdomen.

12.1.2.2 Left Hemihepatectomy

Control the Inflow of the Left Liver Dissect the left Glisson's branches at the left side of the hilar plate, which will avoid injury to the blood vessels and bile ducts if there is anatomical variation of the hepatic portal. Using the confluence of the left Arantius ligament and left Glisson's pedicle branches as a guide, safely and quickly dissect the left Glisson's pedicle branches. Make a small incision at the inferior border of the fissure of the round ligament, and dissect

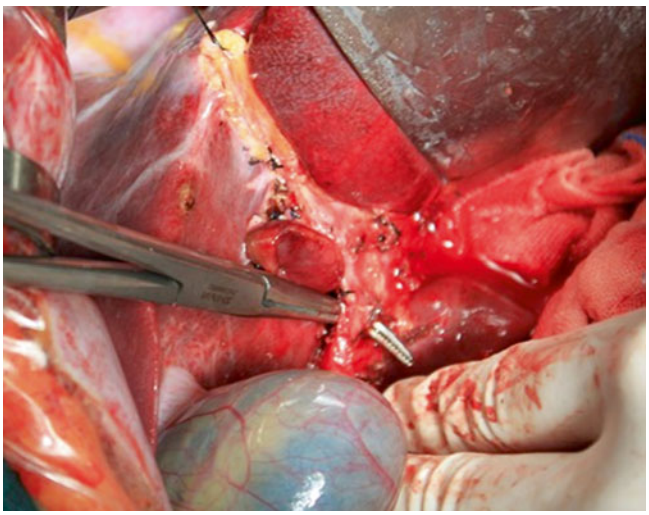

Fig. 12.2 Isolating the left Glisson's branch at the end of left hilar plate

the front confluence of the left Arantius ligament and left Glisson's branch (Fig. 12.1) to expose the back of left Glisson's pedicle branch. Then, use long curved forceps for blunt dissection from site B to site D, encircle the left Glisson's branch with a tourniquet and amputate the left branch (Fig. 12.2).

Parenchymal Transection After occlusion of the left hepatic inflow, a significant ischemic line appears on the liver surface; the hepatectomy starts from this line. Make an incision along the left hepatic vein following an order of a superior-inferior movement and then an inferior-superior movement. Intraoperative ultrasound can help locate the middle hepatic vein when necessary. After exposing the left hepatic vein trunk, amputate it, and reinforce the stump with 5/0 PDS wire. When the tumor affects the caudate lobe and the caudate lobe must be resected, resect the liver along the line as described until arriving in the front of the inferior vena cava. Then, pull the caudate lobe and left liver to the left, expose the front and left side of the retrohepatic inferior vena cava, and ligate the short hepatic vein from inferior to superior. After the back of left hepatic vein is completely exposed, ligate and suture it. Remove the entire specimen, staunch the bleeding, place a drainage tube, and close the abdomen.

12.1.2.3 Right Hemihepatectomy

Control the Inflow of the Right Liver Make a small incision on the right side of the confluence of the caudate lobe, gallbladder bed, and far right side of the hilar plate (Fig. 12.1), up to the level of the hepatoduodenal ligament. Expose the connective tissue at the inferior border of the hilar plate.

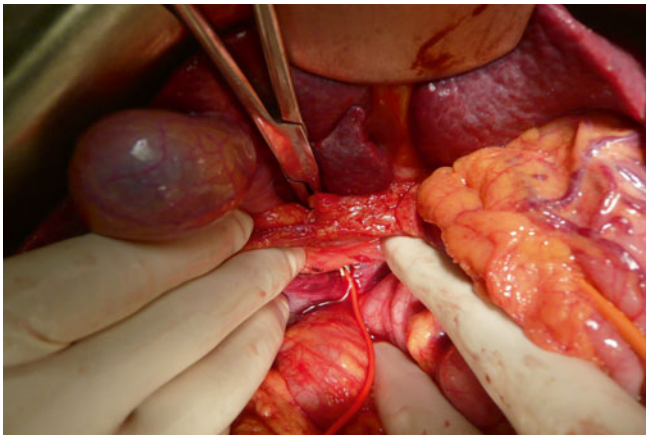

Fig. 12.3 Isolating the right Glisson's pedicle trunkin the right hilar plate

Reveal the caudate branch after careful dissection. Dissect, ligate, and suture this branch; blunt dissection can occur from this branch to incision E until the entire right Glisson's pedicle trunk is dissected. Amputate the trunk, and suture the ends (Fig. 12.3).

Parenchymal Transection After right hepatic inflow is occluded, a significant ischemic line appears on the liver surface. The hepatectomy starts from this line, along the right side of middle hepatic vein following an order of a superior-inferior movement and then an inferior-superior movement. Intraoperative ultrasound can help locate the middle hepatic vein when necessary. After exposing the right hepatic vein trunk, amputate it, and reinforce the stump with 5/0 PDS wire. Remove the entire specimen, staunch the bleeding, place a drainage tube, and close the abdomen.

12.1.2.4 Right Anterior Lobe Resection

The incision is made as a right hemihepatectomy. Then, use curved forceps for blunt dissection along the right Glisson's pedicle and pierce the fissure of Ganz. The fissure of Ganz is the boundary of the right anterior and right posterior branches, which is obvious in 70 % of patients. Therefore, we can use the fissure of Ganz as an anatomical marker for dissecting the right anterior Glisson's pedicle branch and the right posterior Glisson's pedicle branch.

S4 will be cut off when performing a middle hepatectomy or right extensive hepatectomy. The round ligament is a guide when blocking the inflow of S4. The S4 branches come from the left Glisson's pedicle branch (the left portal vein continuation of the round ligament). During dissection of these branches, a small incision is made on the right side at the base of the fissure for the round ligament (Fig. 12.1), and another incision is made at the inferior border of the quadrate lobe near the fissure for the round ligament (Fig. 12.1). Use a right-angle clamp for blunt dissection between A and B, and place a tourniquet around the left Glisson's sheath until the left branch is amputated. Resect the liver at the diaphragmatic surface along the right border of the falciform ligament at the visceral surface along the left border of the round ligament.

12.2 The round Ligament Approach in Hepatectomy

Traditional hepatectomy techniques often start from the hepatoduodenal ligament until the corresponding artery, portal vein, and bile duct are dissected. As we introduced earlier, the round ligament approach starts from the round ligament. First, the fissure of the round ligament is dissected, and the left end of hilar plate is found and isolated. Ligate the structure in the hilar plate. Then, we lower the porta hepatis, which allows complete separation of the hilar plate and hepatic parenchyma so that we can safely and quickly transect hepatic parenchyma. The round ligament approach is applicable for extensive hepatectomy, left hepatectomy, and middle hepatectomy, etc.

12.2.1 Anatomy

The left primary branch of Glisson's pedicle, including the left branch of portal vein, the left hepatic artery, and the left hepatic duct, runs in the left hilar plate and turns upward in the fissure for the ligamentum teres hepatis after giving off branches to segment II at the left-most part of the left hilar plate. The left primary branch of Glisson's pedicle gives off branches to segment III at the left side of the base of the fissure for the ligamentum teres hepatis and branches to segment IV at the right side of the base of the fissure for the ligamentum teres hepatis. Then, it continues with the ligamentum teres hepatis. We can use the ligamentum teres hepatis as a landmark to confirm Glisson's pedicle of some hepatic lobes and hepatic segments and then separate and ligate it out of the liver to selectively block hepatic blood flow. Moreover, we can also use the fissure of the ligamentum teres hepatis and the falciform ligament as a landmark to limit the disconnection of the hepatic parenchyma.

Advantages (1) Using the left approach, dissect the back of the porta hepatis, which can create space for liver parenchyma transection and avoid damaging the retained bile ducts during parenchyma transection. (2) For the patients with hilar adhesions caused by hilar surgery, injury, etc., the left approach is better than the anterior approach.

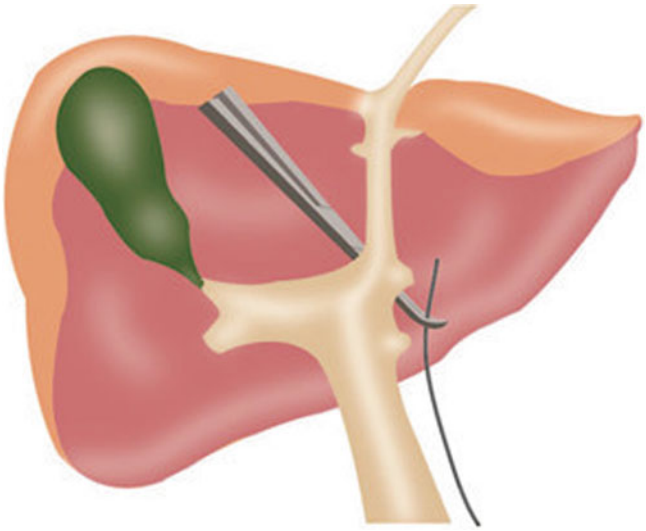

Fig. 12.4 The left main sheath is divided at the left end of the hilar plate

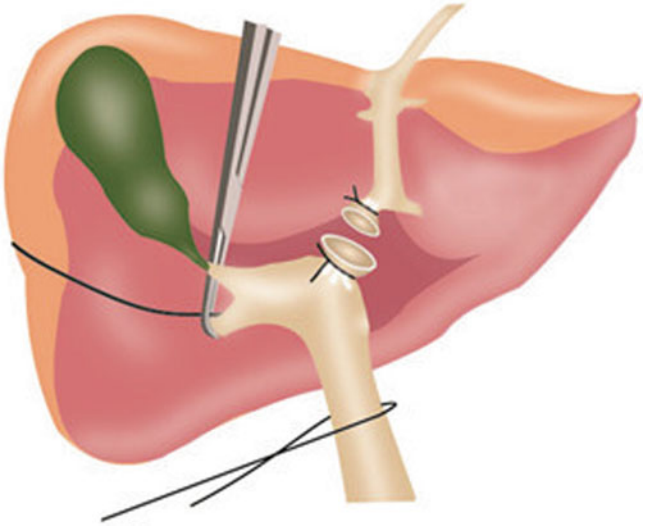

Fig. 12.5 The hilar plate is lowered along the base of segment IV, and a long curved clamp is introduced from the incision left to the cystic plate toward the right edge of the gallbladder bed and penetrates the parenchyma between the anterior and posterior section pedicles to isolate the right anterior section pedicle

12.2.2 Techniques

12.2.2.1 Extensive Left Hepatectomy

Control Inflow of the Liver with the Round Ligament Approach Dissect the ligamentum teres hepatis and find the left end of the hilar plate. Dissect the hilar plate; isolate the left branch of portal vein, left hepatic duct, and left hepatic artery; amputate and suture them one by one (Fig. 12.4). Lower the right side of the hilar plate until it reaches the left side of the gallbladder plate. On the left side of the gallbladder plate, dissect the right anterior Glisson's pedicle branch as described above: amputate and suture them or clamp them first. Address them after Glisson's pedicle has been fully revealed. Pull the hilar plate, which has been stripped from the liver parenchyma to the right side during hepatectomy, inside to create enough space for the surgery and to prevent accidental injury to the bile ducts in the hilar plate (Fig. 12.5).

Parenchymal Transection Because the tumor volume tends to be larger when the patient needs extensive hepatectomy, dissecting around the liver using the traditional surgical approach may cause tumor hematogenous spread, rupture, and even uncontrolled bleeding, which are caused by tumor oppression and liver rotation. Therefore, the anterior approach is a better choice for larger tumors, especially for those that are adhered to the posterior peritoneum or diaphragm. After right hepatic inflow is occluded, the liver parenchymal transection can occur along the hepatic ischemic line, which is between the right anterior branch and the right posterior branch of portal vein. Intraoperative ultrasound can help liver parenchymal transection when necessary. The surgeon should pay attention to protect the right hepatic vein; injuring this vein can cause massive intraoperative blood loss and residual liver dysfunction. The raw surface should be a plane of the exposed right hepatic vein after surgery (Fig. 12.6).

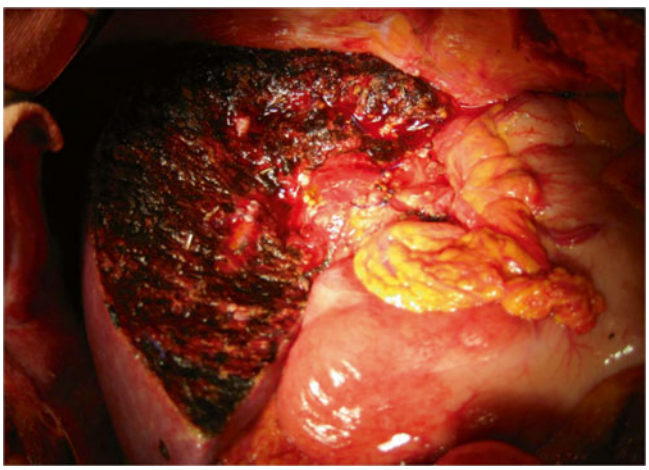

Fig. 12.6 The raw surface of the remnant liver after left hepatic trisectionectomy

12.2.2.2 Right Extensive Hepatectomy

Right extensive hepatectomy can also follow the liver round ligament approach. Dissect and ligate Glisson's pedicle, dominating over segment IV in the fissure for the round ligament (Fig. 12.7), from here to the superior border along the right side, descending along the porta hepatis to the left side of the gallbladder plate. Dissect the right Glisson's pedicle trunk as described above; then, amputate and suture the ends

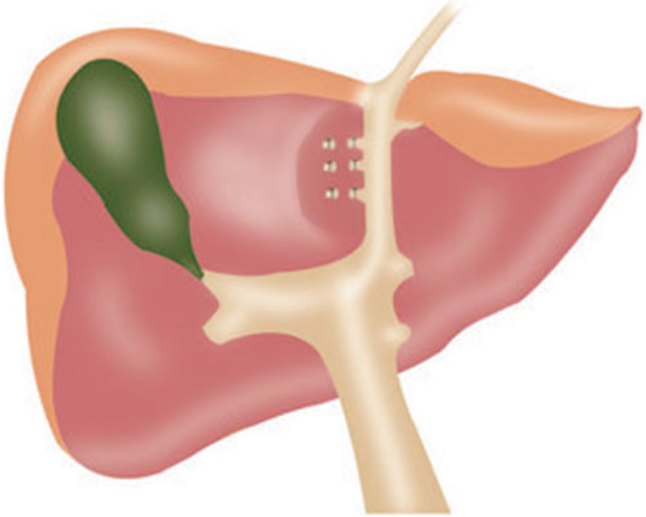

Fig. 12.7 The Glisson's pedicles to segment IV are divided along the fissure for the round ligament

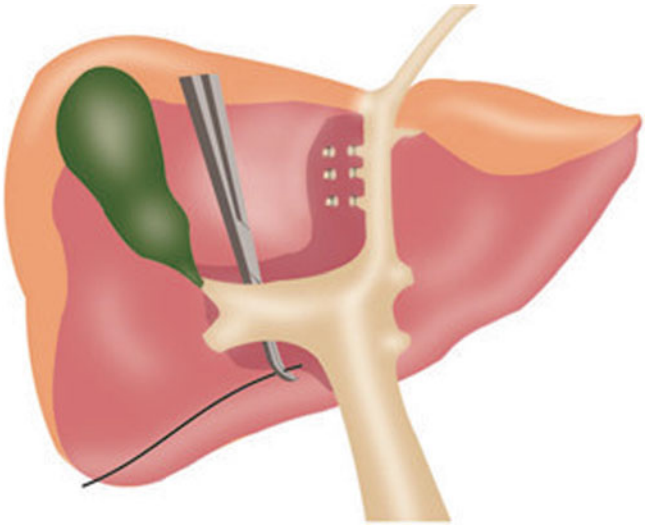

Fig. 12.8 The hilar plate is lowered along the base ofthe caudate lobe and the right Glisson pedicles of segment I is dissected and ligated, after that, the right main sheath is isolated

(Fig. 12.8). Pull the hilar plate to the left during the hepatectomy, and dissect the liver parenchyma along the fissure for the round ligament. The raw surface is the fully exposed right side of the round ligament (Fig. 12.9).

The left approach is also applicable for left liver resection and mesohepatectomy. In conclusion, the main advantages of the left approach are as follows:

1. The left approach provides convenience for dissection along the porta hepatis. When separating the liver tissue, we can separate the porta hepatis from the liver tissue of the operating area, avoiding accidental damage from liver resection.
2. When there is adhesion on the porta hepatis, especially those that were caused by previous hilar surgeries, it is usually difficult to separate the porta hepatis from the anterior and is better to take the left approach to reduce intraoperative bleeding and operative injury.

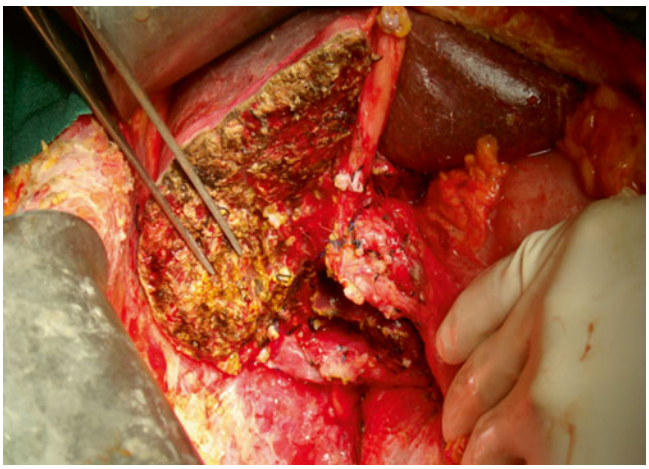

Fig. 12.9 The raw surface of the remnant liver after right hepatic trisectionectomy

Although the two surgical methods described above are excellent for the liver resection of most patients, relative contraindications exist. These techniques should not be used in patients with anatomic variation in the porta hepatis to avoid portal damage. If the tumor is invading the porta hepatis, the Glisson's pedicle approach is usually difficult and may cause tumor rupture; in this case, the traditional method of gradually dissecting porta hepatis is considered better. However, for experienced liver surgeons who are familiar with liver anatomy, the Glisson's pedicle approach and round ligament approach have become important methods of hepatectomy and are applied to tricky surgeries, including triple liver resection and mesohepatectomy, and make these surgeries simple and safe.

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Anatomical Liver Resection

13

Eric C.H. Lai, Stephanie H.Y. Lau, and Wan Yee Lau

13.1 Introduction

In 1952, Lortat-Jacob reported the first successful anatomic right hepatectomy for cancer [1]. It is through better understanding of hepatic segmental anatomy and refinements in intraoperative ultrasound (IOUS) that anatomical segment-based liver resection gradually matures in the past 30 years [2–5]. Segment-based liver resection allows maximal preservation of non-tumorous liver parenchyma while achieving adequate tumor resection margins. Segment-based liver resection then further develops into subsegment-based liver resection.

This chapter illustrates the concept and the techniques of anatomical segment- or subsegment-based liver resection.

13.2 Rationale of Segment-Based Liver Resection

In 1897, Cantlie first described the main anatomical dividing plane between the right and the left livers by showing that it was not along the plane of the falciform ligament but along the principle plane (Cantlie's line, or better Cantlie's plane) which extends from the gallbladder fossa to the inferior vena cava [6]. Couinaud refined the functional anatomy of the liver and demonstrated that the liver can be divided into four sectors and eight segments [7]. The eight segments are numbered clockwise in a frontal plane. The right liver which is nourished by the right hepatic artery and the right portal vein consists of segments 5–8; the left liver, which is nourished by the left hepatic artery and the left portal vein, consists of segments 2–4. The caudate lobe, or segment I, is nourished by branches from both the right and the left hepatic arteries and portal veins. Each of these Couinaud segments receives its own tributaries from the portal pedicle, or portal triad (hepatic artery, portal vein, and bile duct), and drains independently into tributaries of the hepatic veins. Each segment is therefore an independent functional unit [8]. Thus, each Couinaud segment can be resected individually, or in combination with other liver segments. Liver resection basing on liver segments is called segment-based liver resection. Scheele in 1989, in studying corrosive casts of the human liver after filling of the portal structures and subtotal removal of small tributaries, concluded that the portal pedicles leading to the peripheral liver segments 2, 3, 6, and 7 are characterized by a large main trunk and a treetop-like peripheral arborization. In contrast, structures to the central segments 4, 5, and 8 show an early ramification, which is bush-like and fan-shaped, aligned on the body longitudinal axis [9]. Later studies by Lau showed that segment 1, although not mentioned by Scheele, like the other central segments, also has a bush-like or fanlike distribution of the portal triads [10]. As a consequence of these portal triad arrangements, resection of a peripheral liver segment is technically easier than a central liver segment. Also, because of the early branching of the portal triad to a central liver segment, subsegmental resection is technically easier for a central liver segment (1, 4, 5, 8) than a peripheral segment (2, 3, 6, 7). This is fortunate because most of the extended liver resections involve resection of part of a central liver segment/subsegments, e.g., extended right hepatectomy involving resection of part of segment 4, and extended left hepatectomy involving parts of segment 8 and/or 5. Also, isolated partial resection of caudate lobe and subsegmentectomy of segments 4, 5, and 8 is possible, thus opening the door to subsegment-based liver

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resection. The Brisbane 2000 system of nomenclature of hepatic anatomy and resections has also been introduced to provide a universal terminology in order to have better communications among surgeons [11, 12].

There are a number of theoretical advantages of segment-based (or to a lesser extent subsegment based) liver resection [13–18]. The anatomical boundaries between the individual liver segments or subsegments are not crossed by large branches of the portal triads (hepatic artery, portal vein, and bile duct). Therefore, these anatomical boundaries are relatively avascular planes which facilitate surgical resection and decrease intraoperative blood loss. Similarly, by avoiding damages to the main trunks of the portal triad, segment-based (or subsegment based) liver resection avoids leaving behind ischemic liver parenchyma tissues. This decreases the risk of postoperative infection and bile duct fistulation. Also by predetermining the liver segments (or subsegments) to be removed and by following the intrahepatic anatomical plane during parenchymal transection, an adequate resection margin can be guaranteed, while at the same time the largest amount of non-tumorous liver parenchyma can be preserved. This is particularly important for patients with cirrhotic livers. Lastly, segment-based (and to a lesser extent subsegment based) resections have been proposed as means of improving curability of surgical treatment for hepatocellular carcinoma (HCC) [13–18]. Because HCC has a tendency to metastasize via the portal vein, resection of liver parenchyma fed by portal venous branches bearing the tumor is a logical method to eliminate potential intrahepatic metastases. Indeed, vascular invasion and intrahepatic metastases are the risk factors that most strongly influence postoperative prognosis. As early satellite metastases lie in the same liver subsegment or segment as the main tumor, subsegment-/segment-based liver resection should be used to give the best chance of oncological tumor clearance.

In modern liver surgery for HCC, subsegment-/segment-based liver resection is now accepted as the best option for surgical management of HCC, especially in patients with cirrhosis because it optimizes the balance between oncological clearance and the need to spare functioning liver parenchyma. However, its real clinical benefit is still controversial. There is still a lack of good evidence from randomized studies to support this view, and there are also conflicting evidences from non-randomized studies [19–28]. The majority of studies comparing anatomical with non-anatomical liver resections on HCC are reports coming from Japan. In the medical literature, almost half of the published non-randomized studies showed better disease-free survival and overall survival after anatomical liver resection [19–23], while the remaining half of the published non-randomized studies showed similar disease-free survival and overall survival after anatomical and non-anatomical liver resections, and the recurrence pattern after the two types of liver resections were similar [23–28]. However, these data are difficult to evaluate systematically due to the heterogeneities in number of tumors, tumor size, liver function, cirrhotic status, and surgical techniques in these different retrospective studies.

Although it is controversial whether subsegment-/segment-based anatomical liver resection improves survival in patients with HCC, whether to perform anatomical resection or non-anatomical resection in patients with colorectal liver metastases is less controversial. With medical evidences mainly coming from non-randomized studies [29–32], early survival data were in favor of anatomical resection [29], while long-term survival data in almost all studies showed no difference between anatomical and non-anatomical resections [30–32]. This difference may be explained by the difference in tumor biology between HCC and colorectal liver metastases. Metastatic liver lesions develop from blood-borne tumor cells circulating throughout the body. Anatomical liver resection may not offer the same advantage for these lesions as for HCC which arises within a subsegment of the liver and might thus benefit from removal of the complete functional liver unit.

13.3 Techniques of Subsegment-/Segment-Based Liver Resection

Application of principles of subsegment-/segment-based liver resection has been facilitated by advances in liver imaging techniques. In preoperative investigations, ultrasonography (USG), computed tomography (CT) scan, and magnetic resonance imaging (MRI) can relate the location of the tumor to the intrahepatic anatomy. Subsegment-/segment-based liver resection requires a careful preoperative evaluation of the target subsegment/ segment which contains the tumor in relation to the branches of the portal triad which supply and the branches of the hepatic vein which drain the subsegment/segment.

Recent developments in radiological technology have enabled preoperative planning using a three-dimensional (3D) image-processing software. This 3D-CT technique provides accurate visualization of liver segments and their related vascular structures and accurate planning of resected volumes and residual liver volumes. A realistic virtual image of the tumor's location in the liver facilitates a surgeon to visualize the anatomic part of the liver that needs to be resected. Surgeons can also correlate preoperative 3D imaging findings with intraoperative ultrasound findings to plan liver resections. Another advantage of computer-assisted liver surgery is the application of virtual hepatectomy to help designing and planning of operations. However, the need for an accurate alignment between preoperative 3D imaging data and real intraoperative findings remains to be adequately addressed, since the liver is subject to deformation and respiratory movements during surgical procedures [33–35].

Anatomical live resection is traditionally done according to the surface anatomy of the liver, by intraoperative ultra-

sound (IOUS), by superficial dye staining generated by injecting dye into the supplying portal branch followed by cautery markings on the liver surface, or by the ischemic territory generated by shutting off the blood supply to the future resection territory. Despite several methods which have been proposed by liver surgeons, subsegment-/segment-based resection is still technically demanding, including the definition of the subsegment-/segment borders on the liver surface and on the liver parenchymal transection plane.

There are five methods to identify the intersegmental or intersubsegmental plane in the liver:

13.3.1 Surface Anatomy of the Liver

Using the principle plane which runs from the gallbladder fossa to the inferior vena cava, a right or a left anatomical hemihepatectomy can be carried out. If the falciform ligament which separates segments 2 and 3 from segments 4 to 8 is also used, three more anatomical liver resections can be carried out: left lateral sectionectomy (resection of segments 2 and 3), right trisectionectomy (resection of segments 2–5 and 8), and isolated resection of liver segment 4. If necessary, an extended right hepatectomy (resection of liver segments 5–8 + part of segment 4) or an extended left hepatectomy (resection of segments 2–4 + part of segments 5 and 8) can be carried out. A left trisectionectomy (resection of liver segments 2–5 and segment 8) should best be carried out with the help of IOUS to identify and to preserve the right hepatic vein. Using the Takasaki's Glissonian Pedicle Transection Method of hepatic resection [36], the right anterior sectional portal triad and the right posterior sectional portal triad can be isolated and slinged at the porta hepatis. By tightening the sling around the right anterior sectional portal triad, the right anterior section (liver segments 5 and 8) becomes ischemic and changes color and the boundaries can be marked on the liver surface. Similarly by tightening the sling around the right posterior sectional triad, the right posterior section (segments 6 and 7) can be marked on the liver surface. Thus, this Takasaki's Glissonian sheath approach helps to identify the liver surface markings for four more anatomical liver resections: right posterior sectionectomy (resection of liver segments 6 and 7), right anterior sectionectomy (resection of liver segments 5 and 8), central liver resection of liver segments 4, 5, and 8, and left trisectionectomy (resection of liver segments 2 to 5 and 8).

13.3.2 Surface Anatomy + IOUS

This method is to trace the borders of the liver segments on the surface of the liver using surface anatomical landmarks and hepatic and portal venous structures on IOUS [2, 3, 37]. In general, the steps of IOUS in segment-based liver resection are as follows: (1) a general inspection of the whole liver to detect unexpected lesions not detected preoperatively; (2) a systematic anatomical study to trace the three hepatic veins, the portal bifurcation, and its branches so that the individual Couinaud liver segment can be determined (please see latter part of the text); (3) locate the tumor in the liver segment(s); (4) determine the liver segment(s) to be resected; (5) mark the line of parenchymal transection on the surface of the liver; and 6) redetermine the resection margin by measuring the planned liver parenchymal transection plane to the edge of the tumor.

The three major hepatic veins divide the liver into four sectors. The division between the right and the left hemiliver is along a plane which runs from the gallbladder fossa to the inferior vena cava, i.e., the principle plane (Cantlie's line). Inside this principle plane runs the middle hepatic vein which can be shown on IOUS. The left hemiliver is further divided into the lateral sector and the medial sector along a plane which runs the left hepatic vein (left medial sector – segments 3, 4; left lateral sector – segment 2). On surface anatomy, the medial sector is divided by the falciform ligament into segments 3 and 4. Segment 4 lies between the principle plane and the falciform ligament. The right hemiliver is divided into the right anterior and the posterior sectors along a plane which runs the right hepatic vein. Each of these two sectors consists of two segments (right anterior sector – segments 5, 8; right posterior sector – segments 6, 7). There is no surface anatomical landmark in the right hemiliver to identify the individual segments. The individual liver segments (segments 5, 6, 7, 8) in the right hemiliver can be determined by tracing the origins of the upward and downward branching of the right anterior sectoral portal vein (upward to segment 8, downward to segment 5) or the right posterior sectoral portal vein (upward to segment 7, downward to segment 6). The caudate lobe (segment 1) is the dorsal portion of the liver lying posteriorly and embracing the retrohepatic inferior vena cava. It is mainly recognized by its anatomical landmarks.

After marking the liver segments on the surface of the liver, the liver parenchyma is then transected and the pedicles of the vessel and bile ducts of the relevant liver segments are divided during the parenchymal transection. It should be noted that in the use of this method, i.e., segment-based liver resection, it is essential that the surgeons should have a detailed knowledge of the intrahepatic vascular anatomy and the skills in IOUS.

13.3.3 Ultrasound-Guided Puncture of Portal Vein Branch and Injection of Dye

The portal branch supplying the liver segment (or subsegment) to be resected is punctured under ultrasound guidance [2, 3, 38]. A few milliliters of methylene blue or indigo car-

mine dye are then infused into the portal branch. Each portal vein branch is punctured 1–2 cm distal to its origin to avoid dye reflux, and the direction and velocity of the infusion are controlled at IOUS. To prolong dye staining, the hepatic artery is clamped at the hilum before the portal vein branch is punctured. The dye stains the liver segment (or subsegment) corresponding to the limits of the liver transection plane and is marked with electrocautery (Fig. 13.1). Transection is then carried out. Instead of using dye, the other method is to use balloon inflation with occlusion of the targeted portal vein branch after introducing a Chiba needle, a guidewire, and a tract dilator [39]. These techniques require great expertise in interventional USG and for this reason has not gained wide acceptance. However, these techniques rely on making marks on the liver surface to recognize the target territory and thus surgeons have to determine the three-dimensional resectional plane on the basis of the targeted vessels and on occasions based on educated guesswork as to which vessels to puncture. The dying agent may be rapidly washed out, resulting in loss of the stained area. For this difficulty, there are modifications of this technique.

Torzilli et al. reported the technique of ultrasound-guided vessel compression [40, 41]. The procedure was reported to be feasible in all the eligible patients in their study, and a demarcation territory was obtained in all the patients within 1 min of bimanual IOUS-guided compression. The ultrasound-guided vessel compression technique starts with liver mobilization. Afterward, the most peripheral portal pedicle feeding the tumor is identified by IOUS. With this, the level targeted for compression is detected. At this point, the hemiliver where the tumor is located is partially mobilized to allow handling the liver along the dissection. The surgeon's left or right hand is then placed below the right or left hemiliver, respectively, while the IOUS probe handled by the surgeon's other hand is placed above the liver; with IOUS guidance, both hands are positioned at the level of interest which corresponds to the most distal portion of the vessel in relation to its origin but proximal to the tumor to be removed. Using the left/right fingertips and the IOUS probe itself, the surgeon compresses bilaterally the liver at the targeted position, resulting in the compression of the portal pedicle feeding the tumor previously identified. This maneuver is constantly monitored by real-time IOUS probe, and it is maintained until the surface of the targeted liver territory begins to change in color. At that time, the assistant surgeon marks the discolored territory with coagulation, and the compression is released.

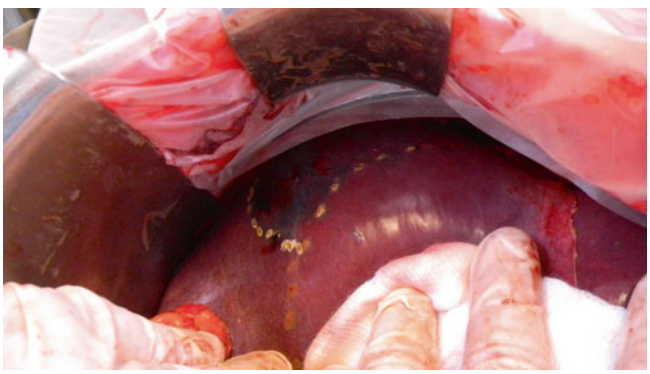

Fig. 13.1 Segment 7 was outlined after indigo carmine dye injection into the corresponding portal branch

Inoue et al. reported a novel application of fused images comprising of a macroscopic view and indocyanine green fluorescence imaging (fusion IGFI) for open anatomical resections making use of the three-dimensional staining ability and a clearer demarcation attained by this method than what can be attained by the conventional technique [42]. Fusion IGFI achieved valid demarcation in 23 of 24 patients (95.8 %), whereas conventional demarcation technique (CDT) achieved valid demarcation in only 10 patients (41.7 %). The IGFI staining technique involves either systemic venous injection of a dye after clamping the inflow to the target vessels (the IV method) or portal puncture and direct injection (the PV method). For the IV method, after dissection of the hepatic hilum, arterial and portal branches of the planned resected hemiliver, section, or segment are exposed and taped. These inflow vessels are first temporarily clamped to confirm the demarcation line and intrahepatic blood flow by US and then ligated and divided for a subsequent intravenous bolus injection of 2.5 mg of ICG. Ten to twenty seconds after the ICG injection, the splanchnic arteries and veins appear enhanced on fusion IGFI, and ICG fluorescence is accumulated in the future remnant territory as counterstaining. For the PV method, after puncturing of the target portal branch, a mixture of 5 ml of indigo carmine, 2.5 mg of ICG, and 0.5 ml of Sonazoid is injected into the branch under contrast-enhanced IOUS guidance with the hepatic artery clamped. The stained region is confirmed by macroscopic inspection, fusion IGFI, and contrast-enhanced IOUS. The IGFI staining technique is chosen on the basis of the CDT required: the IV method is chosen for a hemihepatectomy, sectionectomy, or left-sided segmentectomy where isolation of the target portal branch is usually possible, whereas the PV method is used for a right-sided segmentectomy or resection in which hilar dissection is judged to be difficult due to technical issues.

13.3.4 Preliminary Control of the Vascular Pedicles of the Segment to Be Removed

The main hepatectomies (right and left hepatectomy, right posterior sectionectomy, right anterior sectionectomy) can be performed simply by occlusion of the inflow at the hilum and waiting for a demarcation plane to appear. This approach

is especially useful in resection of the segments of the right liver. The right and the left hepatic pedicles are dissected extrahepatically on the undersurface of the liver. Lowering of the liver plate helps in increasing the extrahepatic length of these pedicles. This technique can also be applied in laparoscopic approach of liver resection [43]. By dissecting and tracing the right pedicle distally, the right anterior sectoral pedicle (segments 5, 8) and right posterior sectoral pedicle (segments 6, 7) can be found. Similarly, by dissecting and tracing the left pedicle distally, the segment 4 pedicle and the segments 2/3 pedicle can be found. Further dissecting distally to expose the pedicles inside the liver (segmental pedicles to the liver segments) requires liver parenchymal transection [44–46]. In most cases, ligating the portal pedicle within the targeted segment from the porta hepatis is difficult, and the ligation needs to be done at a point inside the liver parenchyma. IOUS provides a crude demarcation line of the segment on the liver surface, but an accurate identification is still difficult to achieve. Occlusion of the relevant pedicle by a bulldog clamp results in a change of color of the liver segment. The arterial and portal pedicles are ligated and divided at the end of the parenchymal resection. This technique requires more tissue dissection and longer operating time than the other techniques, and it is technically more difficult in patients with cirrhosis and portal hypertension.

13.3.5 Selective Portal Venous Occlusion Using a Balloon Catheter through a Branch of the Superior Mesenteric Vein

This technique is carried out during open surgery [47]. The liver is completely mobilized. A French 6 balloon catheter is inserted into the portal vein via an intestinal branch of the superior mesenteric vein. The catheter is guided into the corresponding branch of the portal vein (either the right or the left) where the HCC is situated, using the surgeon's hand in the porta hepatis. Once the tip of the catheter is in the intrahepatic portal venous system, further advancement of the catheter into the sectoral and the segmental portal venous branches is done by rotating and advancing the catheter using the trial-and-error method. Guidance of the tip of the catheter into the desired portal venous branch is assisted with ultrasound and the surgeon's hand in the porta hepatis. When the balloon catheter is in the right position, the balloon is inflated with 3 ml. of normal saline to occlude the venous branch. A few milliliters of methylene blue are injected through the catheter to delineate the liver segment to be resected. Any individual liver segment or sector can be identified by the change or absence of change in color after injection of dye, e.g., if the catheter has been directed into the right liver, injection of dye into either the anterior or posterior sectoral branch can identify the right anterior (segments 5, 8) and posterior (segments 6, 7) sectors. Similarly, if the catheter has been directed into the anterior sectoral branch, injection of contrast will stain either segment 8 or segment 5. Thus, by subtraction, the boundaries of an individual segment can be identified. The line of demarcation is marked on the liver surface with a diathermy. The procedure is repeated if more than one liver segment needs to be delineated. The time required to get the catheter in the right position is around 10 min. The hepatic parenchyma is then transected along the line of demarcation. After hemostasis on the raw liver surface, the balloon catheter is deflated and removed. The hole in the portal venous branch where the catheter entered to delineate the resected liver segment is closed. The branch of the superior mesenteric vein is ligated after the catheter is removed.

13.4 Non-anatomical Liver Resection

Non-anatomical resection is a more suitable operation than subsegment-/segment-based liver resection under two situations: first when the tumor is situated at the border of several segments and second when the tumor is small and is situated peripherally at the edge of the liver. Under such a situation, a wedge excision made in the form of an arch or box shape is a simpler operation than a subsegment-/segment-based liver resection. Wedge excision should not be done in a V shape because of the higher chance of the resection margin being involved by tumor on histological study.

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Mesohepatectomy

14

Hong Wu, Yong Zeng, Jianguo Qiu, and Haipeng Meng

14.1 Anatomical Orientation of the Central Liver

The central liver includes the right anterior lobe and the left medial lobe (Fig. 14.1). On the left is the left interlobar fissure, on the right is the right interlobar fissure, and between the two fissures lie the left and right hepatic veins and their branches. On the visceral surface are three structures of the hepatic hilum, namely, the hepatic artery, the portal vein, and the bifurcation of the bile duct. Behind the hepatic hilum is the inferior vena cava. The middle hepatic vein is located in the middle hepatic fissure and drains the blood of the central liver [1].

14.2 Definition of Mesohepatectomy

Mesohepatectomy is the resection of the right anterior and left medial lobes of the liver (IV, V, VIII±I in Couinaud's scheme). The indications for this procedure are tumors that lie between the right anterior and left medial lobes, as well as tumors in the right anterior and left medial lobes that invade the middle hepatic vein which requires en bloc resection.

14.3 Evolution of Mesohepatectomy

In 1965, Wu et al. first reported the use of a mesohepatectomy to treat central hepatic tumor [2].

In 1972 McBride was the first to define mesohepatectomy as resection of Couinaud's segments IV, V, and VIII, which laid the anatomical foundation for this procedure.

In the 1980s, due to the technical difficulty of the procedure and the high incidence of complications, most central hepatic mass lesions were still treated by extended hemihepatectomy or trisegmentectomy [3–5].

In the 1990s, understanding of liver anatomy and relevant surgical techniques evolved, and mesohepatectomy was gradually accepted as a treatment for central hepatic mass lesions. During this period, further investigations were performed regarding the protection of hepatic vascular structures, neoadjuvant chemotherapy, and portal vein embolization [6–9].

In 2002, Chinese scholars suggested that central hepatocellular carcinoma should be defined as a tumor lying within 1 cm of the bifurcation of portal vein, the confluence of the three main hepatic veins to the IVC, or the retrohepatic IVC trunk.

In the early 2000s, with the increasing use of laparoscopic techniques, Machodo et al. were the first to report laparoscopic mesohepatectomy using an intrahepatic Glissonian approach [10].

In 2013, Zeng Yong of West China Hospital was the first to report an anatomical classification of central hepatic mass lesions [11].

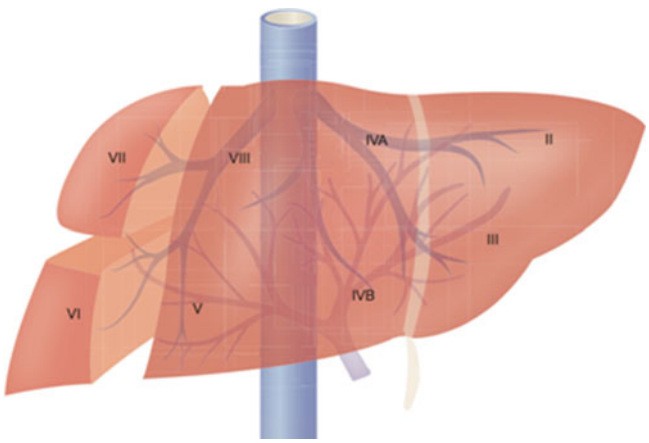

Fig. 14.1 The central liver includes the right anterior lobe and the left medial lobe

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14.4 Indications for Mesohepatectomy

Tumors of the central liver, including primary hepatocellular carcinoma, liver metastasis, hepatic hemangioma, gallbladder carcinoma, and hilar cholangiocarcinoma, as well as other processes such as central liver hepatolithiasis, damage of the central liver which cannot be fixed, chronic liver abscess and hepatic echinococcosis, etc., are all suitable for mesohepatectomy, especially for patients with poor liver function or cirrhosis.

14.5 Conventional Classification of Mesohepatectomy and Its Key Technical Points

14.5.1 In Classical Regular Mesohepatectomy

Glisson's pedicle is first dissected; then, the afferent and efferent canals of the central liver are dissected and divided, and the liver parenchyma is transected.

Advantage: *Precision*

Disadvantage: *Technically demanding*

Key technical points: First dissect the left Glisson's pedicle. Dissect the first porta hepatis, and expose the confluence of the left and right hepatic ducts and the bifurcation of the proper hepatic artery. Dissect along the left hepatic artery until its left medial branch is exposed, and suture and divide this branch. Be careful to protect the left hepatic duct, as it is accompanied by the trunk of the left hepatic artery in the inferior aspect of the ligamentum teres hepatis. Beneath the divided left medial branch of the left hepatic artery is the left medial branch of the left hepatic duct, which should be divided and sutured; alternatively, this branch can be divided during the transection of the parenchyma. The left hepatic artery and the left hepatic duct are gently lifted to expose the left portal branch which lies beneath theses structures, and dissection should be continued anteriorly to expose the left medial branch of the portal vein, which should be carefully clamped and sutured. This completes the dissection process for the left Glisson's pedicle; a similar process should be performed on the right Glisson's pedicle. At the bifurcation of the proper hepatic artery, the common hepatic duct should be pulled to the left to provide a better exposure as the right hepatic artery is commonly found the behind common hepatic duct. The right hepatic artery is dissected along the right portal vein fissure to expose the right anterior and posterior branches of the right hepatic artery, and its right anterior branch points to the gallbladder bed while the right posterior branch points to the bottom right almost vertically [20]. The right anterior branch of the hepatic artery is sutured and divided, and then the right anterior branch of the right hepatic duct, which is commonly found next to the hepatic artery, should be divided and sutured carefully. The division of the right bile duct can also be carried out during transection of the parenchyma. In the end, the liver parenchyma is transected, along with the relevant canals. Now that the central liver is basically devascularized, the dividing line between the central liver and the left lateral lobe, as well as the dividing line between the central liver and the right posterior lobe, can be seen on the surface. The transection line is marked using an electronic knife, and the liver parenchyma is transected using CUSA, a water jet dissector, a LigaSure, or a hemostat. During this process, relatively large relevant canals should be divided and sutured, ligated, or clipped, using titanium clips.

14.5.2 Mesohepatectomy with Transection of the Glisson's Pedicle

Advantage: There is no need to dissect the Glisson's pedicle when dissecting the hepatic pedicle.

Disadvantage: A lack of precision creates a certain risk of subsidiary injury, especially for individuals with complicated anatomical variation of canals entering the liver.

Key technical points: First dissect the gallbladder, and then find the hepatic pedicle of the right anterior lobe at the intersection of the longitudinal axis of the gallbladder and the lower limb of the liver parenchyma. Bluntly dissect the lateral parenchyma to within 0.5 cm of this intersection, and then use straight hemostatic forceps to take a suture from the back of the hepatic pedicle of the right anterior lobe and ligate the pedicle. The dividing line between the right anterior and posterior lobes can be seen on the parenchyma surface. After ligating and dividing the Glisson's pedicles from the right to the round ligament one by one, the left dividing line can be exposed. The key technical point is to avoid opening the Glisson's pedicle; rather, bluntly dissect between the pedicle and the parenchyma. Now several portal branches of the left medial lobe are ligated and divided, while the arteries are not involved. The left ischemic line can be seen after all portal branches of the left medial lobe are ligated. Finally, transect the liver parenchyma [11].

14.5.3 Irregular Mesohepatectomy

Compared with the two procedures described above, irregular mesohepatectomy is less demanding and less complicated. In this procedure, the transection line is directly

marked on the liver surface without dissecting the porta hepatis. The right transection line extends from the notch of the right liver to the inner side of the confluence of the right hepatic vein and the IVC. The left transection line is the right margin of the falciform ligament. The actual transection line is placed 0.5 cm medially to the aforementioned lines, in order to avoid the right and left hepatic veins. This procedure is not precise but still provides satisfactory results. The key point is the use of patience and care during the operation in order to avoid hemorrhage [5, 12].

14.5.4 Laparoscopic Mesohepatectomy

Disadvantage: There is a high incidence of complications such as uncontrolled hemorrhage and bile duct damage because of the special anatomy of the central liver and anatomical variants of the intrahepatic vessels.

Advantage: Anatomical structures are magnified with the laparoscope; thus, regional structures are seen more clearly than in an open procedure. The dissections of the hepatic artery, the portal vein, and the hepatic vein are performed one by one and can be managed by careful dissection using instruments.

Key technical points: Set up pneumoperitoneum in a routine fashion, insert the instruments, and tilt the operating table l5–30° to the left as required. The surgeon stands between the patient's legs, assistants stand by either side of the surgeon, and the instrument nurse stands by the patient's right foot. Five or six ports are created (Fig. 14.2). Normally, the observing port is located 1 cm beneath the umbilicus. The main port is located 2–4 cm beneath the xiphoid when resecting the left aspect of the central liver and dissecting the left lobe's Glisson's pedicle, 4–6 cm beneath the xiphoid when resecting the right aspect of the central liver and dissecting the right lobe's Glisson's pedicle. Two or three ancillary ports are located at the intersections of the right costal margin with the midclavicular line and anterior axillary line. Pretreatment blocking is set up routinely at the porta hepatis, and the transection area is marked according to preoperative imaging, intraoperative exploration, and anatomical markers of the liver. First dissect the porta hepatis. Dissect the hepatoduodenal ligament, and mobilize the common bile duct, the left and right hepatic ducts, the proper hepatic artery and its two branches, and the portal trunk and its two branches, respectively. Clip and divide the left hepatic artery, the left branch of portal vein, and the left medial branch of the left hepatic duct, respectively. Suture and divide the right hepatic artery, the right branch of the portal vein, and the right anterior branch of the right hepatic duct, respectively, in the same way. Then transect the liver

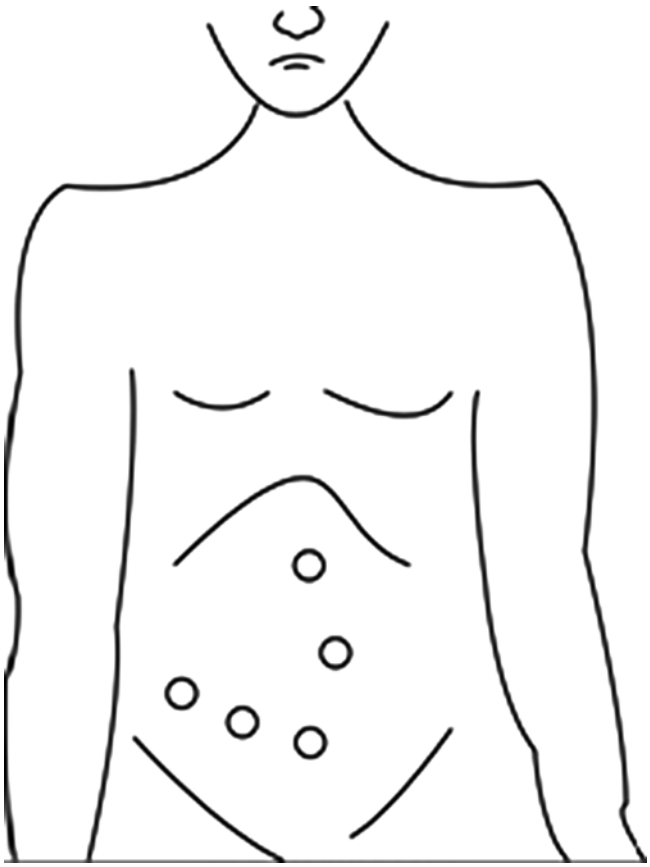

Fig. 14.2 Laparoscopic mesohepatectomy; five or six ports are created

parenchyma, which is commonly performed using a laparoscopic ultrasonic scalpel. Finally, handle the transection and relevant canals using the same method as in an open procedure.

14.6 West China Classification of Central Hepatic Mass Lesions [11]

14.6.1 Background

Because of the shortage of the literature and guidelines regarding mesohepatectomy, as well as this procedure's difficulty and its high incidence of complications, many surgeons prefer to perform extended left or right hemihepatectomy instead. However, extended hemihepatectomy resects 60–70 % of the liver, leading to a high risk of postoperative liver failure and even death [5, 12, 13]. Although hepatectomy has progressed in precision due to techniques regarding donor liver resection, complications such as intraoperative hemorrhage, damage of afferent and efferent hepatic vessels, and postoperative bile leakage still pose great challenges for surgeons. Investigators at West

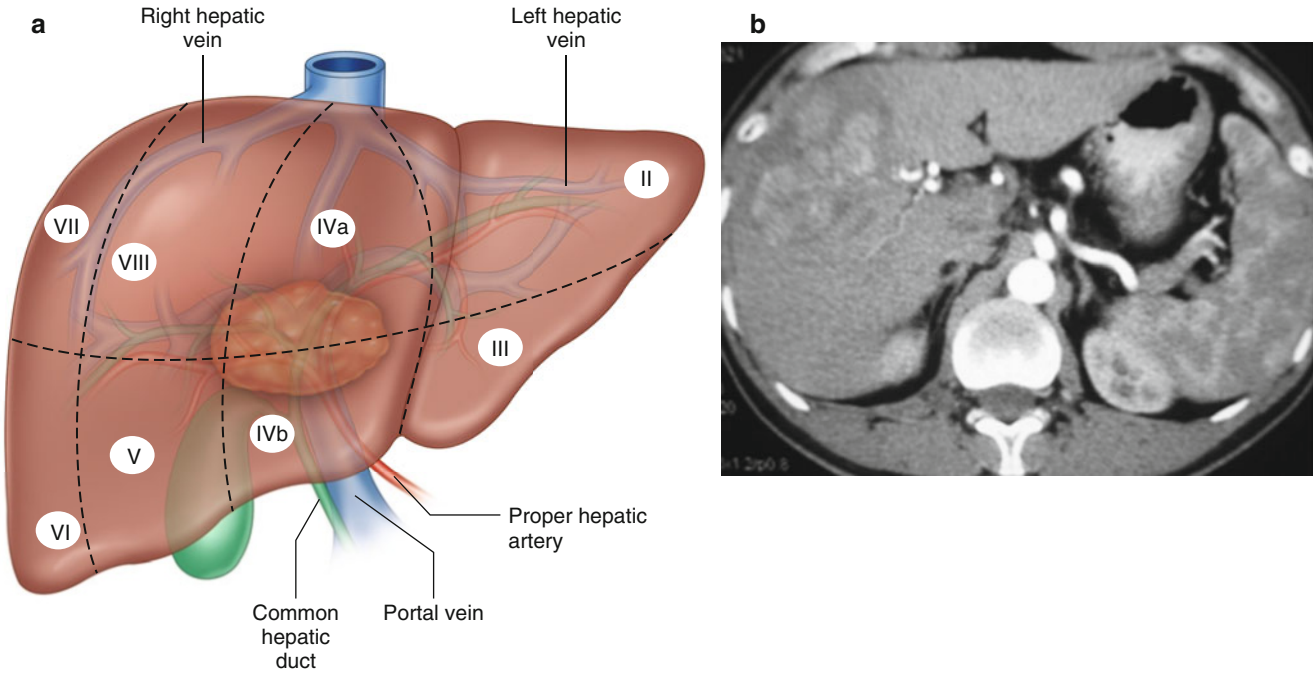

Fig. 14.3 (**a**) Type I is defined as a mass lesion that is proximal to the porta hepatis, approaching the portal vein, bile duct, and hepatic artery. (**b**) Type I is defined as a mass lesion that is proximal to the porta hepatis, approaching the portal vein, bile duct, and hepatic artery

China Hospital of Sichuan University collected clinical data from 356 patients diagnosed with central hepatic mass lesions between Jan 2005 and Dec 2011 and created a classification of mesohepatectomy and key points for each type of procedure, in an attempt to characterize and simplify each type of mesohepatectomy, prevent postoperative complications, and ensure safety [11].

14.6.2 Foundations of the Classification

① Established location of the lesion in the central liver, ② relationship of the lesion to the bile ducts and the portal vein branches of the porta hepatic, ③ relationship of the lesion to the hepatic veins of the second hepatic hilum, and ④ relationship of lesion to IVC.

14.6.3 Classifications

Central hepatic mass lesions are classified into four types. Type I is defined as a mass lesion that is proximal to the porta hepatis, approaching the portal vein, bile duct, and hepatic artery (Fig. 14.3). Type II is defined as a mass lesion lying proximal to the second hepatic hilum, approaching the hepatic veins (Fig. 14.4). Type III is defined as a mass lesion located between the porta hepatis and the second hepatic hilum without invading theses structures (Fig. 14.5). Type III can be further classified into two subtypes according to the relationship between the tumor and the retrohepatic segment of IVC. Type IIIa lesions are defined as tumor located proximal to the liver surface and at least 1 cm from the IVC; IIIb lesions are defined as tumors that are proximal to or invade the IVC. Type IV lesions are mass lesions that approach canals of both the porta hepatis and the second hepatic hilum (Fig. 14.6).

14.6.4 Clinical Significance

Type I: tumors invade the porta hepatis, approaching the left and right branches of the bile duct or portal vein, and require resection of segment IVa and part of segment IV (Fig. 14.7).

Type II: tumors lie proximal to IV second hepatic hilum, approaching the left or right hepatic vein, and require resection of segment IVa and part of segment V (Figs. 14.7, 14.8).

Type III: tumors are located between the porta hepatis and the second hepatic hilum without invading theses structures and require resection of segment IV and parts of segments V and VIII, if necessary. In type IIIa tumors, there is at least a 1 cm gap between the tumor and the IVC; type IIIb: tumors approach the IVC (Fig. 14.9).

Type IV: tumors are relatively large lesions that approach the canals of both the porta hepatis and the second hepatic hilum; these tumors require resection of segments IV, V, and VII±I (Fig. 14.10).

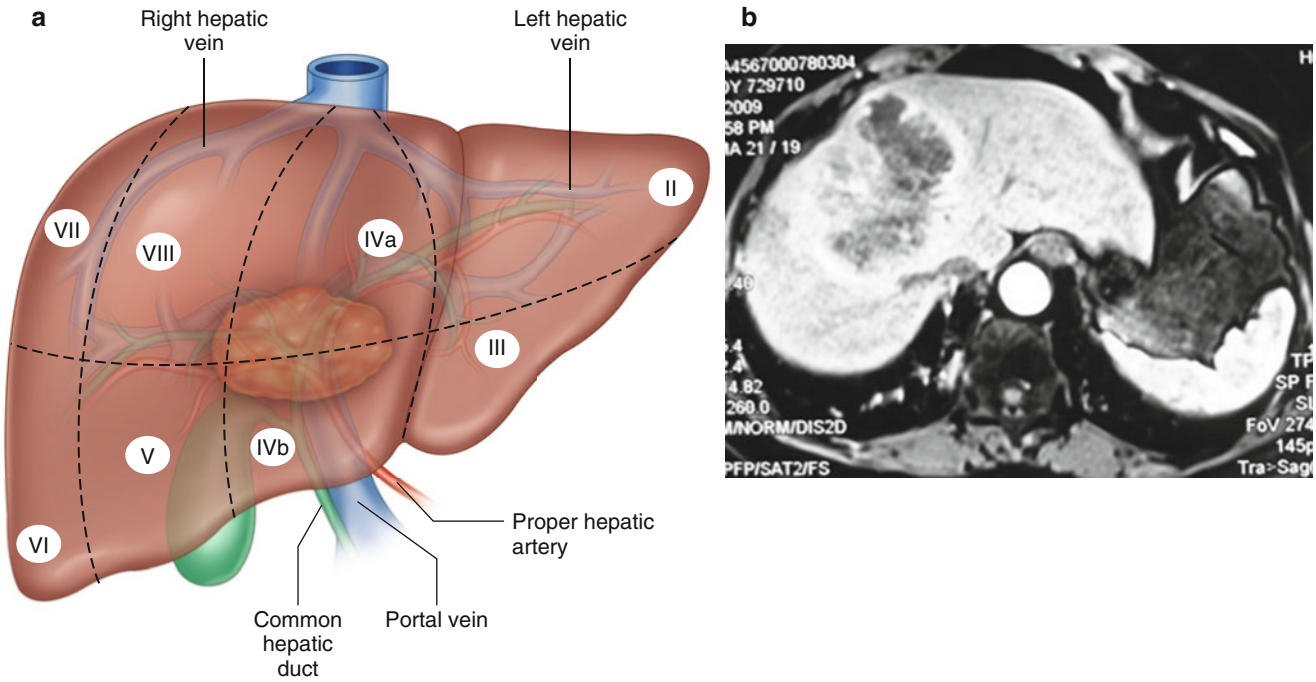

Fig. 14.4 (**a**) Type II is defined as a mass lesion lying proximal to the second hepatic hilum, approaching the hepatic veins. (**b**) Type II is defined as a mass lesion lying proximal to the second hepatic hilum, approaching the hepatic veins

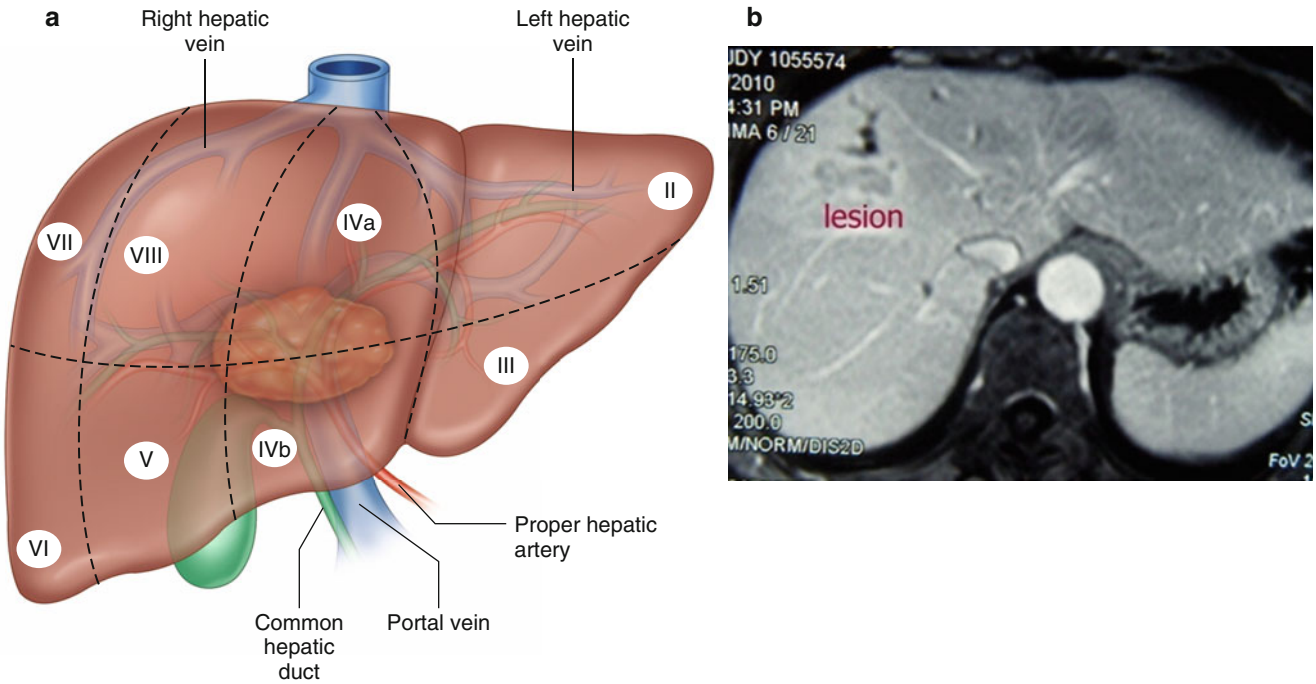

Fig. 14.5 (**a**) Type III is defined as a mass lesion located between the porta hepatis and the second hepatic hilum without invading theses structures. (**b**) Type III is defined as a mass lesion located between the porta hepatis and the second hepatic hilum without invading theses structures

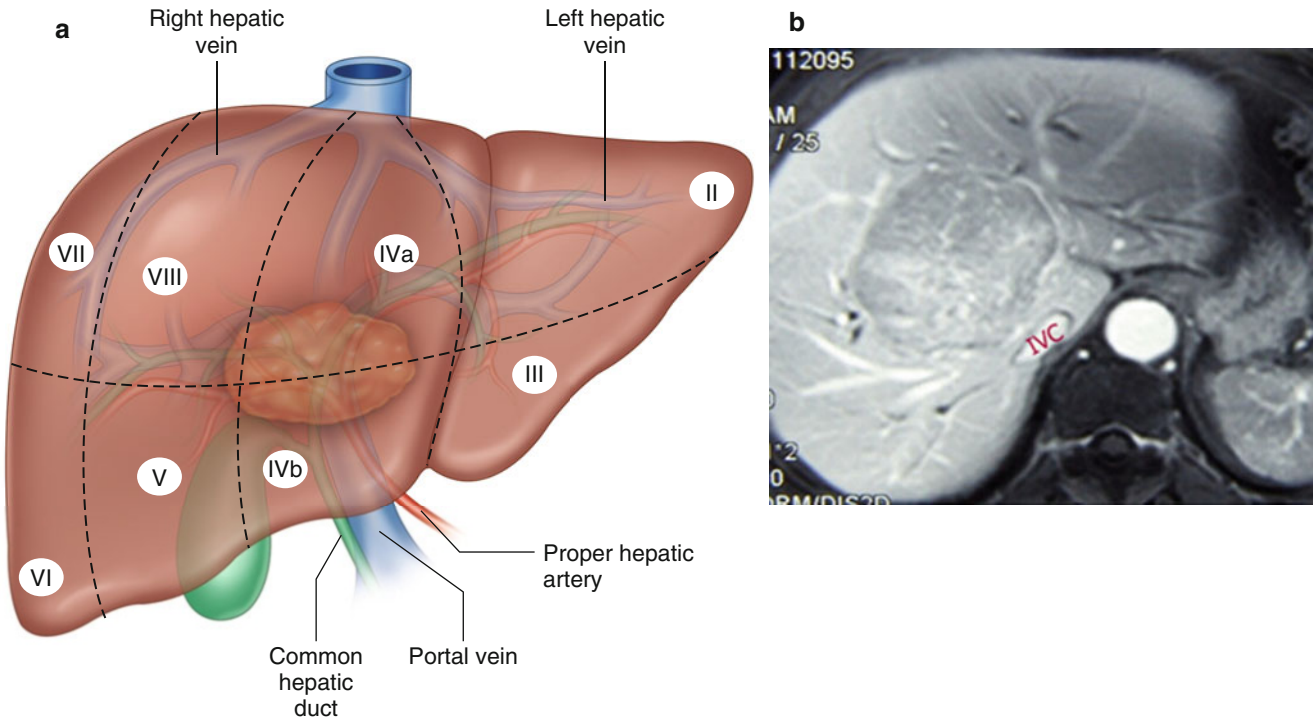

Fig. 14.6 (**a**) Type IV lesions are mass lesions that approach canals of both the porta hepatis and the second hepatic hilum. (**b**) Type IV lesions are mass lesions that approach canals of both the porta hepatis and the second hepatic hilum

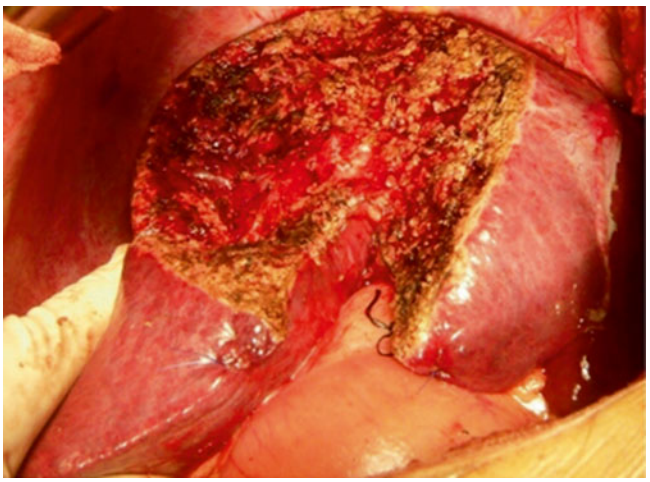

Fig. 14.7 Type I requires resection of segment IVa and part of segment IV

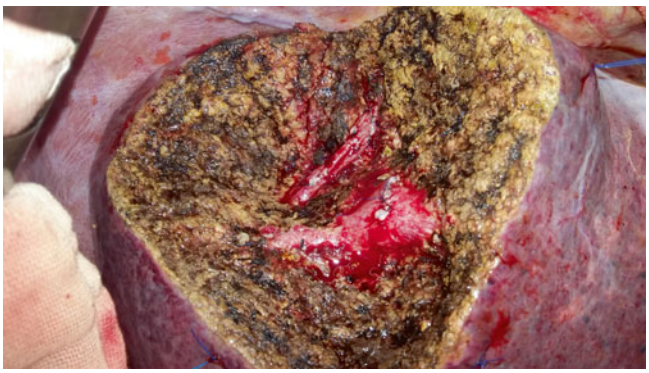

Fig. 14.8 Type II requires resection of segment IVb and part of segment VIII

14.7 Hepatic Vascular Occlusion

Surgery is planned preoperatively according to the aforementioned classification. In type I and type IV tumors, because important structures of the porta hepatis and the second hepatic hilum are invaded, it is difficult to perform hemi-occlusion. If cirrhosis and hemorrhage are not severe, no occlusion is needed. Pringle maneuver or total hepatic vascular occlusion can be performed when cirrhosis is significant.

In type I and type IV tumors, the tumor approaches the canals of the porta hepatis, making it easy to damage the bile duct when dissecting the porta hepatic. In such lesions, there is a higher incidence of postoperative bile leakage than in type II and III tumors. During the operation, normal saline or methylene blue can be injected into the cystic duct to detect bile leakage. If several sites of bile leakage are found, T-tube drainage can be used. However, some experts take a cautious attitude toward T-tube placement and instead choose to place a nasobiliary drain postoperatively.

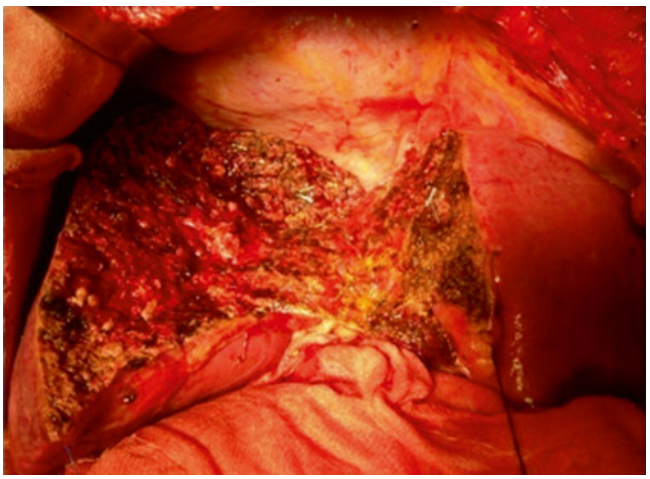

Fig. 14.9 Type III requires resection of segment IV and part of segments V and VIII, if necessary

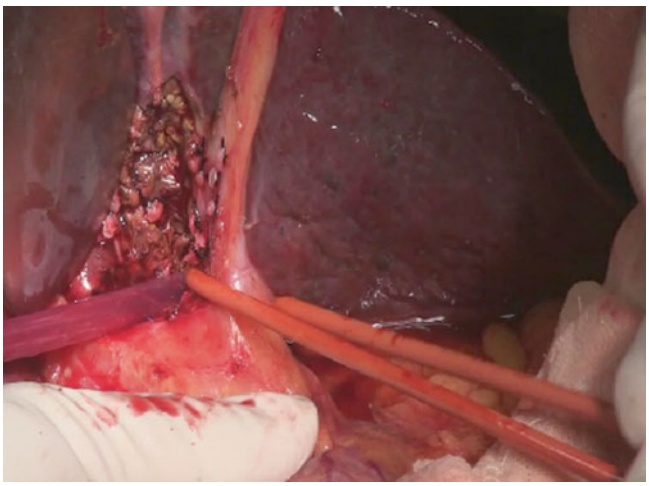

Fig. 14.11 Using "simple hemi-occlusion" was created by Yan in 1994

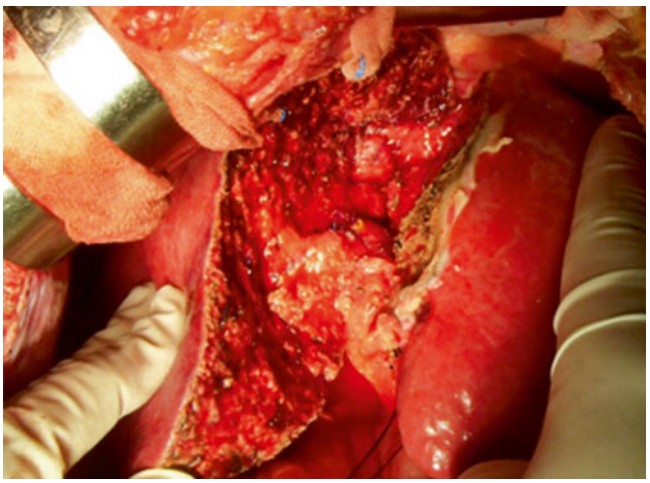

Fig. 14.10 Type IV requires resection of segments IV, V, and VII±I

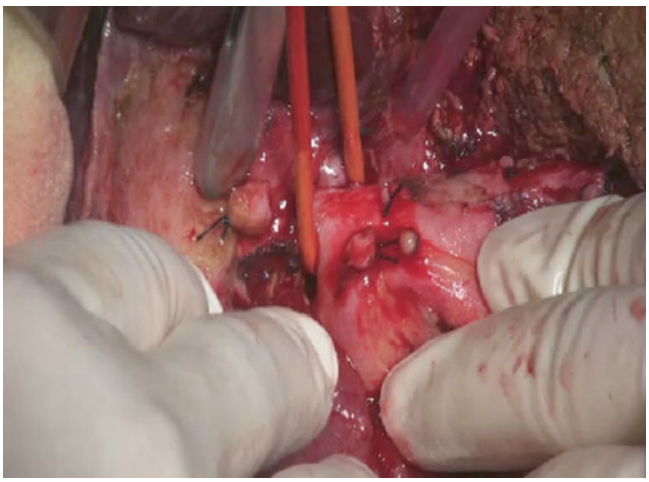

Fig. 14.12 Ligation and divide the right anterior portal branch

In type II and type III tumors, tumor approaches the second hepatic hilum, making it easy to dissect vessels and bile ducts in the left and right hepatic hila of the porta hepatic. In these cases, West China hemi-occlusion is proposed (Fig. 14.11).

14.8 Surgical Techniques

After resection of the gallbladder, the common hepatic duct is mobilized and retracted leftward to expose the right hepatic artery. Dissection continues toward the right portal fissure, exposing the bifurcation of the anterior and posterior branches. Then, dissect along the anterior and posterior portal fissures and divide the right anterior portal branch (Fig. 14.12) and the right anterior lobe branch of the right hepatic artery (Fig. 14.13).

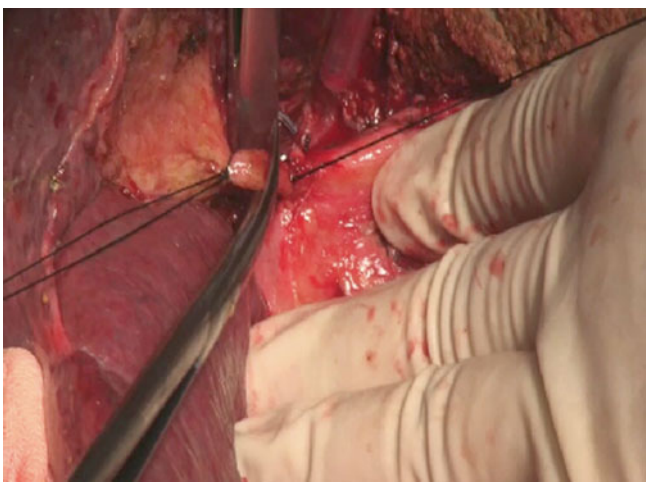

Fig. 14.13 Ligation and divide the right anterior lobe branch of the right hepatic artery

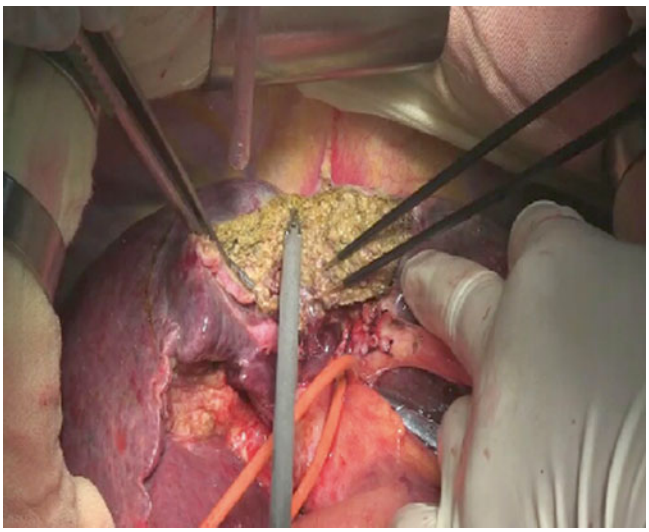

Fig. 14.14 Retract and occlude the left hepatic artery and the left portal vein, and transect the liver parenchyma between the left lateral lobe and the inner lobe from the inferior edge upward

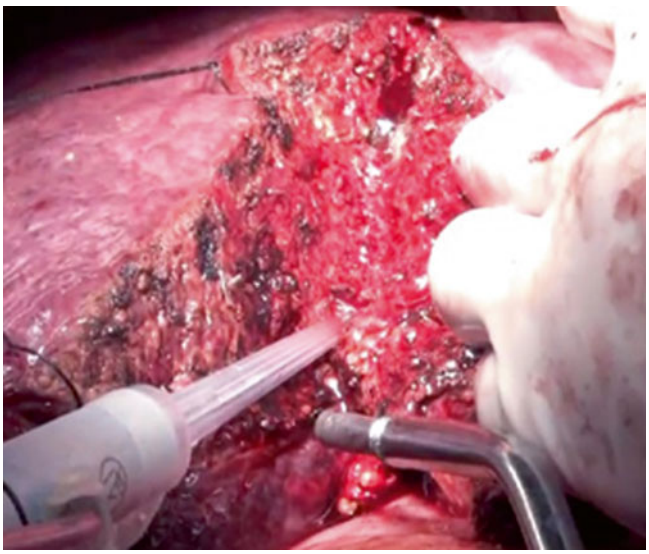

Fig. 14.16 Transection of the liver parenchyma using a CUSA

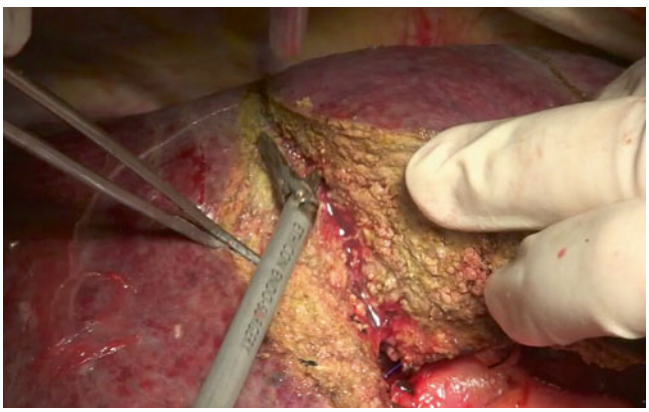

Fig. 14.15 Transect the liver parenchyma between the right anterior and posterior lobes

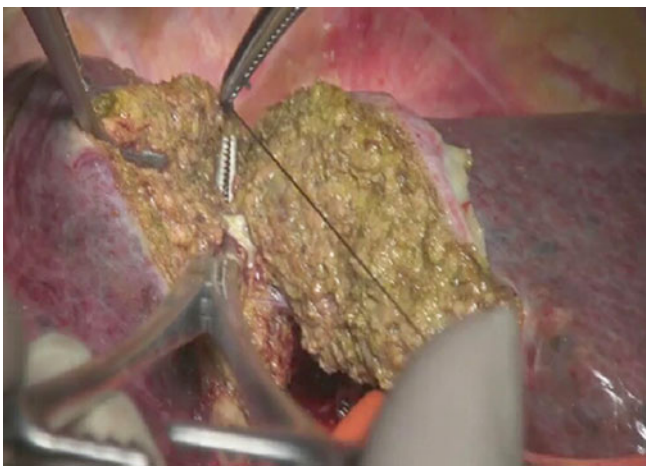

Fig. 14.17 Transection of the liver parenchyma using "hooking with ligation" created by Yan in 1994

Mobilize and retract the canals of the right hepatic hilum as preparation for hemi-occlusion. The middle hepatic vein should be dissected, sutured, and divided. Mobilize and retract the left hepatic artery and its surrounding connective tissue without dissecting the artery, and retract the round ligament of the liver ventrally. Dissect the serosa and connective tissue on the right side of the sagittal section to expose the sagittal section of the portal vein. Suture and divide the portal branches entering the left medial lobe one by one. Retract and occlude the left hepatic artery and the left portal vein, and transect the liver parenchyma between the left lateral lobe and the inner lobe from the inferior edge upward (Fig. 14.14).

When the left section is completed, retract the right hepatic hilum canals for right hemi-occlusion, and transect the liver parenchyma between the right anterior and posterior lobes (Fig. 14.15).

Transection of the liver parenchyma can be completed using instruments such as a CUSA (Fig. 14.16), an ultrasonic scalpel, a water jet scalpel, "hooking with ligation" (Fig. 14.17), or radiofrequency ablation.

14.9 Prevention and Treatment of Complications: Management of Sections and Bile Leakage

14.9.1 Prevention and Treatment of Complications

With developments in surgical techniques and perioperative management, the incidence rates of death and liver

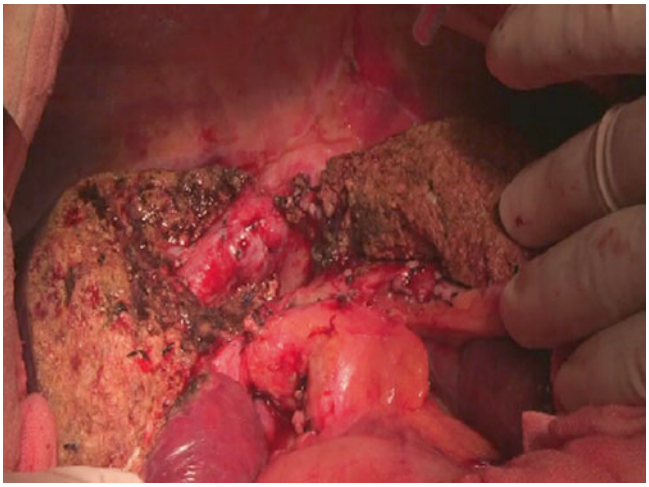

Fig. 14.18 Two large sections left after mesohepatectomy

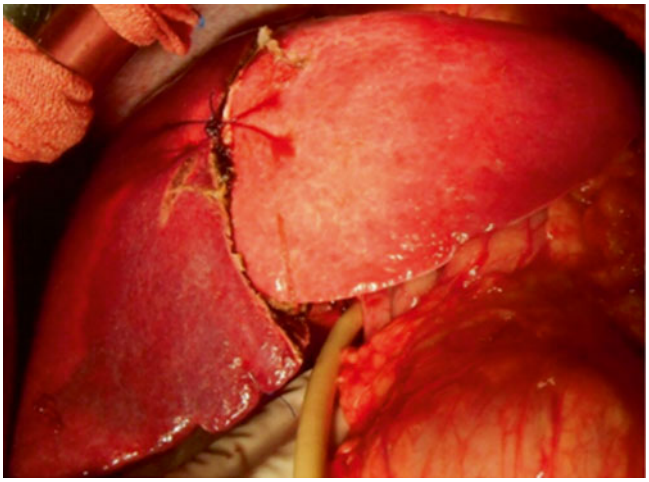

Fig. 14.19 Large sections sutured closed

failure after mesohepatectomy have declined drastically. However, the incidence of perioperative complications is still as high as 5.4–11.3 % [14, 15]. Mesohepatectomy poses great challenges for the prevention of complications, especially relatively uncommon but severe complications, such as sudden onset of pulmonary embolism, ARDS, acute renal failure, and acute liver failure. Intraoperative massive hemorrhage may be the main cause of the aforementioned severe complications. In order to prevent intraoperative hemorrhage and negative consequences of massive transfusion during or after surgery, the hepatic inflow occlusion time when transecting the liver parenchyma can be prolonged appropriately in patients without significant cirrhosis.

14.9.2 Transection of the Liver Parenchyma and Management of the Section

Clump crushing is widely used because of its simplicity and effectiveness. Complicated liver operations demand great efforts to control hemorrhage and preserve normal hepatic tissue. We recommend combined use of a CUSA and an electronic scalpel to ensure safety [16–18]. Many experts believe that after precise surgery, there is no need to routinely suture the sections closed, which can cause ischemia and even necrosis in some cases. We believe that the two large sections left after mesohepatectomy (Fig. 14.18) are inclined to hemorrhage and bile leakage postoperatively and routinely perform suturing and closure (Fig. 14.19). During suturing, the anatomical position of the left and right hepatic veins should be noted. When suturing meets resistance, no force should be used; rather, the suture should be attempted again. Packing and compression may help to control bleeding in the sections.

14.9.3 Prevention and Treatment of Bile Leakage

Bile leakage is the most common postoperative complication of mesohepatectomy, with an incidence of 6.5 %; however, most leaks heal spontaneously after adequate drainage. If the leak still exists after 2 weeks, ERCP can be performed to drain the bile. In order to prevent bile leakage, all bleeding and bile leakage points should be carefully ligated with 5-0 Prolene sutures in an 8-character pattern. After flushing, repeatedly compress the sections with sterile gauze to detect any yellow dots on the gauze. Alternatively, cannulation can be performed through the stump of the cystic duct, and methylene blue can be injected to test for leakage from the section. If bile leakage is found, the leakage point should be ligated with prolene sutures in an 8-character pattern, and a T-tube should be placed in cases of massive leakage. An attempt should be made to suture and close the liver sections, in order to prevent bile leaks into the abdominal cavity; this can lead to biliary peritonitis in cases of postoperative bile leakage (Fig. 14.20, arrow shows pooling of bile).

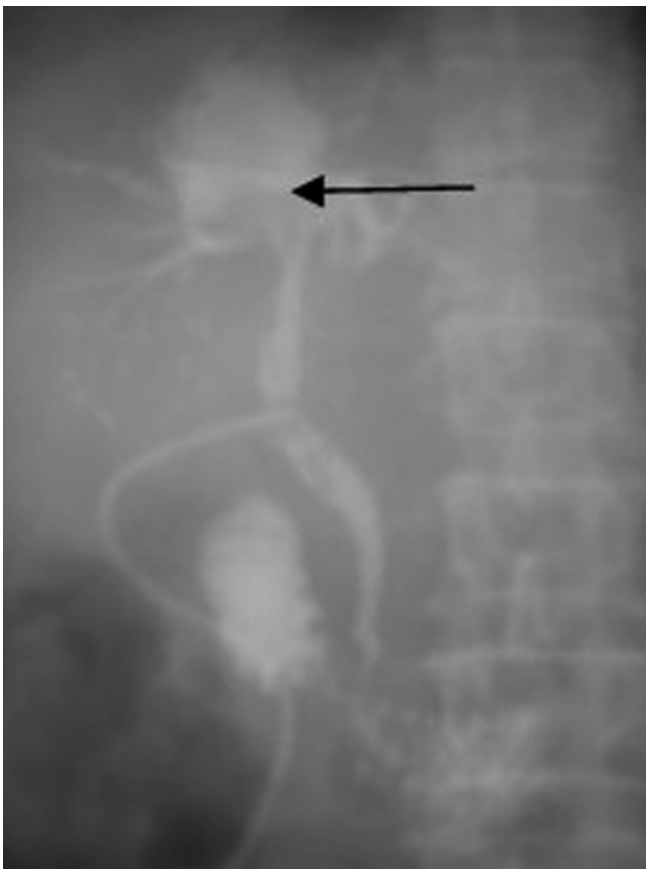

Fig. 14.20 Bile leaks into the abdominal cavity and leads to biliary peritonitis (*arrow* shows pooling of bile)

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Liver Resection for Primary Hepatocellular Carcinoma

15

Tianfu Wen and Wei Zhang

15.1 Background

In China, most patients with primary liver cancer are already outside the Milan criteria at the time of diagnosis and are considered to have advanced liver cancer. Approximately 80 % of the patients have HBV-associated liver cirrhosis; the prevention and treatment of liver damage and hepatic insufficiency is therefore of utmost concern in the perioperative period.

15.2 Requirements for Surgical Resection

Requirements for patients undergoing surgical resection include good general health; the absence of disease involving the heart, lung, kidney, or other essential organs; an established anesthesiology score of 2 or less; normal liver function or only mild liver impairment (Child–Pugh class A or Child–Pugh class B disease that returns to Child–Pugh class A after short-term treatment); adequate liver reserve function (as measured by tests such as an ICGR-15 of under 14 %); and the absence of metastatic disease.

15.3 Contraindications to Surgical Resection

Patients who cannot tolerate surgical resection include those with systemic conditions such as very old age, physical weakness, severe cardiopulmonary dysfunction, or metabolic diseases.

Liver-related contraindications include severe cirrhosis of the liver, liver decompensation (Child–Pugh C), or the presence of insufficient residual liver tissue to be able to maintain metabolism after resection.

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Cancer-related contraindications include multiple tumors or very large tumor; tumors that are associated with thrombus of the main portal vein or bile duct are relative contraindications for resection of liver cancer. Solitary or limited pulmonary metastases can sometimes be removed together with the primary tumor and may not represent an absolute contraindication to liver resection.

15.4 Basic Principles of Surgical Resection

Thoroughness: the tumor should be removed completely, without leaving residual tumor at the resection margin.

Security: the amount of remnant normal liver tissue should be maximized to decrease the risk of complications and mortality.

15.5 Indications for Laparotomy

In cases where the diagnosis of liver cancer is considered to be definite prior to surgical resection, laparotomy is indicated whether the tumor is small or large, located peripherally or in the hilum, superficially or deeply, or in cases of liver cancer with liver cirrhosis or ruptured liver cancers.

In cases where the diagnosis of liver cancer cannot be ruled out, such as the presence of a liver mass with negative AFP or with atypical radiologic examinations, abdominal laparotomy can be considered. According to current medical practice, the harm to liver resection is far less than the harm done by potentially delaying treatment of liver cancer.

15.6 Standards for Radical Resection in Liver Cancer

According to the standard for diagnosis and treatment of primary liver cancer by ministry of health of the people's republic of China (version 2011), radical resections for liver cancer can

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be divided into three standard levels. Level I involves complete removal of all tumors that can be seen with the naked eye, with no residual tumor at the resection margins. Level II resections add the following four criteria: ① the number of tumors is ≦2; ② no tumor thrombus is present at the main portal vein or its primary branches, the common hepatic duct or its primary branches, the hepatic vein trunk, or the inferior vena cava; ③ no hilar lymph node metastases are present; and ④ no extrahepatic metastases are present. In Level III resections, except for the criteria in level II, postoperative follow-up testing is negative; specifically, in patients with increased preoperative serum AFP, AFP should drop to normal after 2 months, and residual tumor must be absent on radiographic examination [1].

15.7 Non-radical Resections for Liver Cancer

The following types of resections are considered non-radical resections: ① the resection of multiple tumors, even in patients who are within the Milan Criteria and even if tumors are limited in half lobe and hemihepatectomy is performed; ② resections in which postoperative pathological results demonstrate vascular tumor emboli, regardless of tumor size; ③ central liver resections (i.e., segments IV, V, and VIII); ④ resections with the presence of lymph node metastasis in porta hepatis, even with simultaneous lymph node dissection; ⑤ the simultaneous removal of involved neighboring organs; and ⑥ the resection of primary liver cancers with portal venous tumor emboli, hepatic venous tumor emboli, inferior vena cava tumor emboli, or bile duct emboli. Close follow-up is necessary to prevent recurrence after surgery [1, 2].

15.8 Essentials of Surgical Procedures

15.8.1 Anesthesia

Currently, continuous epidural anesthesia combined with general anesthesia is the main approach used for liver resection. The benefits of this approach are as follows. (1) Epidural anesthesia is often used for pain relief, while a high concentration of local anesthetics to achieve muscle relaxation by nerve block is avoided, thereby decreasing the effect of limited liver blood flow due to epidural-induced hypotension. (2) General anesthesia is required to provide muscle relaxation and sedation; however, the dosage of general anesthetics is greatly reduced, avoiding large doses of opioid analgesics that can have adverse effects on liver function. However, as thrombocytopenia often occurs in patients with primary hepatocellular carcinoma (HCC), epidural anesthesia is not used routinely.

15.8.2 Operative Position

The supine position is widely used. For right-sided tumor resections in which the exposure is not adequate or the surgeon can't perform easily, the operating table can be tilted left by 10–30° to permit better exposure.

15.8.3 Transfusion Channel

The transfusion channel for liver surgery is a superior vena cava-based system (via the upper extremity veins or the internal or external jugular veins); central venous pressure is monitored when necessary.

15.8.4 Incision

A right subcostal incision is widely used, which may be extended posteriorly to the right or subcostally to the left if necessary, thereby avoiding thoracotomy and reducing postoperative complications. If the patient is thin or if the tumor is small and located in the left or central lobes of the liver, a middle abdominal incision can also be used, reducing trauma and helping the patient recover more quickly.

15.8.5 Surgical Exploration

Exploration of the abdominal organs should begin in the pelvis and then approach the liver tumor. The pelvic organs, colon, intestine, duodenum, and pancreas should be routinely examined to exclude metastases and the presence of primary tumors in other locations. For example, if cancer is noted in the stomach or intestine, tumor resections at these sites can be carried out simultaneously.

Hilar lymph nodes and portal vein tumor thrombosis: HCC less frequently metastasizes to lymph nodes, while intrahepatic cholangiocarcinoma often spreads to nodal sites. Tumor thrombus in the portal vein is confirmed if the portal vein lacks elasticity and no emptiness.

Liver and tumor: It is important for the surgeon to evaluate the size of the liver and the degree of the liver cirrhosis, as well as to assess the future liver remnant and postoperative liver function. After assessing the position, size, and number of tumors, intraoperative ultrasonography is routinely used to identify any masses that were missed on preoperative imaging and identify the resection line. Ultrasound is also helpful in guiding microwave and radio-frequency ablation, as well as alcohol injection into small lesions that lie deep to the liver capsule.

For large tumors on the surface of liver segments VII or VIII, the use of prehepatic vascular occlusion rope is needed, which can prevent the possibility of tumor rupture or hemorrhage.

15.8.6 Skills in Liver Dissection

The dissection of the right liver is often difficult and risky. Divisions of the ligamentum teres, falciform ligament, and part of the coronary ligament to the hepatic vena cava are performed first; then, the right coronary ligaments following the hepatocolic ligament, hepatorenal ligament, and right triangular ligament are divided with electrocautery. The assistant puts his left hand between hepatic flexure of colon and visceral surface of segments V and VI, right hand on the right posterior lobe to rotate the liver to the left side. Dissection is then continued to the right adrenal gland and the lateral wall of the vena cava. The surgeon pinches the tissue in front of the adrenal grand and vena cava with his left thumb and index finger; if the tissue is loose, division can be performed on the surface of the liver. If the tissue is tight, ligation of the tissue on liver side by silks is needed with placement of an angle clamp anterior to the adrenal gland, followed by continuous suturing of the adrenal gland side with 5-0 Prolene. The same method can be used to address the short hepatic veins and the vena cava ligament, and it is safer and easier to explore the cavity between the vena cava and the hepatic veins with Kelly hemostatic forceps, and then a right hepatic vein occlusion rope could be easily placed.

15.8.7 Method of Controlling Bleeding

Intraoperative bleeding control is key to successful liver surgery. It is better to limit the amount of bleeding to no more than 600–800 ml and avoid blood transfusions. To achieve this goal, hepatic inflow occlusion is used for most liver resections to reduce bleeding. Presently, the risk caused by bleeding is believed to be much greater than the risk caused by extended time of inflow occlusion. A typical anatomical hepatic lobectomy or segmentectomy usually begins with hilar dissection of the ipsilateral hepatic artery, portal vein, and bile duct, followed by resection. Currently, intermittent vascular inflow occlusion is widely used and is known as the Pringle maneuver. It allows for 20 min of occlusion alternating with 5 min of liver reflow and can be repeated up to six times until the liver resection is completed, if necessary [3]. For patients without liver cirrhosis, the occlusion time can be extended, if needed. To avoid residual liver ischemic injury and reduce vascular congestion of other organs, continuous normothermic hemihepatic vascular inflow occlusion is used for masses that are limited to one-half of the liver [4, 5]. This technique reduces bleeding and preserves residual liver function using a tourniquet or a nontraumatic hemostatic forceps in the previously dissected ipsilateral hepatic artery and portal veins. During liver resection, blood reflux into the hepatic vein is a major cause of blood loss, which can be reduced if the CVP is maintained at less than or equal to 5 cmH_2O during parenchymal dissection [6]. The operation should be careful and gentle in the area of the right, left, and middle parts of the hepatic vein. There is no need to be panic even damage and hemorrhage occur. Gently press on the vein to stop the bleeding and suture it with 5-0 Prolene; clamping with forceps should be avoided by all means. For large tumors that invade or adhere to the second or third hilum, blocking tapes could be placed at suprahepatic vena cava and infrahepatic vena cava in advance. Additionally, total vascular inflow occlusion can be used to control bleeding if necessary.

15.8.8 No Touch Strategy

Due to the liver's position (high in the abdominal cavity and deep under the diaphragm), the exposure is always difficult with challenging operations. The no touch strategy should be followed, meaning that tumors should not be approached or squeezed when dissecting the liver. Generally speaking, the anterior approach can be used for patients requiring difficult major hepatic resections, especially for tumors that are larger than 5 cm, when flipping the liver is contraindicated [7]. When performing an irregular liver resection, traction lines are sutured on the edge of the tumor, which aids in exposure and dissection and allows the surgeon to avoid holding the tumors directly (Fig. 15.1).

15.8.9 Surgical Margins

Generally, the more generous the tumor margin is, the more thorough the surgery is. Margins in a particular patient depend on the tumor location and size and the degree of the liver cirrhosis. The rate of radical surgery increases with the use of extended surgical margins; however, safety is relatively decreased, as important vascular branches can be damaged due to blind expansion of the scope of the resection. Traditionally, surgical margins should be >1 or 2 cm; however, these boundaries have not been confirmed in current studies [8]. Some professors believe that satisfactory margins can be achieved with R0 resection [9]. Indeed, the use of intraoperative ultrasound is needed to define the tumor margins to avoid the mistakes of missing or cutting through the tumor.

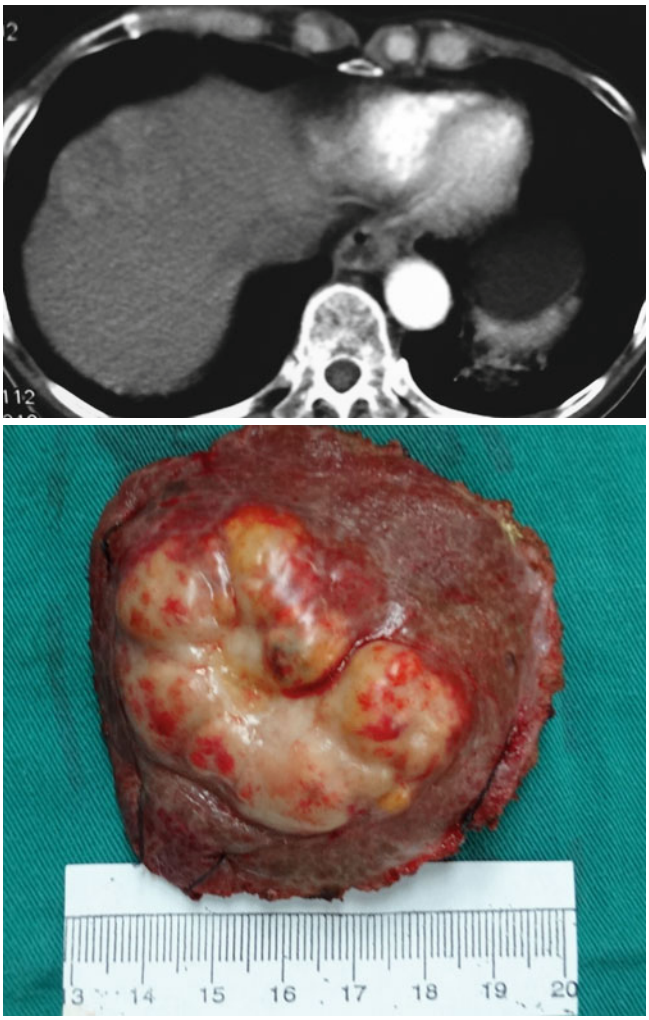

Fig. 15.1 CT shows the liver mass in the central lobe, which is operated by partial resection. On the edge of the tumor, the traction lines are sutured. It is beneficial for exposure and dissection and easy to operate

15.8.10 Methods and Skills for Liver Transection

There are multiple ways to transect the liver: the simple forceps method (using a rectangular clamp hook with ligation and the Kelly clamp crushing method), ultrasonic crushing of the liver parenchyma (using CUSA, water jet, ultrasonic aspirator, etc.), the energy pliers clamp method (BiCamp, LigaSure, etc.), the energy curing transection method (microwave coagulator, Habib 4×, radio frequency, etc.), and a combination of these methods. Actually, there is no difference in complications among these different methods, and surgeons should use the method in which they are most skilled [10]. We recommend the liver parenchyma ultrasonic crushing method, which transects tissue quickly and ensures a handling of the transected bile ducts and vessels, therefore reducing postoperative tissue necrosis and inflammation, especially in complex and larger cross-sectional liver resections. Moreover, this method is the basic technique for precious liver resection and living-donor liver resection [11] (Fig. 15.2).

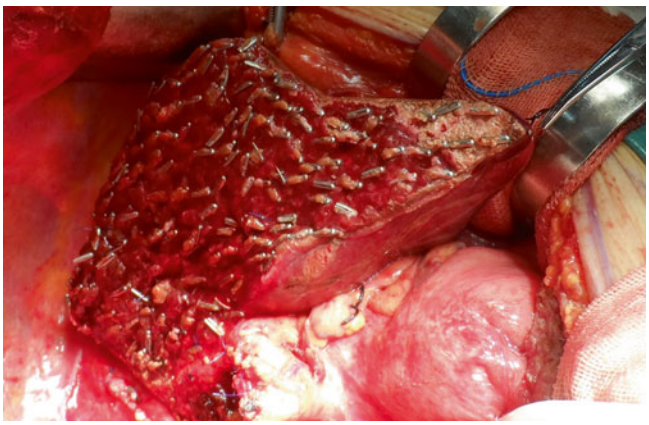

Fig. 15.2 The transected section by right hemihepatectomy with water-jet method

15.8.11 Surgical Strategies

In HCC, intrahepatic metastasis usually occurs via the portal vein. Based on this principle, anatomical liver lobe or segment resections are performed, although it remains unknown whether anatomical liver resection is more radical (Fig. 15.3). Because 80 % of HCC patients also have liver cirrhosis, liver resection often follows the rule of "anatomical left hepatectomy, nonanatomical right." That is to say, left lobectomy or hepatectomy is recommended for left-sided tumors; for right-sided tumors, a right partial hepatectomy is performed. A detailed list of recommendations for resection follows. ① For tumors in segments II and III, an anatomical left lateral lobe resection is performed. ② When the tumor is located at the border of the left lateral and medial lobes, or in cases of deeper tumors or tumors that are larger than 5 cm, an anatomical left hepatectomy is performed. ③ When the tumor is in segments IVa and IVb and is less than 3 cm in size, a partial IVa or IVb segmentectomy is performed. ④ When the tumor is located in the left medial lobe and is larger than 3 cm in size, a IV segmentectomy is performed. ⑤ For tumors that are larger than 5 cm and involve the right lobe, a right hepatectomy is performed. ⑥ In superficial tumors that are smaller than 3 cm, a partial liver resection is performed. ⑦ When the tumor is limited to segments V, VI, VII, and VII and is smaller than 3 cm, a segmentectomy is performed. ⑧ When the tumor involves adjacent segments, a combined liver resection is performed. ⑨ For tumors limited to the caudate lobe, the whole caudate lobe should be resected. ⑩ If a caudate lobe tumor invades the left or right lobe of the liver, a combined liver resection is performed.

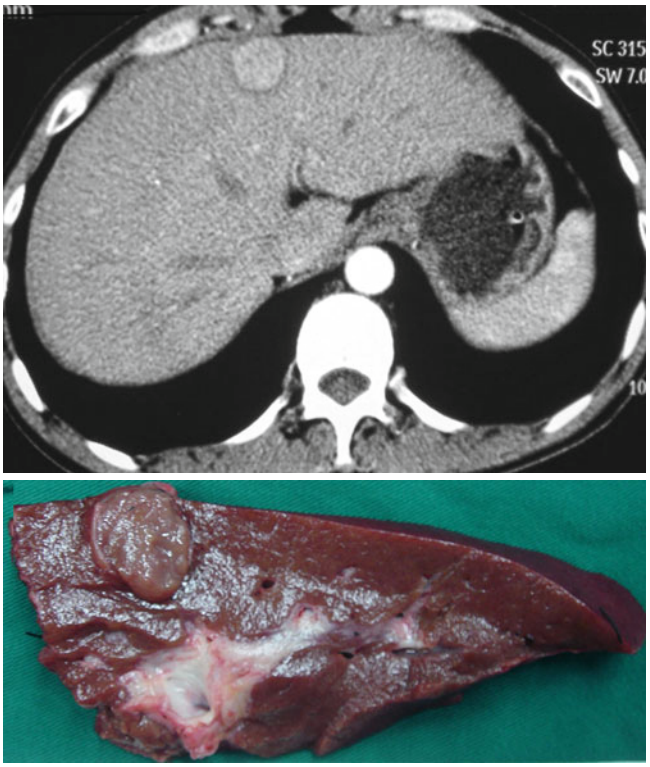

Fig. 15.3 CT shows the liver mass is in the segment IV. The patient could tolerate left hemihepatectomy with a physical and liver condition. The Postoperative pathological report shows moderate differentiated hepatocellular carcinoma with microvascular invasion

Nonanatomical liver resection, or irregular liver resection, includes tumor enucleation, wedge resection, and fusiform excision (Figs. 15.4 and 15.5).

① Tumor enucleation is an option, especially in cases of small tumors that are completely enclosed by a membrane, superficial tumors, or those that are located distant from the vena cava, hepatic vein, or portal vein. The resection follows the membrane, and the tumor is dissected, along with important vessels.
② Wedge resection can be used for tumors that are located at the edge of the liver, and resection of the tumor can be performed along with a 1–2 cm margin of normal liver tissue. Finally, The bile ducts and vessels should be appropriately ligated until the tumor was removed.
③ Fusiform excision can be used for superficial tumors that lie far from the edge of the liver. Resection of the tumor can be performed along with a 1- to 2-cm margin of normal liver tissue, and the liver tissues are dissected and sutured until the tumor is resected completely. Once hemostasis is achieved, the cross section can be sewn together.

15.8.12 Management of the Hepatic Cross Section

Meticulous excision is seldom required to manage the cross section in liver transection. Hemostasis should first be achieved; 5-0 Prolene is liberally used to suture the cross section to stop

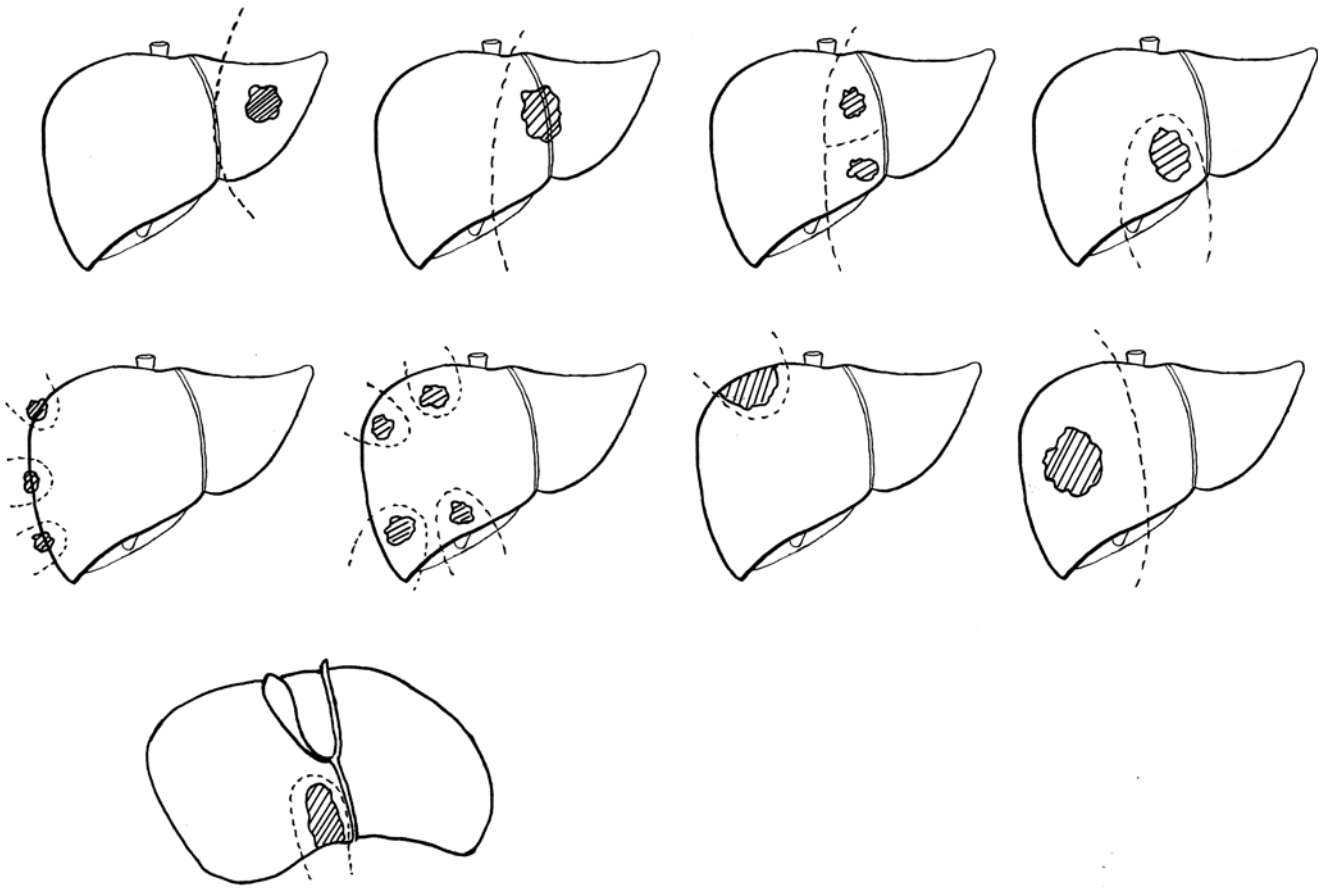

Fig. 15.4 The main approach in liver resection [2]

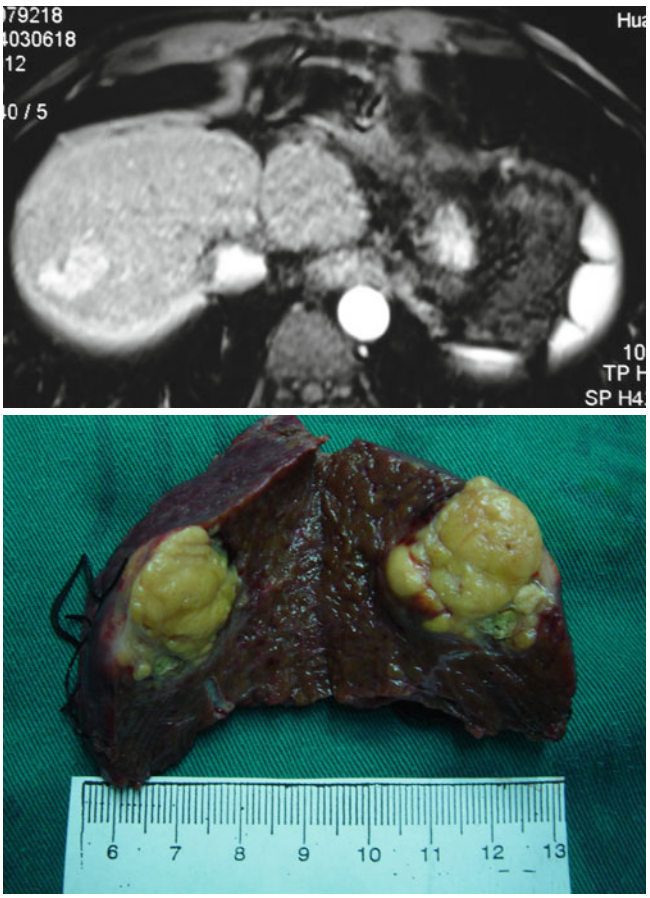

Fig. 15.5 CT shows the liver mass is in segment VII and combined with liver cirrhosis and atrophy, and then the partial resection is performed

bleeding. The presence of bile leakage is then evaluated. In central hepatectomy or nonanatomical resections, water or methylene blue can be injected into the bile duct to determine whether bile leakage is present. If there is bile leakage, the cross section should be sutured. Finally, we use 4-0 Prolene to suture the liver section continuously in four to six rows at a 0.5-cm depth. However, after liver resection, the section is not stitched, and fibrin glue sealant is not used [12].

15.8.13 Placement of Abdominal Drainage

The aim of the drainage is to allow observation of the extent of postoperative bleeding and bile leakage and to reduce effusions in surgical areas and the diaphragm.

15.8.14 Reattachment of the Ligamentum Teres and Falciform Ligament

After right and extended right hepatectomy, the divided sides of the ligamentum teres and falciform ligament are sutured to keep the remnant liver in situ [13].

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Surgical Treatment of Hepatocellular Carcinoma Accompanied with Portal Vein Tumor Thrombus

16

Weidong Jia

16.1 History and Current Situation

In the 1980s, Lee and Lin et al. [1, 2] performed a hepatectomy to treat hepatocellular carcinoma associated with portal vein tumor thrombus (PVTT). At first, this surgery was used only for PVTTs of the first branch of the portal vein and not for PVTTs invading the bifurcation or the trunk of the portal vein.

In the early 1990s, Kumada and Yamaoka et al. [3, 4] reported the surgical treatment of a tumor thrombus in the portal trunk and suggested the following five surgical approaches. (1) Hepatolobectomy: This technique is used when the tumor is located in the left or right liver and the PVTT is confined to the first portal branch. The tumor, PVTT, and relevant portal vein should be resected en bloc. (2) Thrombectomy by balloon catheter: The portal trunk is clamped, and a small incision is then made on its wall. A balloon catheter is inserted into the portal vein through the incision and moved forward all the way through the entire thrombus. The thrombus is extracted by curette or suction. (3) Portal vein bypass: When the thrombus is difficult to extract, the relevant portal branches can be resected en bloc with the thrombus. The autogenous iliac vein can then be used as the bypass graft between the umbilical vein and the portal trunk. (4) Portal vein resection and anastomosis: If the PVTT invades the contralateral first branch of the portal vein, en bloc resection of the PVTT and the portal branch should be performed. Then, an anastomosis should be made between the portal trunk and the stump of the portal vein. (5) Thrombectomy: A biological pump is used to divert the blood of the portal vein and the vena cava to the axillary vein; thus, total hepatic occlusion is achieved. Then, the thrombus is extracted by an incision in the portal vein, and the incision is closed using continuous sutures.

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PVTT in the portal trunk is currently regarded as a sign of end-stage hepatocellular carcinoma, and the tumor itself cannot be removed radically by hepatectomy. Therefore, attempts to surgically extract the PVTT are thought to be unrealistic. The hepatectomy and thrombectomy performed by Kumada and Yamaoka et al. [3, 4] were intended to prevent esophageal variceal bleeding, not to improve survival. Despite a high mortality rate of 11 %, patients who underwent a successful surgery had unexpected 1-, 2-, and 3-year survival rates of 52.2 %, 23.2 %, and 11.6 %, respectively. These rates are significantly higher than in patients who receive conventional therapy [4].

It is difficult to extract the PVTT by balloon catheterization, and cancer cells may metastasize to the distal portion of the portal vein during the procedure. Portal vein bypass, portal vein resection and anastomosis, and open thrombectomy are all difficult and are associated with many complications; these techniques are therefore rarely used or reported [5].

In 2010, Shi et al. [6] improved the method for hepatectomy with associated PVTT. If the PVTT invades the bifurcation or trunk of the portal vein, hepatectomy and PVTT extraction through the stumps of the portal vein can be performed. This surgery is simple and has relatively fewer complications; thus, it is now widely used. The disadvantage is that cancer cells may metastasize to the contralateral portal vein.

Liver transplantation is an effective way to treat end-stage liver diseases. In theory, it not only removes the tumor but also removes the environment that causes the tumor. Thus, transplantation may be a radical treatment for hepatocellular carcinoma with PVTT. However, in clinical practice, there is a very high recurrence rate after liver transplantation for such patients, indicating that PVTT is not suitable for liver transplantation [7]. There is no global consensus that PVTT is a contraindication for liver transplantation [8–12].

In 2003, the Liver Cancer Study Group of Japan (LCSGJ) put forward a classification of PVTT based on clinical and radiological features and advances in surgical knowledge and pathological understanding of PVTT. The classification

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system comprises five types, ranging from Vp0 to Vp4 [13]. In 2007, Cheng et al. [14] at Eastern Hepatobiliary Hospital, Shanghai, classified PVTT into types I0~VI, based on the portion of the portal vein that has been invaded by the PVTT. In 2012, Chen et al. [15] put forward a new classification of PVTT based on the portion of the portal vein invaded by the PVTT as well as surgical outcomes.

The classification of PVTT is conducive to treatment and prognosis prediction. As PVTT classification and the standardization of surgical treatment improve, hepatectomy with thrombectomy has become the main surgical approach for treating hepatocellular carcinoma associated with PVTT.

16.2 Anatomy

16.2.1 Anatomy of the Portal Vein

The portal vein is formed behind the neck of the pancreas via confluence of the superior mesenteric vein and the splenic vein at the level of the second lumbar vertebra. The portal vein then extends to the upper right, crosses the first portion of the duodenum, extends into the hepatoduodenal ligament, and reaches the hilum of the liver just before the epiploic foramen. When extending into the liver, most (82 %) portal veins divide into left and right branches, while some (18 %) divide into three branches.

The left branch of the portal vein extends to the left and into the liver parenchyma, where it divides into the transverse, angle, sagittal, and cystic branches. The transverse branch is approximately 2–3 cm long. Several small veins originate from the transverse branch and travel into the left segment of the caudate lobe. The angle branch is between the sagittal branch and the transverse branch and creates an angle of approximately 90–130°. A vein originates from the angle branch of the left portal vein and runs into the superior segment of the left lateral lobe. This vessel is referred to as the superior segmental branch of the left lateral lobe. The sagittal branch of the left portal vein lies in the venous ligament trench and ranges from 1 to 2 cm in length. Approximately two to four relatively large branches originate from the medial side of the sagittal branch and are referred to as the left medial branches. The cystic branch is linked to the ligamentum teres hepatis and contains the blocked umbilical vein. A vein originates from the lateral side of the cystic part and runs into the inferior segment of the left lateral lobe; this vein is referred to as the inferior segmental branch of the left lateral lobe.

The transverse branch of the left portal vein can be dissected from the transverse trench of the left hilum of liver. The portal branches running into the left segment of the caudate lobe can be found near the origin of the transverse branch. The connective tissue is dissected along the left longitudinal trench and the angle branch, and sagittal and cystic branches of the left portal branch can be exposed. These branches of the left portal vein lie in the left interlobar fissure, near the surface of the left longitudinal trench. Therefore, in a left lateral lobectomy, the resection line should be a safe distance away from the falciform ligament to protect the sagittal and cystic branches of the left portal vein. Additionally, during an extended right hemihepatectomy, the resection line should be toward the medial side of the left longitudinal trench.

The right branch of the portal vein runs within the right side of the transverse trench of the hilum of the liver, extending into the right hemiliver parenchyma. Compared with its left counterpart, the right branch is relatively thick and short, ranging from 1 to 3 cm in length. One to three branches originate from the proximal end of the right portal trunk and run into the right segment of the caudate lobe. These vessels are referred to as the right segmental branches of the caudate lobe. The right anterior portal branches originate from the right portal trunk and divide into two groups, each comprising one to three branches that run to the anterior and posterior portions of the right anterior lobe. The right posterior branch divides into the superior segmental branch and the inferior segmental branch; these branches run to the superior and inferior segments of the right posterior lobe, respectively. Occasionally, when the right portal trunk is not present, the right anterior branch originates from the transverse branch of the left portal trunk or the main portal trunk. In a left hemihepatectomy, if the right anterior branch originates from the transverse branch of the left portal trunk, the transverse branch of the left portal trunk should be dissected on the distal side of the origin of the right anterior branch. In a right hemihepatectomy, if the right anterior branch originates from the main portal trunk, the anterior and posterior segmental branches of the right anterior branch should be ligated and divided separately.

16.2.2 Anatomical Foundation of PVTT Formation

Both ends of the portal system are capillaries. The portal vein runs into the liver parenchyma through the hilum of the liver and divides repeatedly. Ultimately, the portal vein drains into the hepatic sinusoids of the hepatic lobules and travels through the central veins into the hepatic veins. In a cirrhotic liver, the portal blood flow is disturbed, forming the pathologic foundation of PVTT formation. The feeding arteries of the tumor are connected with surrounding small portal branches and the hepatic sinusoids. Tumor arteries cut off the portal perfusion with their high blood pressure, and regional portal hypertension results. Thus, the portal vein becomes the main efferent vessel of the tumor. Cancer cells

infiltrate the efferent vessels, grow in the vessel cavity, infiltrate through the membrane, and eventually metastasize into the portal branch [16]. Other mechanisms of PVTT formation include slow blood flow velocity caused by portal blood flow disturbance, an absence of venous valves, rich nutrients in the portal blood, and the microenvironment of the portal system. PVTTs in the right portal branch invade the portal trunk more frequently than those in the left portal branch because the former is shorter and thicker than the left portal trunk. Moreover, some individuals do not have a right portal trunk, and their right portal branches originate directly from the main trunk. Generally speaking, the prognosis is worse the closer the PVTT is to the main portal trunk. PVTTs are more common in left portal branches, which may be due to the reflux caused by the 90° angle formed between the transverse and sagittal branches of the left portal vein. The occurrence and distribution of PVTTs are associated with the type, size, and distribution of the liver tumor. The occurrence rate of PVTT is highest in diffuse hepatocellular carcinoma, relatively lower in bulky carcinomas, and lowest in nodule carcinomas. The larger the tumor, the higher the occurrence rate of the PVTT is. Tumors in the right hemiliver frequently invade the right portal branches or trunk, while tumors in the left hemiliver frequently invade the left portal branches or trunk. A minority of PVTTs can retrogradely invade the extrahepatic portal trunks, extend into the superior mesenteric and splenic veins, and cause portal hypertension.

Table 16.1 LCSGJ PVTT classification

Type	Location of PVTT
Vp0	No PVTT
Vp1	PVTT in portal branches distal to the second branches
Vp2	PVTT in the second portal branches
Vp3	PVTT in the first portal branches
Vp4	PVTT in the main portal trunk or contralateral portal branch

Table 16.2 PVTT classification of the Eastern Hepatobiliary Hospital

Type	Subtype
Type I0: PVTT in histological examination	
Type I: PVTT invades the second or smaller branches of the portal vein	Type Ia: PVTT invades the third or smaller branches of the portal vein
	Type Ib: PVTT invades the second portal branches
Type II: PVTT invades the first portal branch	Type IIa: PVTT invades the first portal branch of one lobe (the left or right portal trunk)
	Type IIb: PVTT invades the first portal branch of two lobes (the left or right portal trunk)
Type III: PVTT invades the main portal trunk	Type IIIa: the PVTT is no more than 2 cm beneath the bifurcation of the portal vein
	Type IIIb: the PVTT extends more than 2 cm beneath the bifurcation of the portal vein
Type IV: PVTT invades the superior mesenteric vein	

16.3 Classification of PVTT

There are some universally accepted liver tumor classifications regarding treatment, outcome evaluation, and prognosis prediction, including the Okuda system [17], the Cancer of the Liver Italian Program (CLIP) [18], CUPI [19], BCLC [20], HKLC [21], JIS [22], and the TNM staging system [23]. The CLIP [18], BCLC [20], HKLC [21], JIS [22], and TNM staging systems [23] take PVTT into consideration as an important prognostic factor. However, the staging systems do not specify the extent of the PVTT, which hampers PVTT research. Several current proposals of PVTT classification have been put forward. These classification systems are conducive to treatment selection, outcome evaluation, prognosis prediction, and the scientific classification of liver tumors.

16.3.1 PVTT Classification of Liver Cancer Study Group of Japan

In 2003, the Liver Cancer Study Group of Japan (LCSGJ) put forward a classification system for PVTT that describes five types (Vp0–Vp4) according to the clinical, radiological, and pathological features as well as the surgical outcomes [13]. In a retrospective study of 21,711 patients who underwent hepatectomy from 1988 to 1999, the 5-year survival rates of Vp0, Vp1, Vp2, and Vp3–4 patients are 56.5 %, 34.4 %, 27.0 %, and 17.3 % [24], respectively (Table 16.1).

16.3.2 PVTT Classification of the Eastern Hepatobiliary Hospital

Cheng et al. [14] analyzed the clinical data of Eastern Hepatobiliary Hospital and put forward a new PVTT classification system based on the part of the portal vein invaded by the PVTT. In this system, PVTTs are divided into types I0–IV, of which types I–III are divided into two subtypes each (Table 16.2, Fig. 16.1). Research reveals that types I–III have satisfactory surgical outcome, especially types I and II, while types III and IV present poor prognoses. Additional investigation suggests that this classification system is more accurate with respect to

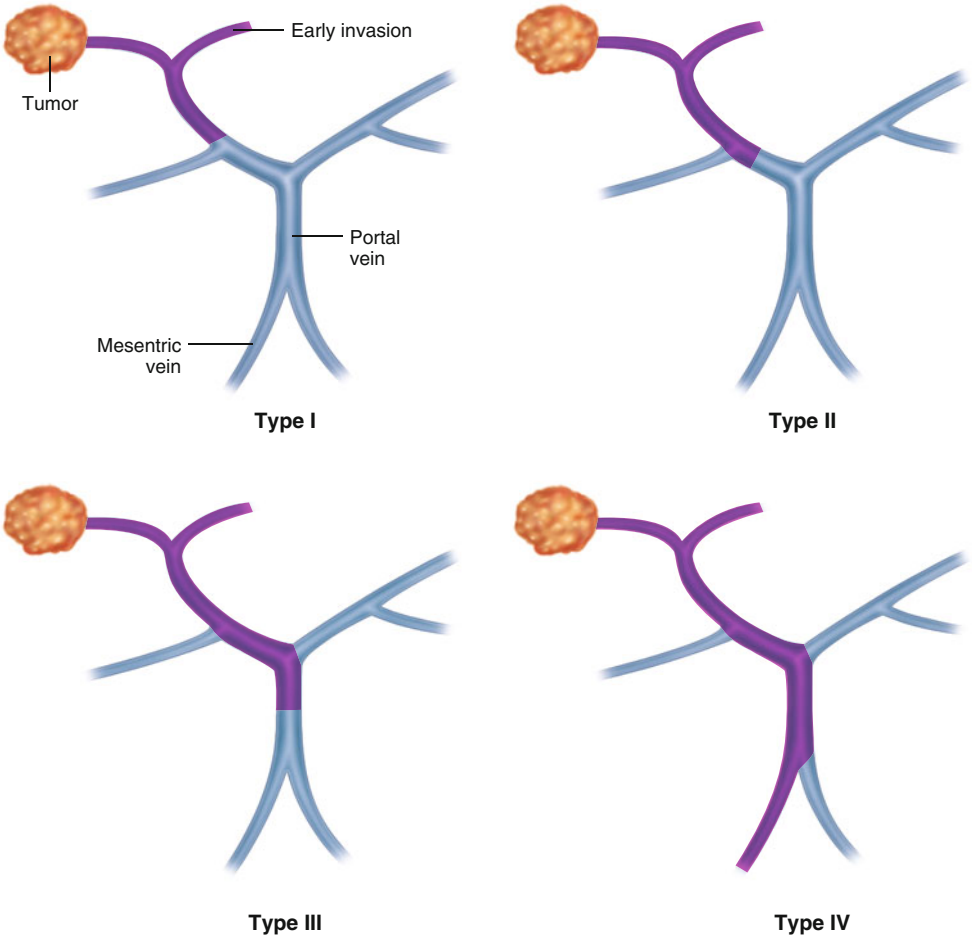

Fig. 16.1 PVTT classification of the Eastern Hepatobiliary Hospital

Table 16.3 Other PVTT classifications

Type	Location of the PVTT
Type A	Within the resection area
Type B	Extends to the first portal branches, exceeding the resection line by 1–2 cm
Type C	Extends to the main portal trunk or the contralateral portal branches

stratification and prognosis prediction than the TNM, CLIP, and JIS systems [25].

16.3.3 Other Classification of PVTT

Some scholars divide PVTT into types A–C, based on the tumor's location and surgical outcome [15] (Fig. 16.3). Hepatectomy is suggested for type A. Hepatectomy and thrombectomy via the stumps are performed in type B. In type C, the wall of the portal trunk should be incised to extract the PVTT. The mean postoperative survival time is 9 months in type A and B, while it is only 5 months in type C (Table 16.3).

16.4 Preoperative Evaluation

16.4.1 Radiological Evaluation

1. Due to its high sensitivity and specificity, ultrasound is the preferred radiological examination for PVTT. Due to its advantages, such as it being simple, intuitive, noninvasive, radiation-free, and inexpensive, it is also the most widely used examination method. Ultrasound can clearly demonstrate the cavity and blood flow of the portal vein. Ultrasound can also detect abnormal echoes and distinguish them from the thrombus caused by cirrhosis based on its blood supply and properties. Pulsatile blood flow detected by color Doppler flow imaging makes the diagnosis of PVTT easier (Figs. 16.2, 16.3, 16.4, and 16.5).
2. Computed tomography (CT) is one of the most important radiological examinations for the diagnosis and differential diagnosis of liver tumor. CT can reveal the morphology and blood supply of the liver tumor and is conducive to detection, identification, staging, and posttreatment follow-up. In the diagnosis of PVTT, CT can provide information of the tumor's size, location, and relationship with

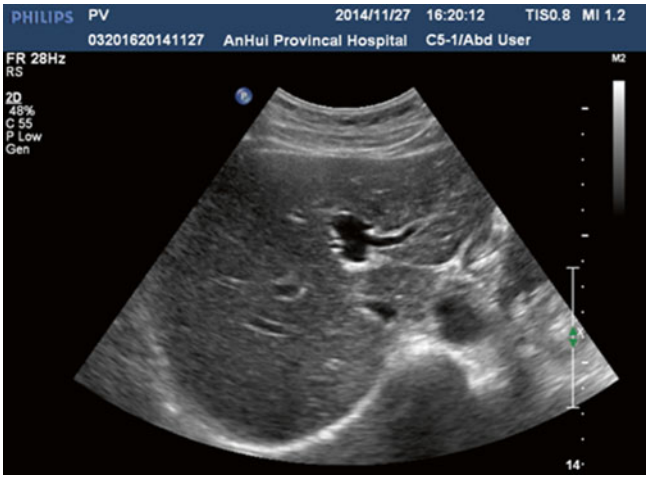

Fig. 16.2 Normal sonography of the portal vein. The left portal branch is unobstructed with no PVTT in the cavity

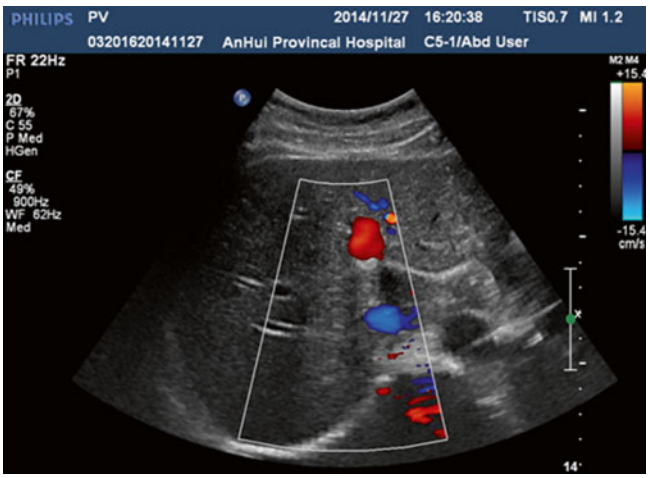

Fig. 16.3 Normal sonography of the portal vein. Colorful blood signal is present in the cavity of the left portal vein, indicating patency

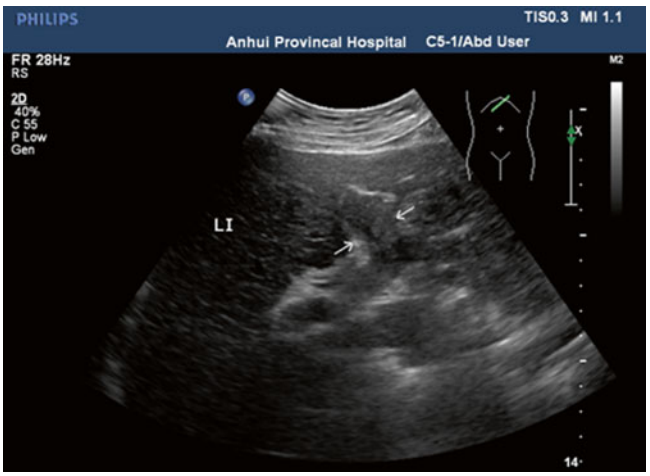

Fig. 16.4 Gray-scale ultrasonography of PVTT, PVTT in the left portal branch (*arrows*)

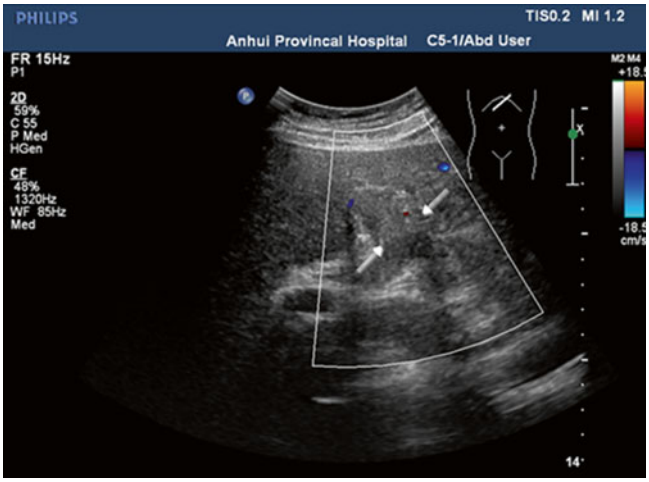

Fig. 16.5 Color Doppler ultrasonography of PVTT, color Doppler ultrasonography detects no blood signal in the left portal branch due to PVTT occlusion. There is little blood in the periphery of the related portal vein (*arrows*)

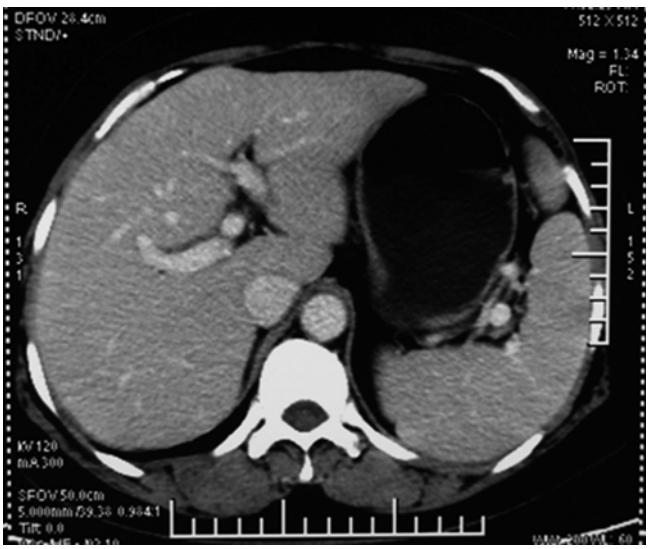

Fig. 16.6 Normal CT image of the portal vein. The cavities of the left and right portal branch are clear, with no filling defect

adjacent large vessels. In addition, CT can help identify the mass lesion in the portal vein and differentiate PVTT from thrombus (Figs. 16.6 and 16.7). CT, especially dynamic enhanced spiral CT, has relatively high resolution, which facilitates the precise localization of PVTT. The CT indications of portal vein thrombus are a thickened cavity and a low-density filling defect in the cavity. Indirect indications are enhanced portal vein wall, the formation of collateral circulation, and cavernous transformation of the portal vein.

3. Magnetic resonance imaging (MRI) has the same value as CT in PVTT diagnosis. MRI can provide cross-sectional,

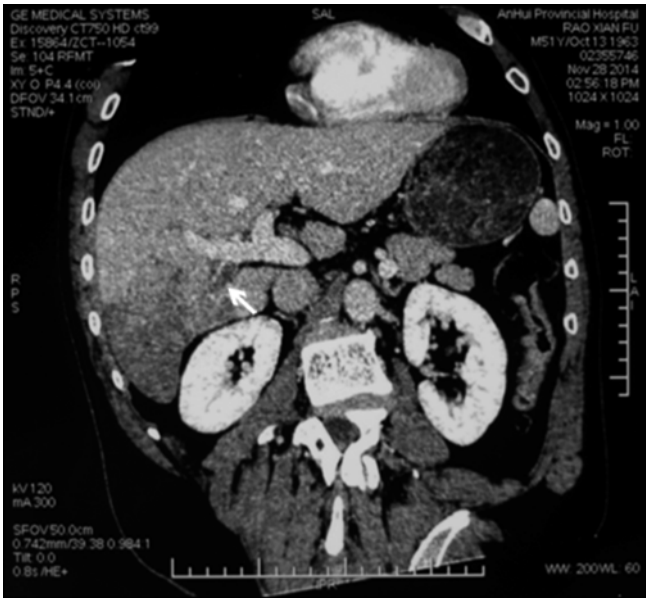

Fig. 16.7 CT image of PVTT. The tumor is located in the right liver, with a PVTT in the right posterior branch of the portal vein. The *arrow* marks the filling defect in the cavity of the right posterior branch of the portal vein

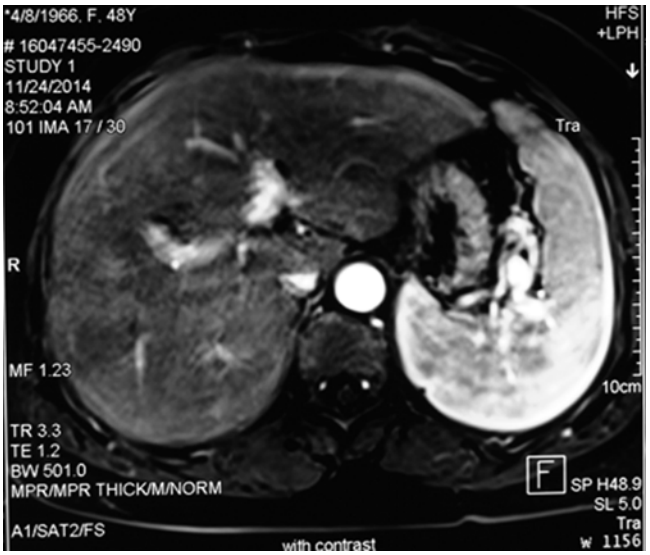

Fig. 16.8 Normal MRI image of a portal vein. The cavities of the left and right portal branch are clear, with no abnormal signal intensity

coronal, and sagittal images and evaluate the size and location of the PVTT. It can also evaluate the extent of portal vein occlusion. On MRI, PVTT exhibits normal signal intensity or hypointensity on T1WI image and hyperintensity on T2WI image, with no significant post-enhanced changes. This pattern is similar to the pattern of the liver tumor. MRI has high sensitivity and specificity for PVTT (Figs. 16.8 and 16.9).

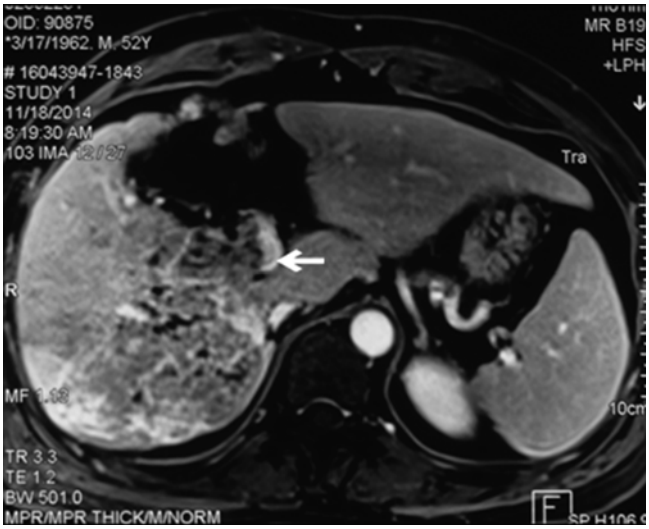

Fig. 16.9 Image of a PVTT. The tumor is located in the right liver, with a PVTT in the right posterior branch of the portal vein. The *arrow* marks hypointensity on enhanced MRI in the cavity of the right posterior branch of the portal vein. The hypointensity extends to the bifurcation of the portal vein

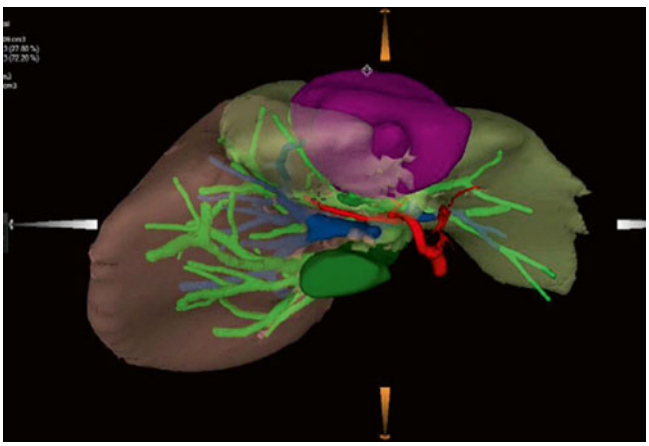

Fig. 16.10 3-D image reconstruction of PVTT. The tumor is located in the left liver, with a PVTT in the left portal branch. The *arrow* marks the total occlusion of the left portal branch by the PVTT

4. The liver surgery planning system has some advantage in the diagnosis and treatment of liver tumors associated with PVTT. The liver surgery planning system can calculate the liver remnant and simulate the liver surgery based on: (1) the preoperative overall assessment of hepatic functional reserve, (2) images of the tumor and liver anatomy, and (3) the local condition of the tumor and its relationship with adjacent important vessels [26]. 3-D image reconstruction reveals a defect in the portal vein when it is occluded by a PVTT. If the PVTT is significant, PVTT reconstruction can be performed (Fig. 16.10). A CT image is shown in Fig. 16.11.
5. PET-CT combines PET with CT. PET reveals the biochemical and metabolic condition of the hepatic mass

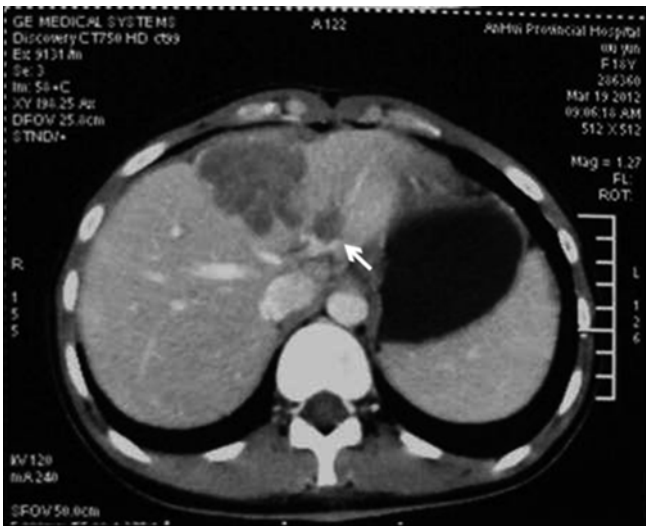

Fig. 16.11 The tumor is located in the left medial lobe, with a PVTT in the left branch of the portal vein (*arrows*)

lesion and can precisely locate the lesion. PET-CT provides cross-sectional images of the whole body in one examination and has advantages with respect to sensitivity, specificity, and precision. Thus, PET-CT can diagnose and detect metastasis in the early stage. In theory, PET-CT can differentiate PVTT from thrombus. However, in clinical practice, the diagnostic accuracy of PVTT is unsatisfactory, and this technique now serves only as a supplemental examination.

16.4.2 Assessment of Hepatic Functional Reserve

Post-hepatectomy liver failure is an important cause of perioperative mortality and is the main predictor of short-term survival of patients with hepatocellular carcinoma associated with PVTT. A precise assessment of the hepatic functional reserve is very important for selecting the treatment protocol, determining the resection scope, and reducing the risk of post-hepatectomy liver failure.

Many methods are now available for evaluating the hepatic functional reserve. Apart from plasma biochemical tests and scoring systems (e.g., the *Child-Pugh score and the MELD score*), the indocyanine green (ICG) excretive test can objectively demonstrate the hepatic functional reserve and provide an important reference value with respect to the selection of the method and timing of surgical treatment [27]. Generally speaking, a Child-*Pugh* A patient with an ICGR15 of <10 % can tolerate a large-volume liver resection of four segments. A Child-*Pugh* A patient with an ICGR15 of 10–19 % can tolerate a large-volume liver resection of 2–3 segments. A Child-*Pugh* A patient with an ICGR15 of 20–29 % can tolerate liver resection of only one segment. When the ICGR15 is 30–39 %, the patient can only tolerate a small regional liver resection. When the ICGR15 is ≥40 %, only enucleation is permitted [28].

The ICG excretion rate varies greatly with the hepatic blood flow. Therefore, the factors that influence hepatic blood flow, such as PVTT, post-portal vein embolization, and regional blood flow disturbance, all influence the test results. The location of the PVTT and the extent of the occlusion should be considered preoperatively [29].

Calculating the volume of the remnant liver by CT or MRI is a simple but effective way to assess the hepatic functional reserve and can help predict and prevent post-hepatectomy liver failure.

Zurich University combined portal hypertension, the Child-Pugh score, the future liver remnant, the ICGR15 value, and the condition of liver parenchyma (i.e., with or without cirrhosis) and put forward a relatively objective and reasonable method for assessing hepatic functional reserve [30].

In 2011, Chinese experts reached a consensus with respect to the preoperative assessment of hepatic functional reserve. In this consensus, ICGR15, the Child-Pugh score, radiological evaluation of liver parenchyma and vessels, and the calculation of liver volume are combined to form an evaluation system to determine the safe limit of liver resection. This consensus is very important for the individualization of the method and the scope of liver resection [31].

16.4.3 Preoperative Evaluation

The patient's overall condition, the preoperative hepatic functional reserve, the location of the tumor, and the condition of the PVTT are all factors that influence the surgery and the prognosis.

The general condition of patients can be evaluated using the ECOG scoring system. Other aspects that need assessment are nutrition; water-electrolyte balance; acid-base balance; and the conditions of vital organs, such as the heart, lungs, and kidneys.

Preoperative evaluation of hepatic functional reserve is conducive to assessing the patients' tolerance level of hepatectomy and thrombectomy, thus providing a basis for surgical planning and reducing post-hepatectomy liver failure.

Radiology not only plays an important role in preoperative hepatic functional reserve evaluation but also determines the PVTT classification. Ultrasound, CT, and MRI can show the lesions of the liver parenchyma, assess the hepatic functional reserve, and indicate the safety of liver surgery. In addition, these methods can classify the PVTT, help with

surgical planning, and predict the prognosis. CT can also provide a 3-D reconstruction, allowing a simulated hepatectomy via the liver surgery planning system.

16.5 Surgical Indications

According to the BCLC strategy for staging and treatment, early-stage hepatocellular carcinoma (stage 0-A) is indicated for radical resection. PVTT belongs to stage C, which requires targeted therapy with sorafenib instead of surgery [20]. The updated Japan Society of Hepatology (JSH) 2010 guidelines for the management of hepatocellular carcinoma proposed PVTT in the portal branches as an indication for hepatectomy [32]. In 2014, the NCCN Clinical Practice Guidelines in Oncology proposed that large-vessel invasion is indicated for hepatectomy, despite debate [33]. In 2014, Hong Kong University proposed the Hong Kong Liver Cancer staging system with treatment stratification. The proposed indications for hepatectomy are a single tumor, diameter ≤ 5 cm, intrahepatic vessel invasion, and Child-Pugh A [21].

There is no consensus regarding the surgical indications for hepatocellular carcinoma accompanied by PVTT. Generally accepted indications are: (1) the general condition is fine, with no organic disease of vital organs; (2) liver function is normal or only slightly damaged (Child-Pugh A), or Child-Pugh B improves to Child-Pugh A after short-term treatment; and (3) the liver tumor is localized without metastasis. Based on the PVTT classification proposed by LCSGJ, Vp1, Vp2, and Vp3 are indicated for resection, while Vp4 is a relative indication. Based on the PVTT classification proposed by Cheng et al. in Eastern Hepatobiliary Hospital, types I, II, and III are indicated for resection, while type IV is a contraindication.

16.6 Preoperative Preparation

1. Medical history and physical examination: In the patient's medical history, low back pain caused by liver tumor metastasis should be given special attention. Upon physical examination, lung metastasis, ascites, and cachexia should be given special attention. Several tests should be run, such as routine blood work, blood biochemistry, blood coagulation, serum AFP, abdominal ultrasound, CT, MRI, and PET-CT, when necessary.
2. Evaluation of hepatic functional reserve: Child-Pugh scoring combined with an ICG excretive test is most widely used. Vitamin K and prothrombin complex concentrate are administered to those with coagulation abnormities. Albumin is administered to those with hypoproteinemia. For those with damaged liver function, treatment aimed at improving liver function should be continued until it is essentially normal. Vitamins, glucose, and albumin should be given to undernourished patients. Anemia should be treated.
3. Evaluation of the function of the vital organs, such as the heart, brain, and kidney: Seek professional help when necessary to reduce surgical risk.
4. Administration of laxatives to clean the gut the day before surgery, if necessary.
5. Preparation of blood for intraoperative transfusion according to the scope of resection.

16.7 Operative Method Options

Among all of the treatments for PVTT, surgery has the highest probability of cure. Most PVTT growth occurs from the original tumor to the portal trunk, which is the foundation for radical resection. This procedure removes the tumor and the PVTT in one operation. There are three widely used operative methods, which are described below.

16.7.1 Hepatectomy

Hepatectomy is the most radical operation and consists of resecting the tumor and PVTT en bloc. This procedure can be performed if the PVTT does not extend beyond the first branch of the portal vein and the patient's general condition and liver function are suitable for left or right hemihepatectomy. For tumors in the right anterior lobe, a right anterior lobectomy can be performed in which the PVTT is resected together with the right anterior portal branch if the PVTT does not exceed beyond the right anterior portal branch. Similarly, for tumors in the right posterior lobe, if the PVTT does not exceed beyond the right posterior portal branch, a right posterior lobectomy can be performed in which the PVTT is resected together with the right posterior portal branch.

16.7.2 Hepatectomy + PVTT Extraction through the Liver Cross Section

This procedure applies to PVTT extending to the portal bifurcation or trunk, exceeding the resection line by 1–2 cm. After resecting the liver, occlude the portal trunk and open the portal stumps on the liver cross section to extract the PVTT by clamping, flushing, or suction. If blood exits from the stump during reperfusion, the portal vein is most likely clear. Intraoperative ultrasound can detect whether the PVTT is totally extracted. Before extraction, the contralateral portal

branch is temporarily occluded to prevent cancer cell metastasis to the contralateral portal vein.

16.7.3 Hepatectomy + Thrombectomy through the Portal Trunk

If the PVTT extends to the portal trunk or the contralateral portal branch, the portal trunk needs to be incised to extract it. Expose the portal trunk and its left and right branches, occlude the proximal end of the portal trunk, and incise it from its bifurcation. If the PVTT adheres loosely to the vessel wall, it can be extracted gently. If the adhesion is tight, en bloc resection can be considered. The resected portal vein can be mended using an autogenous vein, vascular prostheses, or autogenous peritoneum. End-to-end anastomosis of the portal vein is another option [5].

16.8 Detailed Surgical Procedures

16.8.1 Hepatectomy

Consider a case of left hemihepatectomy as an example. This case is an 18-year-old female patient with a history of HBV infection since childhood. The serum AFP level is 17,654 ng/ml, the Child-*Pugh score is* A, ICGR15 is 3.9 %, and the diagnosis is hepatocellular carcinoma associated with PVTT. The tumor is located in the left medial lobe, with a PVTT in the left branch of the portal vein not exceeding the first portal branch. Anatomical left hemihepatectomy is performed, and the left portal branch is resected en bloc with the PVTT. A 3-D reconstruction image is shown in Fig. 16.10, and a preoperative CT image is shown in Fig. 16.11.

1. The patient is placed in a supine position. Measures are taken to keep the patient warm, and elastic stockings are put on to prevent deep venous thrombosis. Make an oblique incision beneath the right costal margin; resect to the xiphoid to directly expose the inferior vena cava. After exploring the abdominal cavity, intraoperative ultrasound is routinely performed to detect the number and size of the lesion, its relationship with surrounding vessels, and other small lesions beyond the planned resection area (Figs. 16.12 and 16.13).
2. The ligamentum teres hepatis, falciform ligament, left coronary ligament, left triangular ligament, hepatogastric ligament, and part of right coronary ligament are divided. The left hemiliver is mobilized, and the tumor is exposed (Fig. 16.14).
3. The hepatoduodenal ligament is dissected. The cystic artery and cystic duct are mobilized, ligated, and divided. The gallbladder is resected (Fig. 16.15).

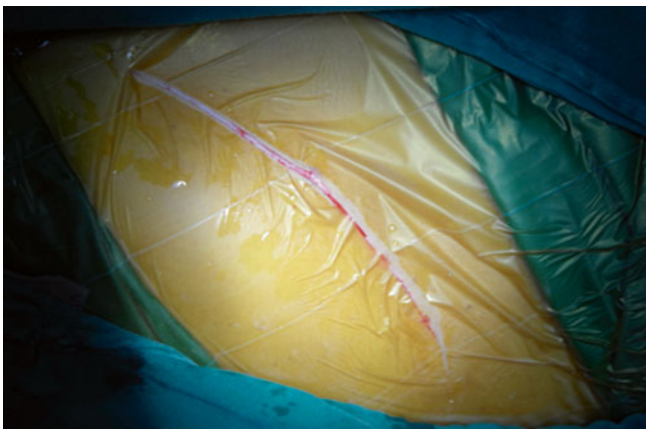

Fig. 16.12 An oblique incision is made beneath the right costal margin

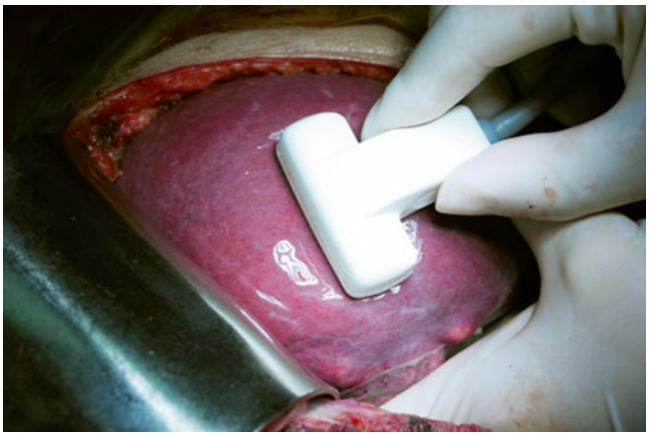

Fig. 16.13 Intraoperative ultrasound is routinely performed

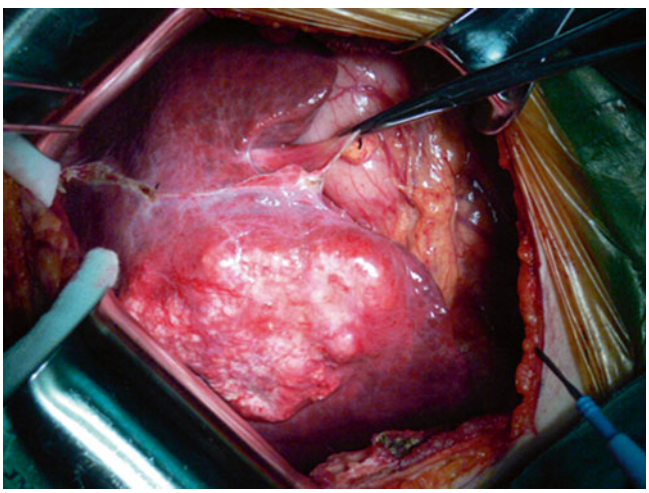

Fig. 16.14 The left hemiliver is mobilized, and the tumor is exposed

4. The porta hepatis is dissected. The left hepatic artery and the left branch of the portal vein are separated, suspended, double ligated, and divided (Fig. 16.16).

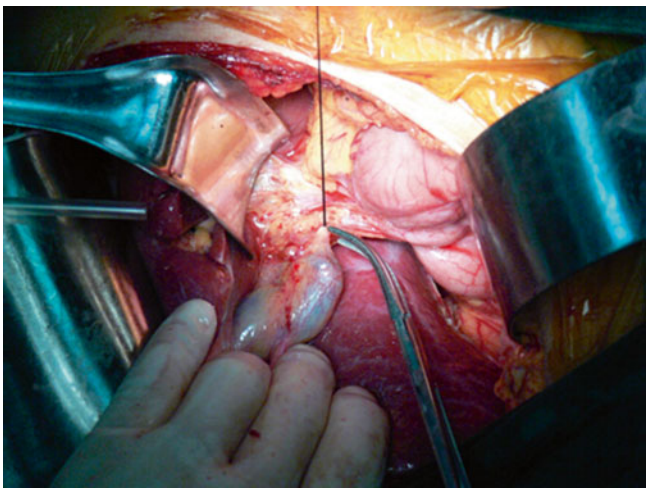

Fig. 16.15 The cystic duct is mobilized, ligated, and divided

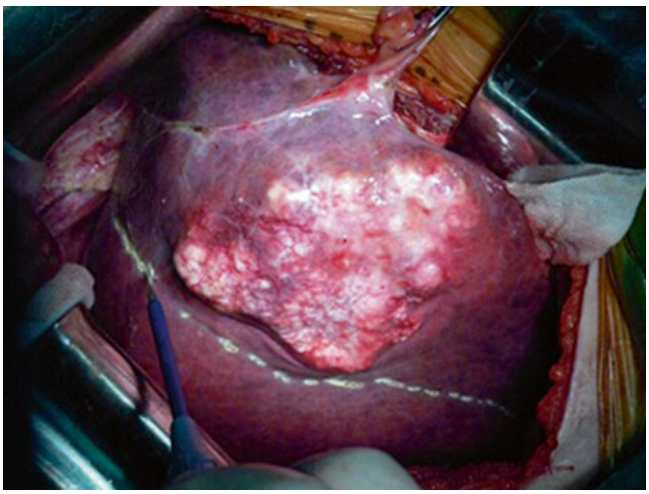

Fig. 16.17 The dividing line between the left and right hemilivers is *marked*

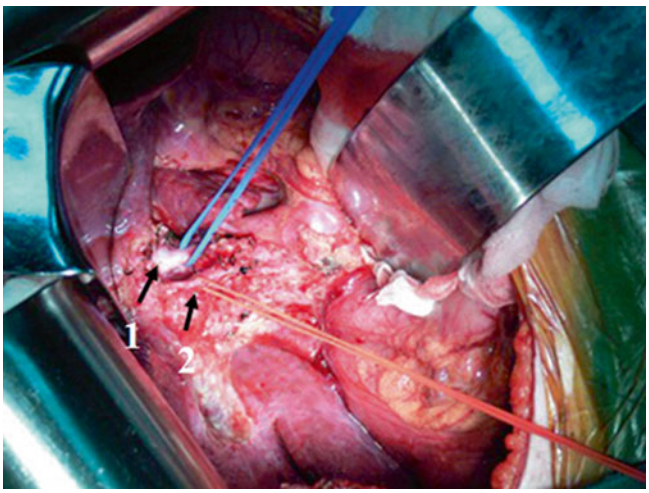

Fig. 16.16 The left hepatic artery and the left portal branch are suspended separately (*1* the left portal branch; *2* the left hepatic artery)

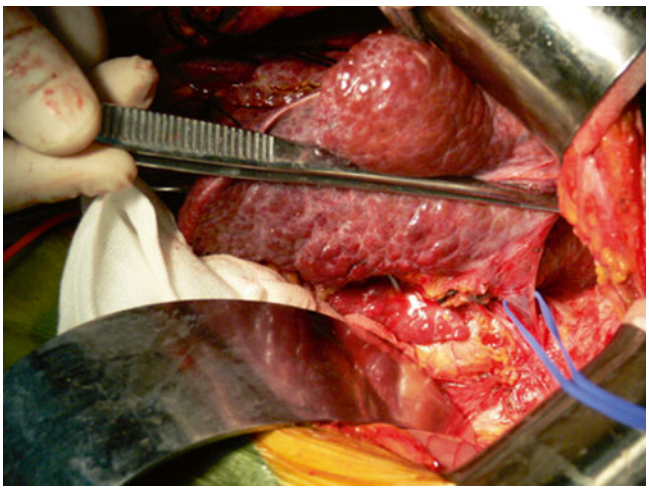

Fig. 16.18 The left hepatic vein is suspended

5. After dissection of the left portal branch and the left hepatic artery, an apparent ischemic line indicating the interlobar fissure can be observed. Mark the line with an electronic knife (Fig. 16.17).
6. The second hepatic hilum is dissected. The common trunk of the middle and left hepatic veins is exposed. The Arantius ligament is divided. The left hepatic vein is exposed, dissected, and suspended (Fig. 16.18).
7. Suture along the two sides of the marked line for traction. Transect the liver parenchyma using an ultrasonic scalpel and CUSA. The relevant vessels and bile ducts are ligated and divided.
8. The hepatic vein of segment IVA is dissected, suspended, ligated, and divided (Figs 16.19 and 16.20).
9. The left hepatic vein is divided, and the stump is continuously sutured using 4-0 Prolene (Fig. 16.21).

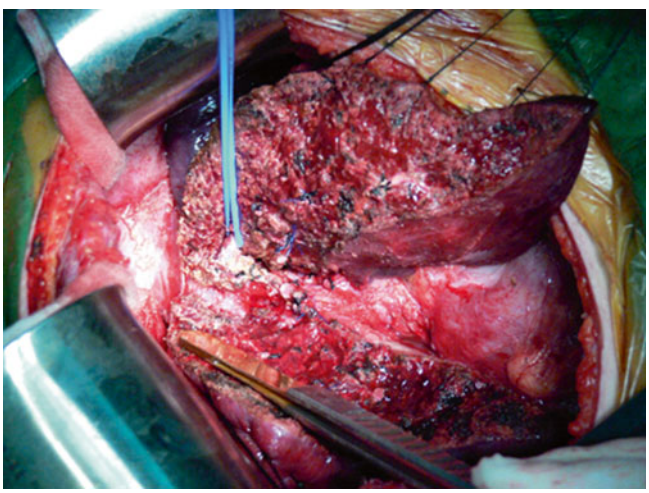

Fig. 16.19 The hepatic vein of segment IVA is suspended

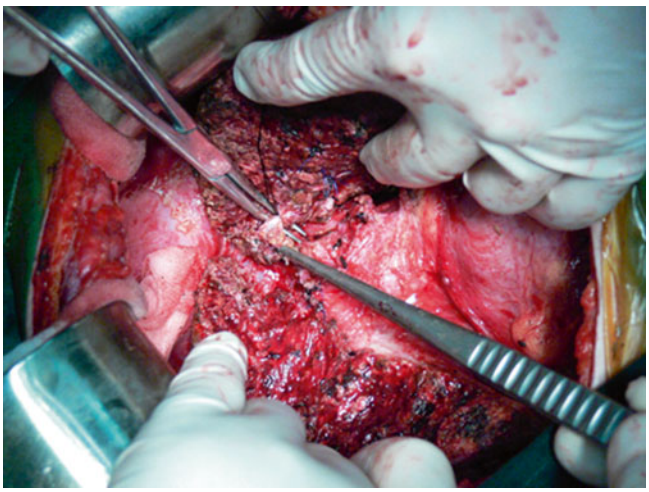

Fig. 16.20 The hepatic vein of segment IVA is divided

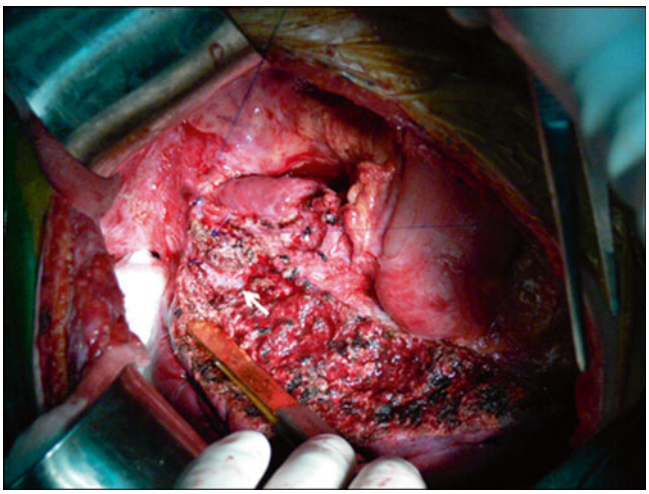

Fig. 16.22 The liver parenchyma is transected. Liver cross section closure and abdominal drainage are not routinely necessary (*arrow* marks the proximal end of the MHV)

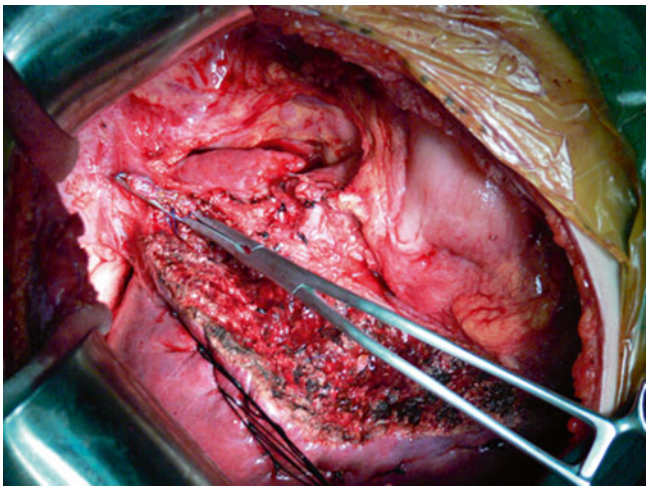

Fig. 16.21 The left hepatic vein is divided

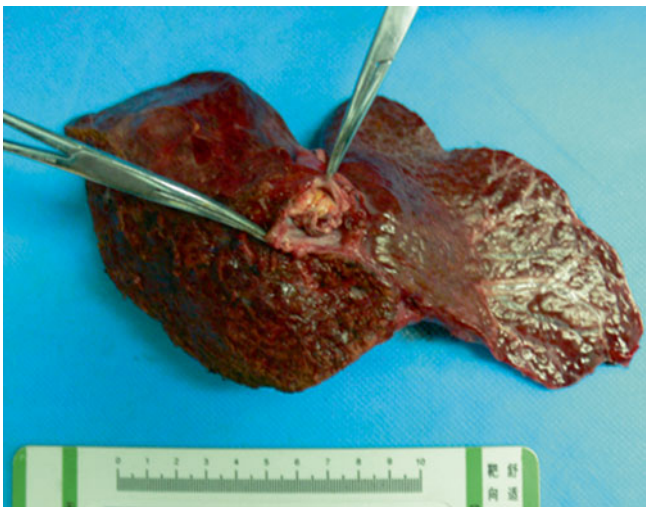

Fig. 16.23 The resected specimen

10. The left hemiliver is resected. The distal portion of the middle hepatic vein is resected, while the proximal part is preserved. Due to the frequently encountered anatomical variants of the hilar bile ducts, we advocate routine dissection of the left hepatic duct inside the liver to prevent bile duct injuries. After left hemihepatectomy, any bleeding on the cross section is ligated. Liver cross section closure and abdominal drainage are not routinely necessary (Fig. 16.22).
11. The resected specimen is shown in Fig. 16.23, with PVTT in the left portal branch.

16.8.2 Hepatectomy + PVTT Extraction Through the Liver Cross Section

Take right hemihepatectomy as an example. This case is a 52-year-old male patient with a history of HBV infection of 20+ years. His serum AFP is 41,129 ng/ml, the Child-*Pugh is* A, and the ICGR15 is 7.4 %. The diagnosis is hepatocellular carcinoma associated with PVTT. The tumor is located in the right posterior lobe, with PVTT in the right portal branch extending to the portal bifurcation. Anatomical right hemihepatectomy is performed, and the PVTT is extracted through the liver cross section. Preoperative CT image is shown in Fig. 16.24.

1. An oblique incision is made beneath the right costal margin. After exploring the abdominal cavity, routine intraoperative ultrasound examination is performed. The ligamentum teres hepatis, falciform ligament, right coronary ligament, right triangular ligament, hepatocolic ligament, and hepatorenal ligament are divided. The IVC is

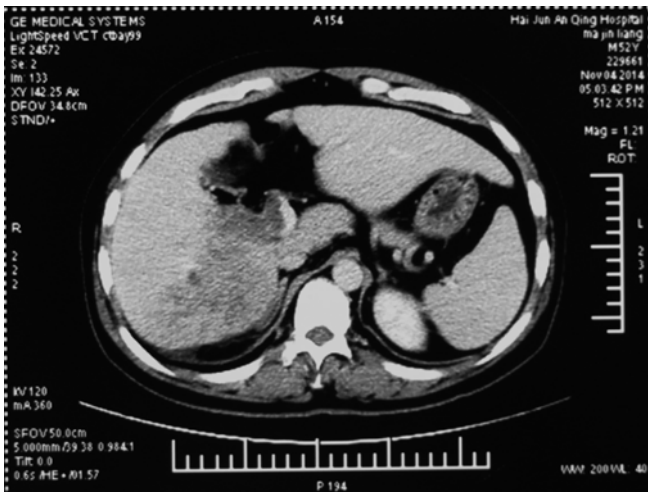

Fig. 16.24 The tumor is located in the right posterior lobe, with PVTT in the right portal branch extending to the portal bifurcation

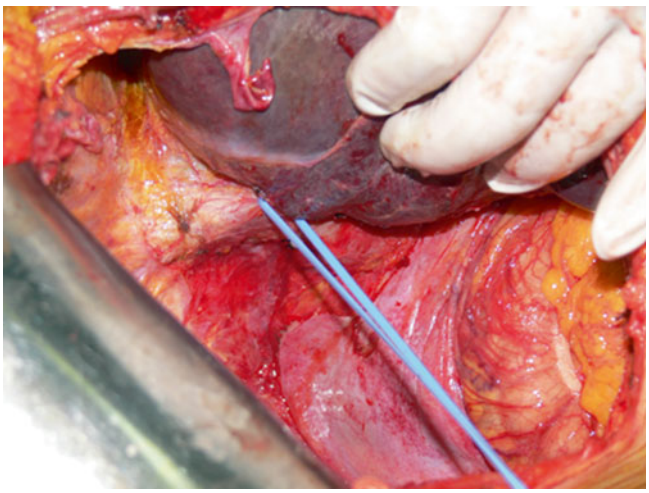

Fig. 16.26 The right hepatic vein is dissected in an extrahepatic manner and suspended

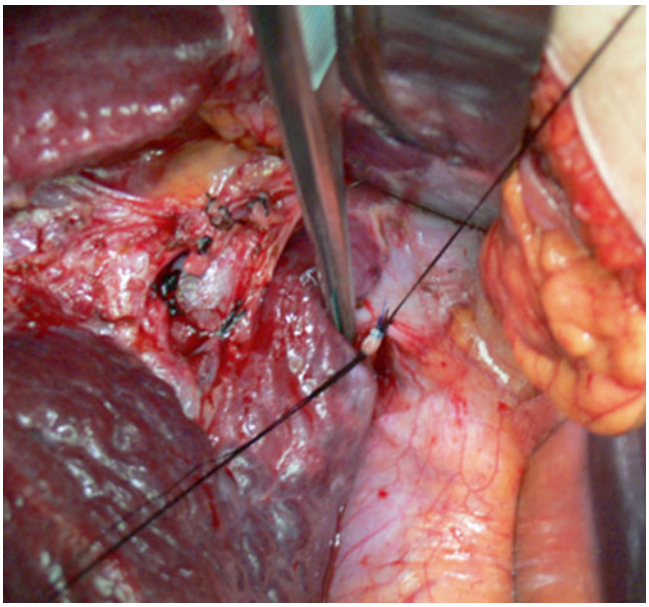

Fig. 16.25 The short hepatic veins are ligated and divided

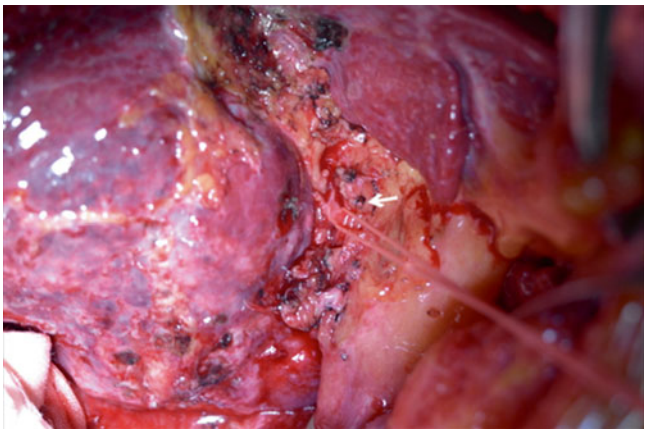

Fig. 16.27 The right hepatic artery is suspended (*arrows*)

exposed by dissecting the bare area. The right hemiliver is mobilized, and the gallbladder is resected in the way described for the left hemihepatectomy.

2. The short hepatic veins are ligated and divided. The Makuuchi ligament is divided. The right hepatic vein is dissected in an extrahepatic manner and suspended (Figs. 16.25 and 16.26). Then, precisely dissect the second and third hepatic hila.
3. The porta hepatis is dissected. The right hepatic artery is mobilized and suspended (Fig. 16.27).
4. The portal trunk and its two branches are dissected and suspended (Fig. 16.28).
5. The right hepatic artery is double ligated and divided. The ischemic line appears on the liver surface, indicating the interlobar fissure. Mark the dividing line with an electronic knife (Fig. 16.29).
6. Suture along the two sides of the marked line for traction. Transect the liver parenchyma using CUSA. The trunk of the MHV should be preserved. The relevant vessels and bile ducts are ligated and divided. The hepatic vein of segment VIII is dissected, suspended, ligated, and divided. The right hepatic vein is transected, and its stump is continuously sutured with 4-0 Prolene until the right hemiliver is totally resected. The right hepatic duct is dissected inside the liver, as is routine, to prevent hilar bile duct injuries (Figs. 16.30 and 16.31).
7. The left portal branch and the proximal end of the portal trunk are clamped using Hemoclips. The PVTT is extracted from the stump of the right portal branch using forceps combined with a curette (Figs. 16.32 and 16.33).

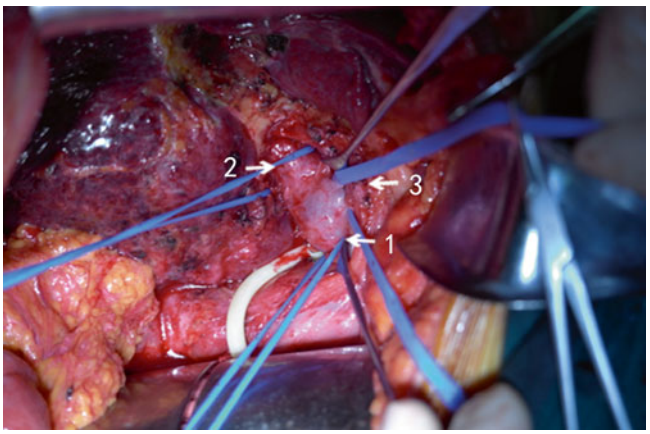

Fig. 16.28 The portal trunk and its two branches are suspended (*1* portal trunk, *2* right portal branch, *3* left portal branch)

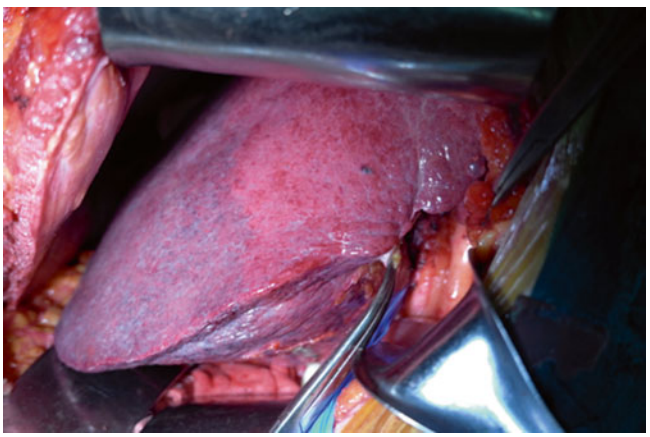

Fig. 16.29 The ischemic line appears on the liver surface

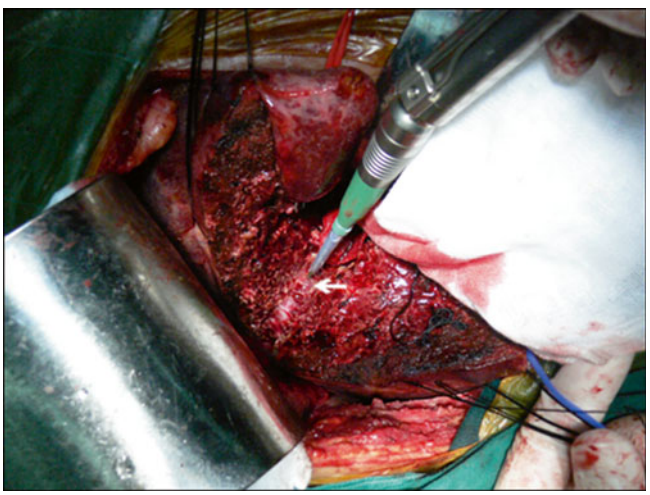

Fig. 16.30 The liver parenchyma is transected using CUSA, while preserving the trunk of the MHV (*arrows*)

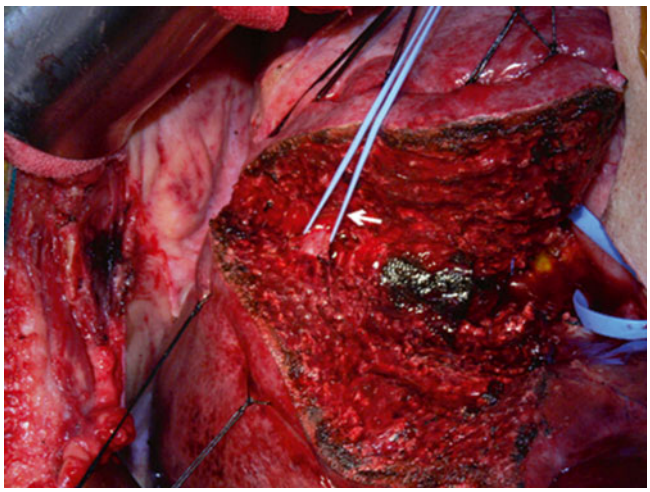

Fig. 16.31 The hepatic vein of segment VIII is suspended (*arrows*)

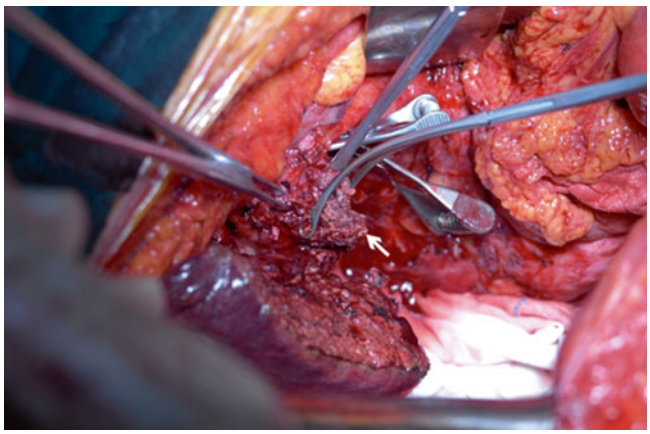

Fig. 16.32 The PVTT is extracted from the stump of the right portal branch using forceps (*arrows*)

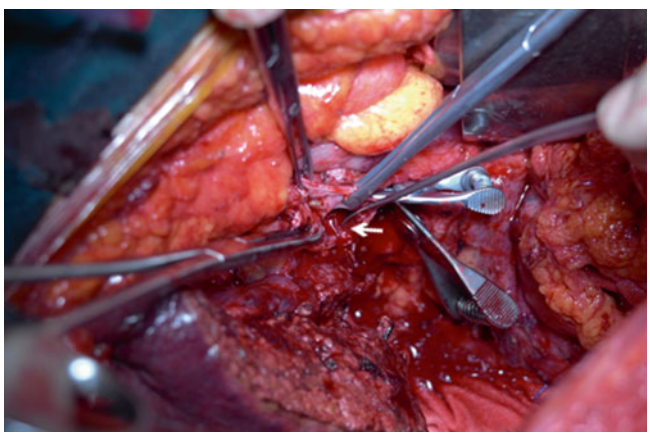

Fig. 16.33 The PVTT is extracted from the stump of the right portal branch using a curette (*arrows*)

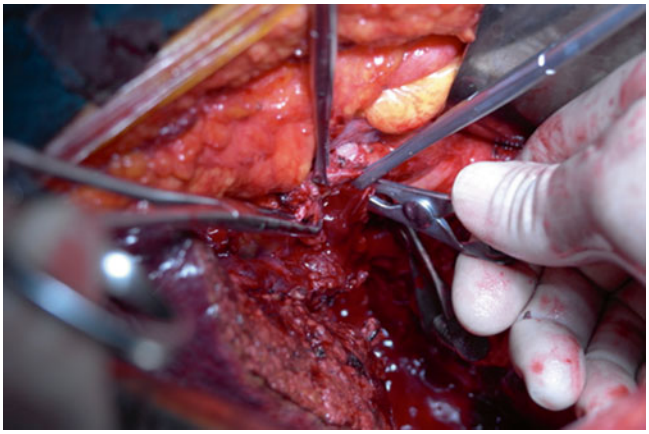

Fig. 16.34 The portal trunk is released to flush out the PVTT debris

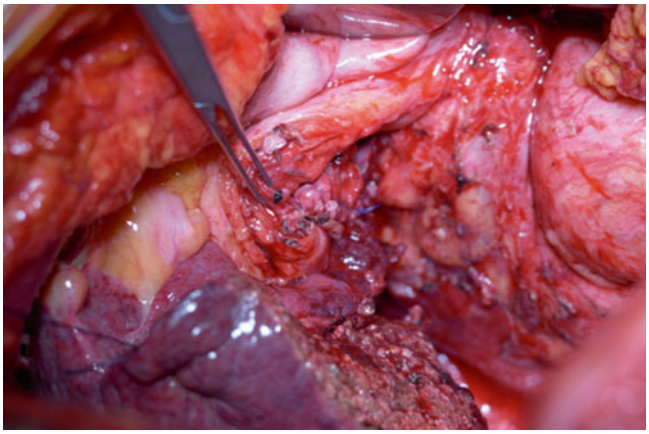

Fig. 16.36 The sections are not sutured closed

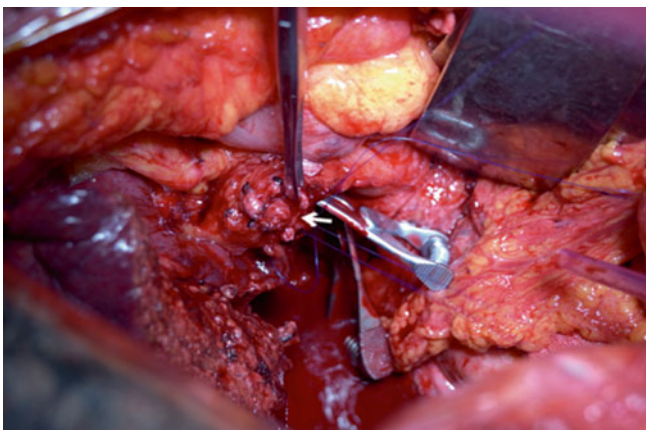

Fig. 16.35 Close the stump of the right portal branch by continuous suture (*arrows*)

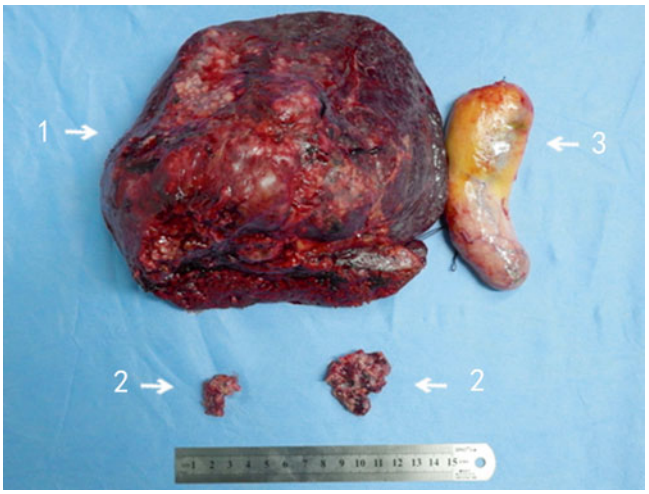

Fig. 16.37 The resected specimen and PVTT (*1* tumor, *2* PVTT, *3* gallbladder)

8. After extraction of the PVTT, the portal trunk is released to flush out the debris of the PVTT. Then, release the left portal branch. Ensure that there is no PVTT remaining; then, close the stump of the right portal branch by continuous suture with 5-0 Prolene (Figs. 16.34 and 16.35).
9. Ligation and argon plasma coagulation can be used for hemostasis of the liver cross section. The sections are not sutured closed. Abdominal drainage can be used depending on the situation (Fig. 16.36).
10. The resected specimen is shown in Fig. 16.37.

16.8.3 Hepatectomy + Thrombectomy

Consider a right hemihepatectomy and thrombectomy as an example. This case is a 59-year-old male patient with a history of HBV infection for 21 years. The serum AFP is 3227 ng/ml, and the Child-*Pugh score is* A. The diagnosis is hepatocellular carcinoma associated with PVTT. The tumor is located in the right anterior lobe, with PVTT in the right portal branch extending to the portal bifurcation. Anatomical right hemihepatectomy and thrombectomy are performed. Part of the wall of the portal vein is resected and mended by autologous peritoneum. A preoperative CT image is shown in Fig. 16.38.

1. The patient is placed in a supine position. Make a reversed L-shaped incision on the right upper abdomen. Routine intraoperative ultrasound examination is performed. The ligamentum teres hepatis, falciform ligament, right coronary ligament, right triangular ligament, hepatocolic ligament, and hepatorenal ligament are divided. The right hemiliver is mobilized, and the gallbladder is resected. The first, second, and third hepatic hila are dissected.

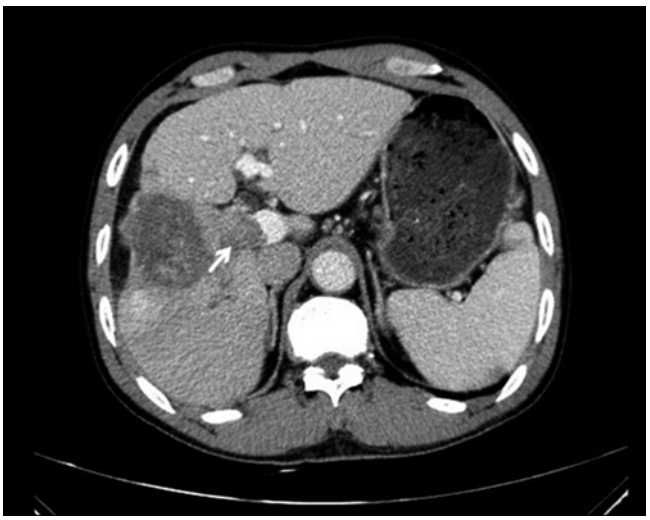

Fig. 16.38 The tumor is located in the right anterior lobe, with PVTT in the right portal branch extending to the portal bifurcation (*arrows*)

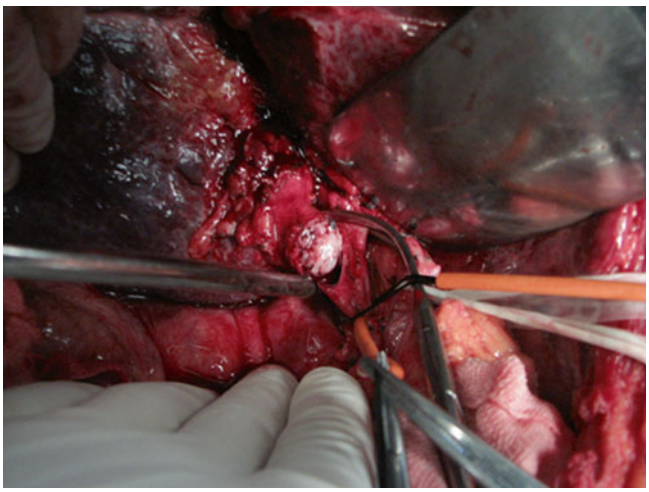

Fig. 16.40 Part of the anterior wall of the portal vein is resected en bloc with the PVTT

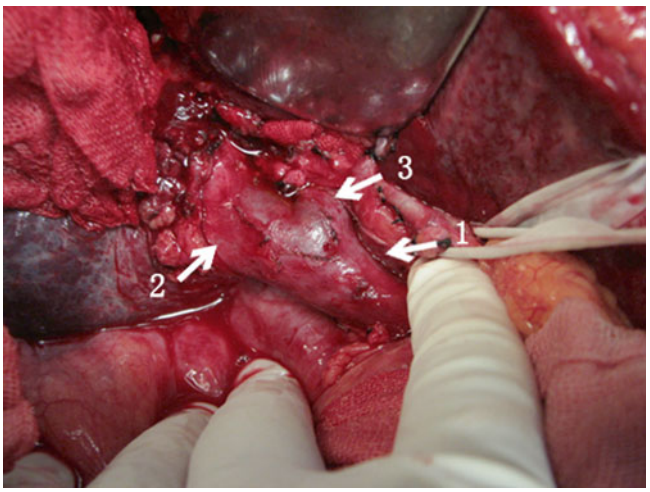

Fig. 16.39 The portal trunk and its two branches are separated (*1* portal trunk, *2* right portal branch, *3* left portal branch)

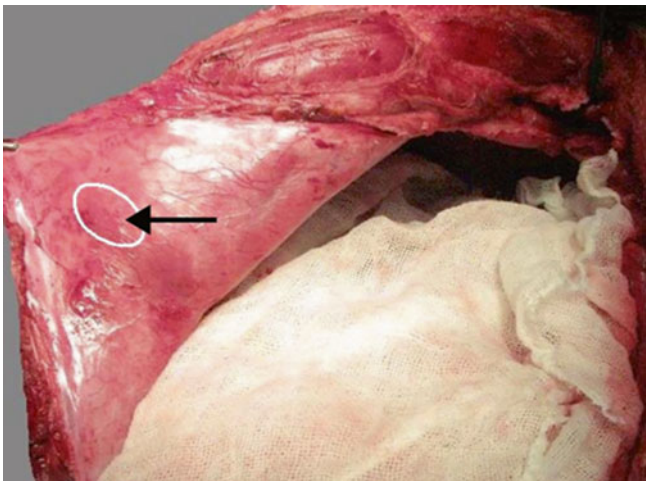

Fig. 16.41 An appropriate patch of peritoneum is taken from the upper right abdominal wall together with the posterior layer of the sheath of rectus abdominis (*arrow* marks the peritoneum to be resected)

Then, a right hemihepatectomy is performed using the aforementioned procedures.

2. The portal trunk and its two branches are dissected and separated (Fig. 16.39).
3. The left portal branch and the proximal end of the portal trunk are occluded. The anterior wall of the portal bifurcation is incised to extract the PVTT. If the PVTT and the wall adhere tightly, they can be resected en bloc (Fig. 16.40). After extraction of the PVTT, the portal trunk is released to flush out possible PVTT debris.
4. An appropriate patch of peritoneum is taken from the upper right abdominal wall together with the posterior layer of the sheath of rectus abdominis. The defect of the portal wall is mended with the patch by intermittent sutures of 6-0 Prolene (Figs. 16.41, 16.42, and 16.43). The inner surface of the patch should face the cavity.
5. The portal trunk and its left branch are unobstructed in the follow-up two months postoperatively (Fig. 16.44).

16.9 Points for Attention During Operation

1. Before extracting the PVTT from the left or right portal branch, the contralateral portal branch should be temporarily occluded to prevent cancer cells from metastasizing to the contralateral portal veins.
2. Forceps and suctions can be used to extract the PVTT. PVTTs that adhere loosely to the portal wall can

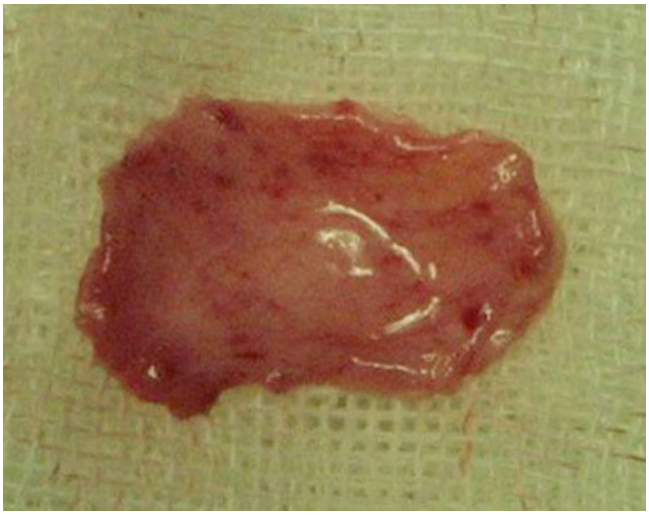

Fig. 16.42 The resected autologous peritoneum

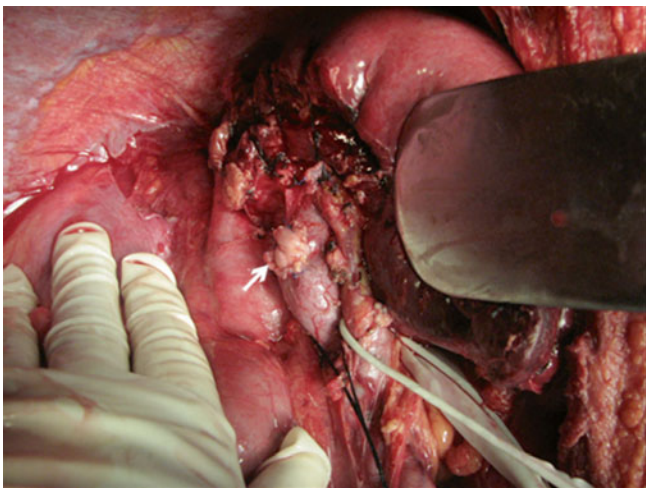

Fig. 16.43 The defect of the portal wall is mended with the patch of autologous peritoneum (*arrows*)

be easily extracted. Then, shave the portal wall gently with the curette to eliminate the PVTT residue. Organized PVTTs adhere so tightly to the portal wall that it is very difficult to separate them. In that case, the relevant portal wall needs to be resected en bloc with the PVTT. The portal vein is then mended with the autologous vein, autologous peritoneum, or vascular prostheses. End-to-end anastomosis of the portal vein using 6-0 Prolene can be performed when necessary.

3. When extracting the PVTT from the stumps of the portal vein, the portal trunk is temporarily reperfused to flush out possible PVTT debris. Normal saline is routinely used to flush the portal cavity. No blood or insufficient blood flowing out of the portal vein indicates that there is still PVTT occluding the portal trunk, and the extraction should be continued until blood gushes out. The portal trunk should be incised to extract the PVTT in case of difficulty in extracting it from the stumps.
4. For patients who require en bloc resection of the portal vein and the PVTT, a reversed L-shaped incision of the upper right abdomen is recommended to facilitate resecting the autologous peritoneum patch. The resected autologous peritoneum patch must include the back layer of the sheath of rectus abdominis to ensure its strength [34].

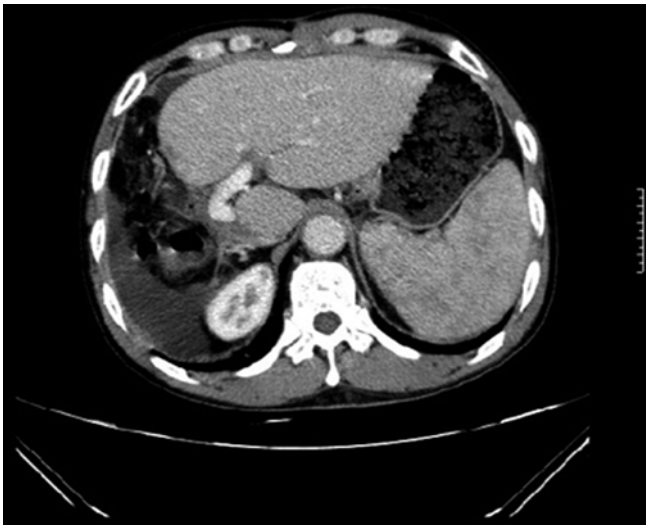

Fig. 16.44 The portal trunk and its left branch are unobstructed

16.10 The Treatment of Complications

1. Postoperative bleeding: Reasons for postoperative bleeding include less than thorough intraoperative hemostasis, infection, and necrosis of the liver cross section and coagulation abnormities caused by poor liver function. Bleeding should be detected and treated in the early phase, and the causes should be identified. For vessel bleeding, the wound should be opened to ligate or suture the bleeding vessels. For massive errhysis, hemostasis can be obtained by compressing with a hemostatic sponge or gauze. For patients with hemorrhagic tendency, coagulation drugs and fresh blood should be administered.
2. Biliary peritonitis: A small amount of bile will leak from the liver surface, which will stop spontaneously in 3–7 days under adequate drainage. If the ligature falls off or necrosis of the large bile ducts on the liver surface occurs, bile leakage and biliary peritonitis will result. Therefore, the hepatic ischemic time should be minimized in the operation, the bile ducts should be securely ligated, and the drainage should be adequate. Once diagnosed as biliary peritonitis, surgical drainage should be performed.

3. Liver failure: Post-hepatectomy liver failure is a common severe complication of liver resection. The clinical manifestations are constant fever, dysphoria, deepening jaundice, aggravating ascites, hemorrhagic tendency, oliguria, and even coma. Liver failure often occurs in patients who are given large amounts of anesthetic, with poor preoperative liver function, and heavy surgical injury. Liver-protecting measures should be taken, such as administration of glucose, vitamins, branched-chain amino acid, and hepatoprotective medicine; protein intake restriction; oxygen inhalation; antibiotics; and colonic irrigation.
4. Upper gastrointestinal hemorrhage: Cases with PVTT are often complicated by portal hypertension and resultant esophageal and gastric varices. Upper gastrointestinal hemorrhage may occur several days postoperatively. The treatment is the same as for esophagogastric variceal hemorrhage. If the bleeding is caused by a peptic ulcer or stress ulcer, the treatment should be based on respective principals.
5. Subphrenic infection: The possible causes are less than thorough intraoperative hemostasis, inadequate drainage, and early extubation. The diagnosis can be made by ultrasound combined with CT. The infection can be controlled by ultrasound-guided catheter drainage and antibiotics.
6. Hydrothorax: Hydrothorax, especially right pleural effusion, is common after hepatectomy. The causes include hypoproteinemia, lymphatic obstruction caused by massive dissection around the liver, wounds of the diaphragm and the liver, and irritated pleura. The clinical manifestations are mild fever, chest congestion, and even dyspnea. Chest X-ray or ultrasound can demonstrate the location and quantity of the effusion. A small amount of effusion needs no treatment. A large amount of effusion can be treated by ultrasound-guided drainage or closed thoracic drainage if it recurs.

16.11 Evaluation of Surgical Outcomes

PVTT is one of the most dangerous complications of hepatocellular carcinoma and can result in portal hypertension, deterioration of liver function, intrahepatic and extrahepatic metastasis, and postoperative tumor recurrence. The natural course of hepatocellular carcinoma accompanied by PVTT is only 2.7–4.0 months. Surgery is still the most effective treatment.

Chen et al. [35] reported the surgical outcomes of 438 PVTT patients. Among them, 286 PVTTs (group A) were within the resection area or extended to the first branches of the portal vein and surpassed the resection line by no more than 1 cm. One hundred fifty-two PVTTs (group B) invaded the trunk of the portal vein. The recurrence rate of group B at 6 months postoperatively was 77 % and was much higher than in group A (11.3 %). Additionally, the recurrence rate of group B at 1 year postoperatively, 78.8 %, was also much higher than the 45.0 % of group A. The 1-, 2-, 3-, and 5-year overall survivals were 58.7 %, 39.9 %, 22.7 %, and 18.1 % for group A and 39.5 %, 20.4 %, 5.7 %, and 0 % for group B, respectively.

Shi et al. [6] retrospectively analyzed the data for 406 patients of hepatocellular carcinoma who underwent surgery. The numbers of cases with types I, II, III, and IV tumors were 139, 169, 78, and 20, respectively. Among all patients, the 1- and 3-year overall survival rates were 34.4 % and 13.0 %, respectively, and the 1- and 3-year disease-free survival rates were 13.3 % and 14.7 %, respectively. In type I patients, the 1- and 3-year overall survival rates were 52.1 % and 25.1 %, respectively, and the 1- and 3-year disease-free survival rates were 21.1 % and 4.4 %, respectively. In type II patients, the 1- and 3-year overall survival rates were 38.2 % and 17.7 %, respectively, and the 1- and 3-year disease-free survival rates were 13.6 % and 6.4 %, respectively. In type III patients, the 1- and 3-year overall survival rates were 24.7 % and 3.6 %, respectively, and the 1- and 3-year disease-free survival rates were 3.0 % and 0, respectively. In type IV patients, the 1- and 3-year overall survival rates were 18.3 % and 0, respectively, and 1- and 3-year disease-free survival were both 0. The aforementioned studies suggest that PVTTs that invade the portal trunk or mesenteric vein have a much worse surgical outcome.

Ikai et al. [36] reported 78 Vp3-4 (i.e., PVTT in the first portal branch or portal trunk) cases. After hepatectomy and thrombectomy, these patients achieved a mean survival time of 0.74 years and a 3-year overall survival rate of 21.7 %. Matono et al. [37] reported 29 Vp4 (i.e., PVTT in the portal trunk) patients. After hepatectomy and thrombectomy, these patients achieved 1-, 3-, and 5-year overall survival rates of 62.1 %, 24.1 %, and 17.2 %, respectively. Ban et al. [38] reported 45 Vp3 and Vp4 patients. After hepatectomy and thrombectomy, these patients achieved 1-, 3-, and 5-year overall survival rates of 35.3 %, 41.8 %, and 21.2 %, respectively. The independent prognostic factors were serum AFP level, serosal invasion, and intrahepatic metastasis. For Vp4 patients, hepatectomy combined with thrombectomy not only prevents acute occlusion of the portal vein but also achieves a survival benefit comparable with that of Vp3 patients. Chok et al. [5] reported the surgical outcomes of 88 PVTT patients. The mortality rate was 3.4 %, and the postoperative complication rate was 37.5 %. The operative method had no influence on the survival, complication, or recurrence rates.

The literature reports are all retrospective, with no prospective randomized controlled studies. The literature varies greatly with respect to the surgical outcome. Generally

speaking, apart from type IV, surgery is superior to conventional therapy [39]. Many factors influence the surgical outcome, such as PVTT type, serum AFP levels, and intrahepatic metastasis. Although the safety of the operation has improved tremendously, postoperative recurrence is inevitable due to PVTT residue or intrahepatic metastasis. Reducing the recurrence rate and improving long-term survival are challenges faced by surgeons [39].

We advocate combining hepatectomy with other treatments, such as HAI, radiation therapy, chemotherapy, molecular-targeted therapy, and immunotherapy, on the basis of restricted indications. The appropriate patients should be appropriately treated at the appropriate time. Individualized multidisciplined treatment mode based on evidence-based medicine may be the direction of development for the treatment of hepatocellular carcinoma accompanied by PVTT.

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Liver Resection of Secondary Liver Cancer

17

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Metastatic liver cancer, also known as secondary liver cancer, is formed by metastasis from cancer of other organs to the liver and is an indicator of late-stage malignancy. Metastatic liver cancer, if untreated, can result in a poor outcome. The median survival time of patients with this diagnosis is no more than 2 years, with patients rarely surviving for more than 5 years [1]. Optimal treatment for metastatic liver cancer remains a challenge in the modern era. Although multiple therapeutic methods such as surgical resection, liver transplantation, chemotherapy, transhepatic portal or arterial embolization, intratumor local injection, hyperthermic and hypothermic therapy, and gene therapy have been introduced, only surgical resection has achieved satisfactory results.

17.1 Origin of Metastatic Liver Cancer

Half of primary malignancy cases result in metastatic liver cancer, which outnumbers cancers of metastasis to the lung and all other organs. Metastatic liver cancer is commonly present in multiple lesions, though solitary lesions can exist. Metastases arrive at the liver via the portal vein, hepatic artery, the lymphatic system, or through direct invasion. Blood from the gastrointestinal tract and pelvic organs flows into the liver through the portal venous system. Malignancies of other sites such as breast cancer, lung cancer, renal cancer, neuroendocrine tumors, and malignant melanoma can metastasize to the liver. This is attributed to the dual blood supply of the liver. Cholecystic cancer or pancreatic cancer metastasizes to the liver directly and through the lymphatic system. Metastatic liver cancer most frequently originates from gastrointestinal carcinoma. Approximately 60 % of gastrointestinal malignancies and 35 % of breast malignancies metastasize to the liver. The incidence of metastatic liver cancer upon autopsy is 20.0–64.5 times that of primary hepatic cancer in western countries and approximately 1.2 times that of primary hepatic cancer in China.

17.2 Surgical Resection for Metastatic Liver Cancer

17.2.1 Indications and Contraindications for Operation

Surgical resection, an effective treatment for metastatic liver cancer, is considered likely to benefit patients in the overall course of the disease process. Surgical resection can only be considered when the following requirements are met:

1. The patient is in good condition with normal heart, lung, liver, and kidney function.
2. Solitary nodule or multiple metastases are defined within hemiliver.
3. The primary tumor is operable or already removed.
4. No extrahepatic metastases are present, or existing extrahepatic metastases are considered treated or likely to be treated effectively.
5. Lesions recurring after surgical resection, if present and localized, are considered candidates for reoperation when the patient meets the requirement for surgery.

The 5-year survival rate of patients undergoing resection for metastatic liver cancer is between 25 and 49 % [2–4]. Recurrence and metastasis occurs in 70–80 % patients undergoing operation despite the fact that surgical resection is considered the most effective option among available therapies. Reoperation can be considered in recurrent cases when surgical requirements are met. Patients with recurrent metastases

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in the remnant liver, if operated, can obtain outcomes comparable to those resulting from initial hepatectomy [5, 6]. Compared with initial hepatectomy, the incidence of complications and hospital death after second hepatectomy is not significantly different, although prolonged operation time and increased bleeding volume are likely to occur during the second hepatectomy.

Past conventional beliefs hold that the presence of metastases in each hemiliver, the existence of more than three metastatic nodules, a diameter of metastases beyond 5 or 10 cm, and the coexistence of extrahepatic metastases are each contraindications for hepatectomy [7, 8]. However, these are not currently considered absolute contraindications. The assessment of patient safety prior to operation and the potential success of radical resection should be given priority when surgical resection is considered in suitable cases. According to Vauthey et al. [9], surgical resection for metastatic liver cancer in non-cirrhotic patients is feasible when liver function is normal, and 25–30 % of remnant liver by volume can be preserved.

Extrahepatic metastasis has long been viewed as a contraindication for surgical resection. In 2003, Elias et al. [10] reported that negative resection margin (R0) occurred in 77 of 111 (69 %) of patients who underwent surgical resection for metastatic liver cancer originating from the colon or rectum while concomitantly undergoing operations for extrahepatic metastases. The 5-year survival rate was reported to be 29 %, suggesting that extrahepatic metastases do not compromise 5-year survival outcome. Surgical resection is generally thought to be suitable in patients with metastatic liver cancer and extrahepatic metastases when R0 is predicted and extrahepatic metastases are responsive to chemotherapy as well as postoperative treatment is effective and available. However, the outcome of patients with hilar lymph node metastasis, especially in cases with retroperitoneal lymph nodes involvement, is worse than single extrahepatic metastasis. It is controversial whether surgical resection is contraindicated in patients with more than three metastatic nodules or whether an upper number limit of nodules should be used as a contraindication to surgery. Some argue that the number of metastatic nodules is a significant predictor, claiming that patients with three or four metastatic nodules are inappropriate for surgical resection because hepatectomy would elevate mortality and reduce 5-year survival rate. However, some research indicates that the number of metastatic nodules is unrelated to patient outcome. Moroz et al. [11] reported that 5-year survival rate was not significantly different between 22 cases with 4–7 nodules (39 %) and 91 cases with 1–3 nodules (30 %) among 123 patients undergoing hepatectomy for metastatic liver cancer from the colon or rectum. This study also found that local infiltration and recurrence after operation are independent of the overall outcome of patients with metastatic liver cancer. Several research studies with large sample sizes have demonstrated that mortality and the incidence of complications after surgery do not increase as the number of metastatic nodules grows [12, 13]. These studies suggest that three or more than three metastatic nodules are not an absolute contraindication to surgical resection.

In conclusion, hepatectomy for metastatic liver cancer is indicated only when the primary tumor has already been removed or is able to be removed simultaneously. Advanced age alone is not a contraindication. Senile patients with cardiac and lung comorbidities cannot tolerate surgical trauma and should therefore not be considered for hepatectomy. A presurgical understanding of the size, position, and blood supply of the tumor, as well as the relationship of the tumor with hepatic conduits, facilitates establishing an accurate surgical strategy.

17.2.2 Timing of Surgical Resection

No consensus has been reached as to whether hepatectomy should be performed simultaneously with or following the operation for the primary tumor when metastasis and primary lesion are detected concurrently. Advocates for concomitant hepatectomy believe that patients who postpone hepatectomy risk losing the opportunity for surgical resection because hepatic metastases may transfer again. In contrast, advocates for postponed hepatectomy believe that mortality and the incidence of complications will increase and that removal of micrometastases may be incomplete when concomitant hepatectomy is performed. Postponed hepatectomy is recommended to be performed 2–3 months after the operation of the primary tumor, due to the belief that concomitant hepatectomy would increase surgical complications and mortality [14]; furthermore, there may be concealed micrometastases that make scheduled concomitant hepatectomy and the goal of radical cure unachievable [15]. Growing evidence indicates that concomitant hepatectomy is as safe as staged hepatectomy [16] and leads to comparable outcomes [17] with current improved surgical technique and detection methods. For this reason, the timing of surgical resection should depend on patient conditions such as physical tolerance for undergoing surgical procedure, the sites and size of primary and metastatic cancer lesions, and whether incision facilitates exposure during hepatectomy.

For patients whose hepatic metastases come from gastrointestinal tumors and who are suitable for concomitant hepatectomy, hepatic metastases should be removed prior to the removal of the primary gastrointestinal lesion. This is indicated for several reasons. First, the low central venous pressure that is usually adopted to decrease bleeding during hepatectomy impairs splanchnic blood flow. To decrease the duration of low perfusion to gastrointestinal anastomoses, gastrointestinal surgery is performed directly following hepatectomy, thus allowing for the rapid recovery of central venous pressure after these procedures have been

successfully performed. When the gastrointestinal procedure is performed before hepatectomy, hilar occlusion can result in gastrointestinal anastomotic engorgement that impairs anastomotic healing. Additionally, hepatectomy is not as prone to contamination as gastrointestinal surgery, and surgical instrument replacement is therefore not required when moving from a hepatic to gastrointestinal surgical site. Several incision sites can be considered in concomitant hepatectomy, including a median incision between the xiphoid process and pubic symphysis and a subcostal oblique incision combined with a right paramedian incision.

17.2.3 Resection Margin

Arguments exist as to whether negative resection margin (R0) should be achieved in surgical resection for metastatic liver cancer. It is highly debatable whether R0 is required and what the optimal distance between the cutting edge and the tumor in hepatic metastases resection should be if R0 is determined to be necessary. It is generally believed that R0 contributes to reduced recurrence of cutting edge and intra- and extrahepatic metastasis, as well as contributing to improved outcome overall. However, current studies show that positive resection margin does not correspond with an increased risk of cutting edge and intra- and extrahepatic recurrence, nor does positive resection margin relate to recurrence-free survival and overall survival [18]. Some believe that a margin greater than 1 cm can improve survival, while others argue that the difference in outcome between short and distal margin cases is insignificant when negative resection margin is assured. As a result, a margin <1 cm should not be viewed as a contraindication on preoperative evaluation [19]. Further studies are required to determine the minimal margin that guarantees a negative resection margin.

17.2.4 Surgical Methods

17.2.4.1 Conventional Open Hepatectomy

Serial well-designed retrospective studies have shown that hepatectomy can dramatically improve the longevity of patients with metastatic liver cancer and even cure those with cancers of gastrointestinal origin. Despite this, prospective randomized controlled trials investigating the effect of surgical resection on metastatic liver cancer are currently unavailable. In 1963, Woodington et al. [20] first reported a 5-year survival rate of 20 % in 20 patients undergoing hepatectomy for metastatic liver cancer of various origins, including the colon, stomach, gallbladder, pancreas, and malignant melanoma. Since then, surgical resection has been increasingly accepted as treatment for metastatic liver cancer, especially when other therapies prove unsuccessful. Meanwhile, the outcome of patients with metastatic liver cancer undergoing surgical resection improves with an improved understanding of hepatic segmentation and an enhancement of surgical technique and postoperative care. Martinet et al. [21] reported that 5-year survival rate reached 25–40 % after hepatectomy in patients with hepatic metastasis from the colon and rectum; however, operable metastases were found in no more than 20 % of the cases. Cummings et al. [22] analyzed the clinical data of 13,599 patients with colorectal carcinoma and metastasis to the liver and found that hepatectomy was appropriately performed in only 833 cases (6.1 %). This resulted in a 30-day mortality of 4.3 % and a 5-year survival rate of 32.8 %, which was significantly higher than the 5-year survival rate in those without hepatectomy (10.5 %). Thelen et al. [23] reported that 1-, 3-, and 5-year survival rates were 77 %, 50 %, and 42 %, respectively, in patients undergoing hepatectomy for liver metastases from breast cancer. In another study, after retrospective investigation of the postoperative data of 1452 cases undergoing liver metastases from sites other than colorectal or neuroendocrine tumors, Adam et al. [24] found that 5- and 10-year survival rates were 36 % and 23 %, respectively, and 5- and 10-year disease-free survival rates 21 % and 15 %, respectively. The median survival time was 35 months, and the median disease-free survival time was 13 months. Among these liver metastasis cases, 460 cases (32 %) were from breast cancer with 5- and 10-year survival rates of 41 % and 22 %, respectively, and a median survival time of 45 months. Additionally, 230 cases (16 %) were from gastrointestinal cancer with a 5-year survival rate of 31 % and a median survival time of 26 months, 206 cases (14 %) were from urinary cancer with a 5-year survival rate of 48 % and a median survival time of 51 months, 148 cases (10 %) were from malignant melanoma with a 5-year survival rate of 22 %, and 84 cases (6 %) were from biliopancreatic cancer only, with those from ampullary cancer achieving an acceptable 5-year survival rate of 46 %. Five-year survival of patients with liver metastases from unknown source was 38 %. Patients with liver metastases from breast cancer who were treated surgically obtained an improved 5-year survival rate. Extended hepatectomy, anatomic hepatectomy, hepatic segmentectomy, and partial hepatectomy are technical options for liver metastases. Normally, the maximum volume of removed hepatic tissue is 60–65 % [25, 26]. The advantage of a partial hepatectomy in comparison to more aggressive techniques is that postoperative liver failure is uncommon due to the preservation of remaining functional liver tissue.

17.2.4.2 Laparoscopic Hepatectomy

The development of minimally invasive surgical techniques exemplified by laparoscopic cholecystectomy has gained momentum in recent years, and surgeons treating liver cancer using these minimally invasive techniques have achieved

some success. Minimally invasive surgeries such as laparoscopic hepatectomy and laparoscopic radioablation have been launched to treat liver cancer. Laparoscopic hepatectomy, characterized by causing minimal trauma and an accelerated recuperation after operation, is as effective as open hepatectomy and therefore shows great potential. However, laparoscopic hepatectomy does introduce new challenges. The procedure is technically demanding, requires sophisticated manipulation, and makes control of bleeding from the hepatic cutting face difficult due to the difficulty of achieving hilar occlusion under laparoscopy. Additionally, absence of optimal instruments for laparoscopic hepatectomy retards the advancement of this procedure. Laparoscopic hepatic malignancy resection, hand-assisted laparoscopic hepatectomy, and laparoscopic hepatic tumor radioablation are commonly used. Controversy over complications such as tumor implantation around the trocar used in laparoscopic hepatic tumor resection and dissemination of tumors by pneumoperitoneum has yet to be resolved. Explanations for these complications include that (1) laparoscopic instrument contamination by tumor cells could cause indirect implantation on other viscera or puncture sites and that (2) tumor cells evaporated by CO_2 gas inside the abdomen could implant on other viscera or puncture sites. When continued pneumoperitoneum is established, a gas leak at puncture sites or vacuum while finalizing the operation could help spread detached tumor cells.

17.2.4.3 Liver Transplantation

Currently, there is not adequate experience from which to draw conclusions about the success of treatment of metastatic liver cancer using liver transplantation. Tumors that reoccur early after liver transplantation lead to poor long-term outcome. According to statistics from European and American countries, the 1-year survival rate in patients undergoing liver transplantation for liver metastases from various sources except neuroendocrine system was only 5 % [27]. Liver transplantation is optional for liver metastases from the neuroendocrine system because of poor infiltrative characteristic of these metastases. Patients who undergo liver transplantation for inoperable liver metastases from the neuroendocrine system after the primary tumor has been removed may enjoy long-term regression or even healing [28]. Recipient criteria should be strict when liver transplantation is used to treat liver metastases due to a shortage of livers available for transplant. Only patients with no extrahepatic metastases who have failed to show improvement after pursuing other treatment options should be considered.

17.2.4.4 Surgical Therapy for Inoperable Liver Metastases

An inoperable liver metastasis is generally defined as a metastatic tumor involving 70 % of the liver or more than 6 segments as well as branches of portal vein and hepatic veins. It is now believed that for cases deemed inoperable upon diagnosis, surgical resection after the tumor has been downsized by neoadjuvant chemotherapy can improve survival and life quality [29]. A serial study by Bismuth et al. [30, 31] showed that neoadjuvant chemotherapy could downstage liver metastases and makes a greater number of inoperable liver metastases operable. This study further suggested that neoadjuvant would revolutionize oncologic surgery.

17.3 Summary

Prognosis of metastatic liver cancer depends on the site and malignancy of the primary tumor, the involved volume of the liver, existing extrahepatic metastasis, and patient systemic condition. In general, patients diagnosed with liver metastases will die within 1 year. Compared to this, those patients with liver metastases originating from the gastrointestinal tract have a better outcome. Patients with multiple liver metastases commonly die 2–3 years after diagnosis and only 16 % patients with solitary liver metastasis survive more than 5 years. To achieve maximum remission, improve life quality, and prolong longevity of patients with liver metastases, combined therapy based on operation is used only when the primary tumor has been resected as much as possible.

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Hepatectomy for Hepatic Hemangioma

18

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18.1 History and the Present Status of Hepatic Hemangioma Surgery

Hepatic hemangiomas (HHs) are the most common type of benign liver tumor, with an incidence of ~3–20 % [1]. Among the different pathological types of HH, cavernous hemangioma is most commonly seen in clinics, and tumors are often discovered by ultrasound or contrast-enhanced CT in physical examinations. The majority of HH patients have no clinical symptoms, but some suffer from upper abdominal pain and discomfort. Although surgical resection is often adopted for the treatment of HHs, there are still no consensus in terms of surgical indications. Other treatment methods include radiofrequency ablation, hepatic artery embolization, suture and ligation, hepatic artery ligation, and microwave coagulation. For a small number of patients with diffuse HHs or unresectable giant HHs, liver transplantation can be performed if liver decompensation occurs.

18.2 Classification of HH

Classification by pathological types:
- Cavernous hemangioma (most common)
- Sclerosing hemangioma
- Hemangioendothelioma
- Capillary hemangioma

Classification by tumor size:
- Small hemangioma <5 cm
- Large hemangioma 5–10 cm
- Giant hemangioma >10 cm
- Diffuse hemangioma

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Determining the classification of HHs has implications for the development of surgical programs.

18.3 Diagnosis

HHs lack specific clinical manifestations and rarely present abnormalities during examinations of relevant tumor markers. The majority of HH cases are found by physical examinations. Imaging examination (including upper abdominal ultrasound, upper abdominal contrast-enhanced CT, and upper abdominal MRI) is the primary approach to diagnose HHs.

18.3.1 Ultrasound Examination

HHs appear hyperechoic on color Doppler ultrasound. The hyperechoic region often has a lattice-like structure, uniform density, regular shape, and clear boundary, with a partially complete capsule. A relatively large cross section of the hemangioma may be lobulated, and the internal echoes are mainly hyperechoic. The hypoechoic region may be tubuloreticular or present with an irregular nodular or banding pattern. In some cases, the hyperechoic region of calcification is associated with posterior shadowing due to intravascular thrombosis in hemangiomas with organization or calcification.

18.3.2 Contrast-Enhanced Ultrasound

For HH patients who appear atypical in ordinary color Doppler ultrasound examinations, the diagnosis can be confirmed by a contrast-enhanced ultrasound examination. The typical manifestations of hemangioma in contrast-enhanced ultrasound examinations are as follows: nodular or ring

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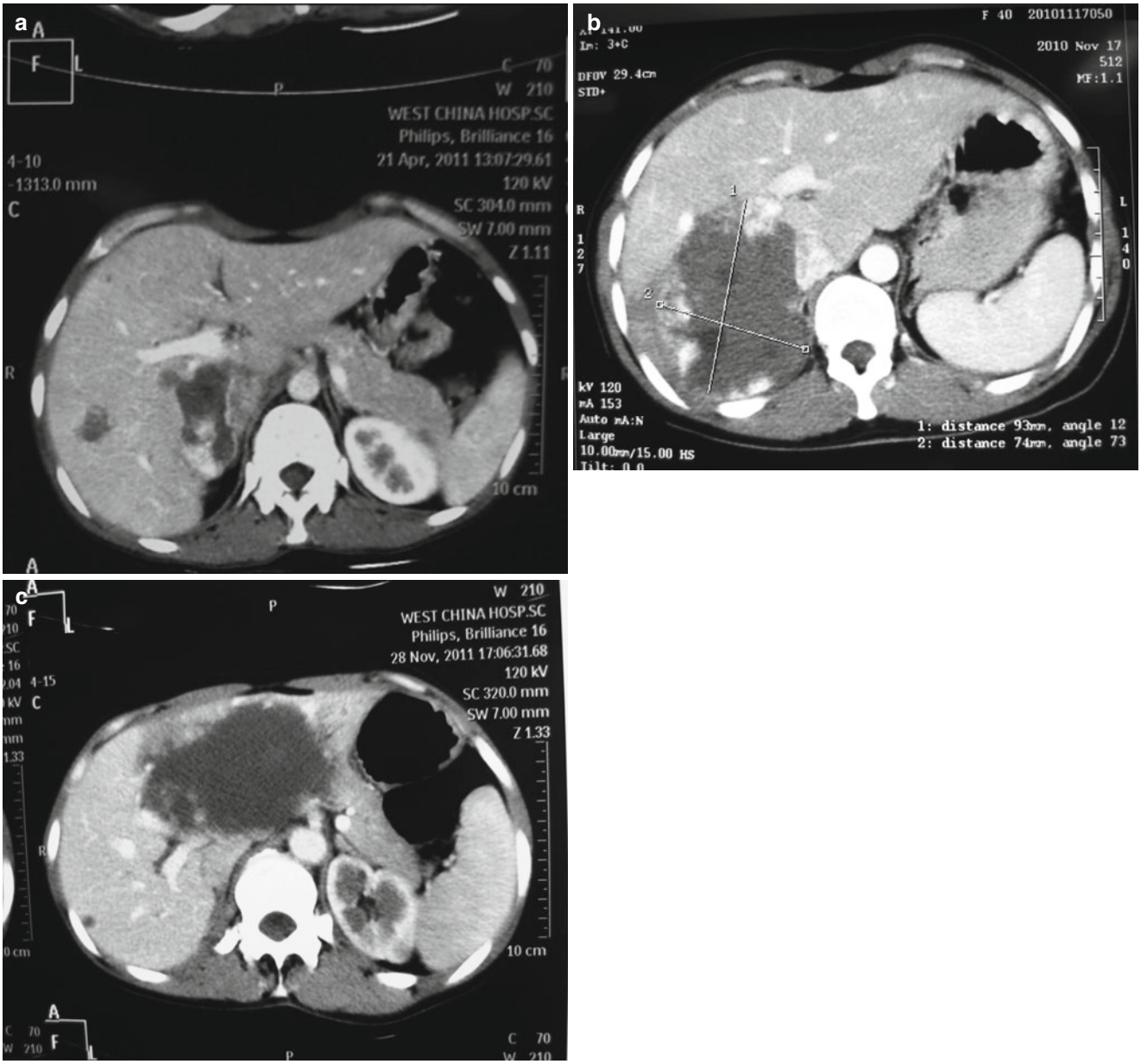

Fig. 18.1 (**a**–**c**) Contrast-enhanced CT image of a HH. (**b**) (*1*) represented the maximum diameter of the hepatic hemangioma (93mm); (*2*) represented the minimum diameter of the hepatic hemangioma (74mm)

enhancement of the liver margin at the arterial phase, the extent of enhancement gradually extends toward the tumor center over time, and the tumor mass remains in an enhanced state at the enhanced portal venous and delayed phases, with echoes equal to or higher than the surrounding liver tissue.

18.3.3 Contrast-Enhanced CT/MRI Examination

Typical HHs follow a "fast-in and slow-out" trend in contrast-enhanced T1-weighed CT/MRI examinations. Specifically, nodular or ring enhancement of the tumor margin is present at the arterial phase; the enhancement expands toward tumor center at the portal venous phase; and the tumor mass shows enhancement at the delayed phase, with higher density than the surrounding normal liver tissue (Fig. 18.1).

Liver biopsy is a contraindication for patients suspected of this disease.

18.4 Surgical Indications

When should surgery be performed for an HH? What size of HH should undergo surgical resection? These questions remain controversial, and no consensus has been reached to date. Foreign researchers define tumors >4 cm in diameter as giant hemangiomas. The idea is that a tumor >4 cm at the hepatic margin or hilum is easy to rupture or may compress the hilar bile duct and blood vessels, for which surgical

treatment is preferred [2]. Domestic scholars deem that surgical treatment is needed for tumors >10 cm with rapid growth over a short-term period, tumors >5 cm located at the margin of the left external lobe or the right hepatic lobe, or tumor masses with nearly half of the mass protruding out of the liver. Currently, our medical center adopts the following surgical indications for HHs:

1. For tumors with a diameter <5 cm, with or without clinical symptoms, short-term clinical observation is suggested.
2. For tumors with a diameter 5–9 cm with right upper abdominal pain and discomfort or tumors located at the hepatic margin (right or left external lobe), surgical resection is considered.
3. For tumors with a diameter >10 cm, surgical resection is recommend.
4. For tumors with a significant increase in diameter in a short-term period during clinical observation, regardless of tumor diameter, surgical resection is considered.

18.5 Surgical Options

The biological behavior of HHs is consistent with the manifestations of benign tumors. Therefore, there is no vascular invasion or intrahepatic and extrahepatic metastasis in clinical cases of HH. Depending on the growth location and tumor size of HH and the classification of the liver segments, the surgical options for HH presently include the following:

Non-anatomical liver resection – suitable for giant hemangiomas confined to half of the liver, exceeding half of the liver, or in multiple liver segments (Fig. 18.2)

Liver segment resection – suitable for hemangiomas confined to one or two hepatic segments

Caudate lobe resection – suitable for hemangiomas in segment I

Radiofrequency ablation, hepatic artery embolization, suture and ligation, hepatic artery ligation, and microwave coagulation – not widely used

Liver transplantation – used for a small number of cases with diffuse HHs or unresectable giant HHs that present with liver function decompensated

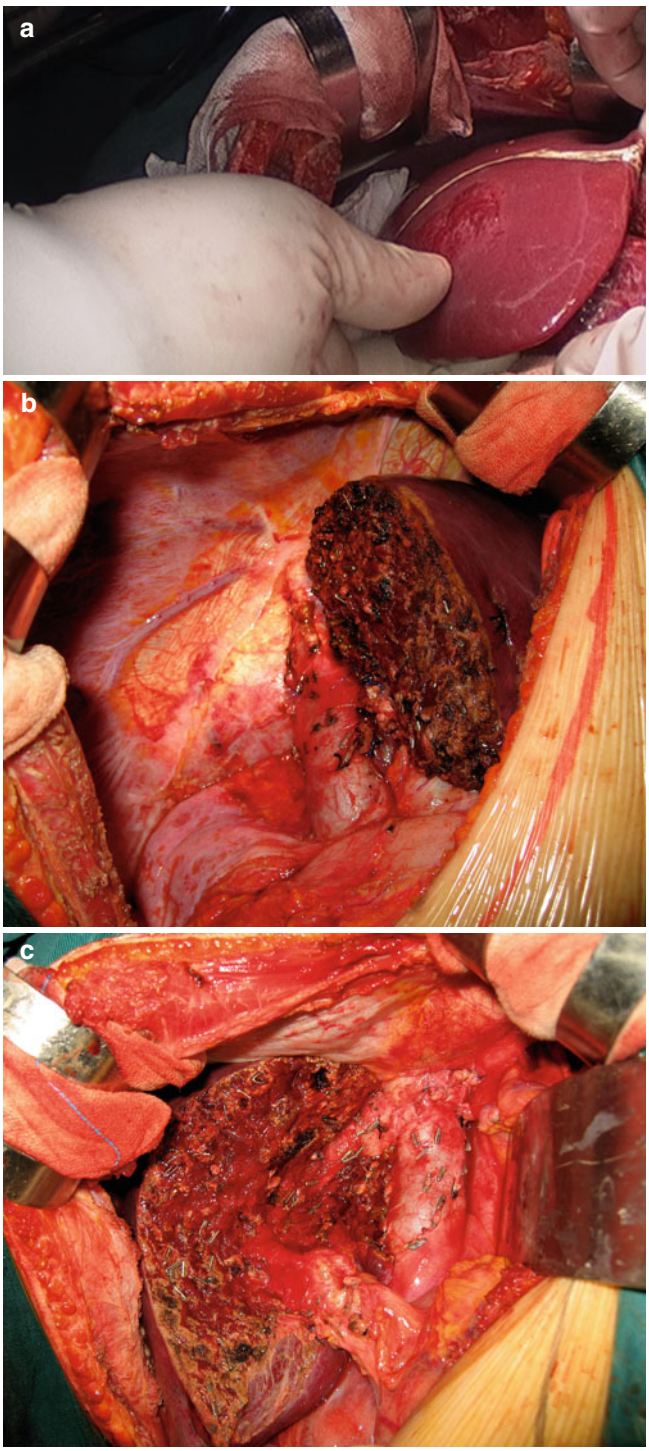

Fig. 18.2 (**a**–**c**) Non-anatomical liver resection

18.6 Surgical Techniques

18.6.1 Local Resection or Liver Segment Resection

The Pringle maneuver or "simple hemi-occlusion" technique is used for liver transection (Fig. 18.3); "hooking with ligation" is used for parenchymal transection (Fig. 18.4) [3, 4].

When a Cavitron Ultrasonic Surgical Aspirator (CUSA) or Water Jet is used for liver parenchymal transection, vascular occlusion or hemi-occlusion should not be performed because a major resection costs much more time. However, when the "hooking with ligation" method is used for parenchymal transection, a shorter time is spent (always less than 30 min); therefore, total hepatic occlusion and sometimes hemi-occlusion were adopted during resection (Fig. 18.5).

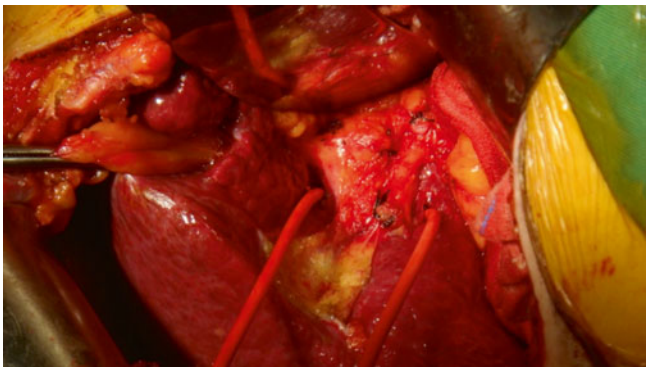

Fig. 18.3 "Simple hemi-occlusion"

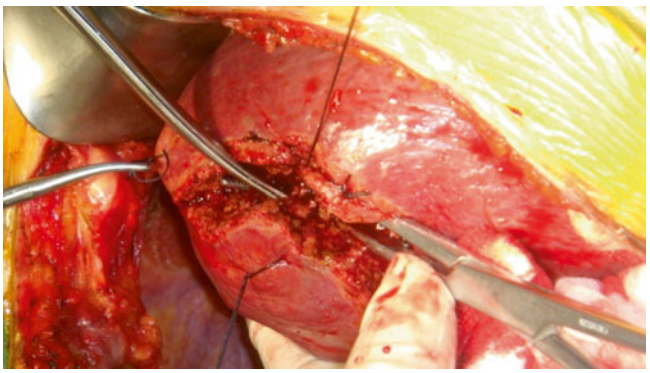

Fig. 18.4 "Hooking with ligation" for liver parenchymal transection

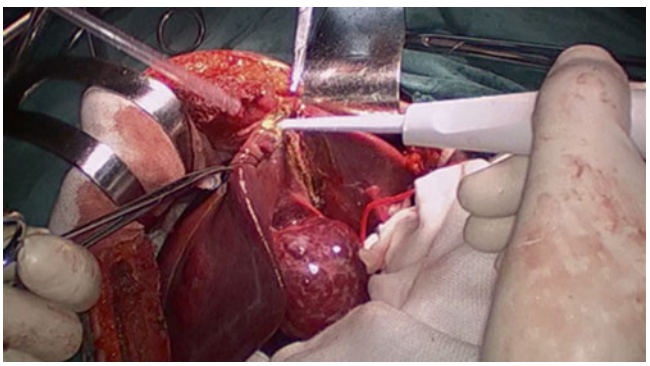

Fig. 18.5 Water Jet for liver parenchymal transection

18.6.2 Caudate Lobe Resection

Figures 18.6, 18.7, and 18.8.

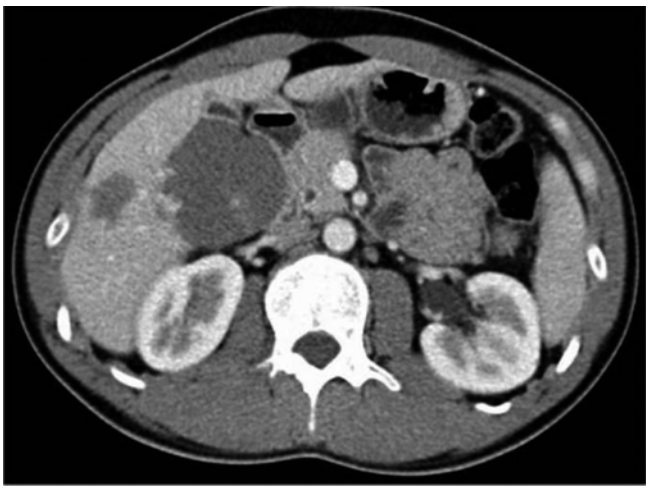

Fig. 18.6 CT image showing a hepatic hemangioma confined to segment I

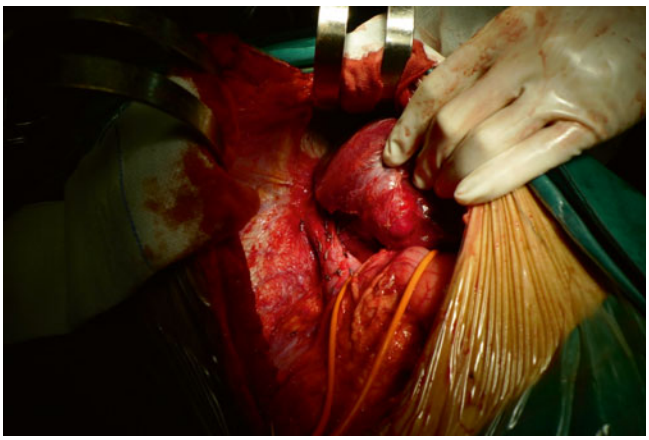

Fig. 18.7 Photo showing a hepatic hemangioma confined to segment I

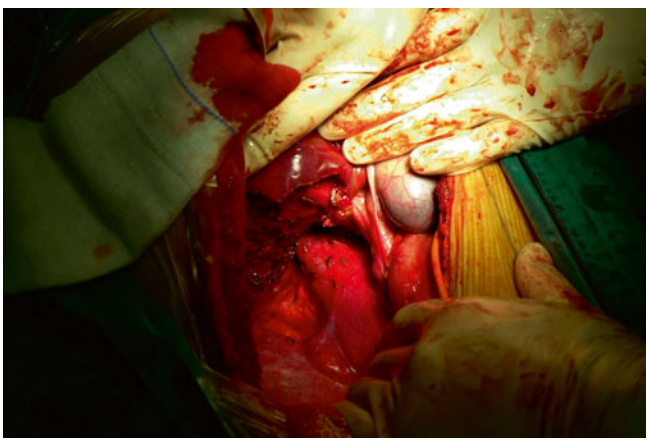

Fig. 18.8 Photo showing a hepatic hemangioma confined to segment I after resection

18.7 Complications and Treatment

The complication rate following a hepatectomy for HH is substantially low, with almost no deaths in hospitalized patients. Cases of death due to liver failure are rare. The primary causes for postoperative liver dysfunction are related to small residual liver volume, postoperative infections, vascular complications, and bleeding.

18.8 Long-Term Follow-Up Results

HHs are benign liver tumors for which surgical resection can achieve a curative effect without recurrence. Patients with liver transplantation can also be cured and survive for a long-term period if no severe complications occur after surgery.

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Liver Resection in Hepatic Hydatid Disease

19

Zheyu Chen

19.1 History and Current Situation

Hepatic hydatid disease is also called echinococcosis of the liver. It is a kind of parasitic zoonosis caused by infection with the larva of echinococcus in the visceral organs of human beings and other animals. After infection with echinococcus has occurred, the larva of echinococcus can parasitize many organs in the body. The liver is the most commonly affected organ and accounts for approximately 70 % of cases, followed by the lung, which accounts for 20 % of cases. It can be also observed in other organs, such as the brain, heart, kidney, orbit, and bone marrow cavity, which accounts for approximately 10 % [1]. Hepatic hydatid disease has been reported all around the world, and the prevalence is more severe in pastoral areas. Most of the locations where hydatid disease is prevalent are pastoral areas where economic conditions and medical conditions are very poor, and most patients are herdsmen who have no ability to afford hospitalization costs. Therefore, hepatic hydatid disease has become a severe public health problem in epidemic areas. Over the past few years, the thriving development of immigration and tourism has caused a high level of migratory movement, which has resulted in reports of hepatic hydatid disease in many non-epidemic areas [2, 3]. For this reason, the disease is becoming a global public health problem [4, 5]. Sixteen species and 13 subspecies of echinococcus have been found so far, but only five of them have important clinical significance: *Echinococcus granulosus*, *Echinococcus multilocularis*, *Echinococcus oligarthrus*, *Echinococcus vogeli*, and *Echinococcus shiquicus*, which were recently discovered in Shi Qu County of Sichuan Province [6]. Among them, *E. granulosus* is the most commonly reported all around the world. Infection with *E. granulosus* causes cystic echinococcosis, which is most commonly found in a clinical environment. *E. multilocularis* is rarely reported worldwide, but the incidence is very high in the Ganzi prefecture of Sichuan Province. Alveolar echinococcosis caused by *E. multilocularis* develops like a malignant tumor. It is a type of highly pathogenic disease that leads to high mortality, which has important clinical significance. This chapter focuses on these two kinds of echinococcosis.

19.2 Structure and Anatomy of an Echinococcus Cyst

If people eat the eggs of the echinococcus tapeworm, the larvae hatch under the effect of gastrointestinal fluid. Most of the larvae will be killed by the immune system after entering into the liver. A few of them escape from the immune system and continue to develop into cystic echinococcosis or alveolar echinococcosis.

A mature cyst of *E. granulosus* consists of an endocyst and a pericyst. An endocyst consists of a germinal layer that surrounds the fluid-filled central hydatid cavity and the laminated membrane outside. The germinal layer is actually the identity of echinococcus. The germinal layer can produce brood capsules, which develop into daughter cysts after dropping into cystic fluid. Daughter cysts have the same structure as their mother cyst except that they have no pericyst. The germinal layer can promote the growth of the cyst by absorbing nutrients from cystic fluid, and it has the ability of secreting cystic fluid. The laminated membrane is located in the outer layer of the germinal layer and has no cellular structure. It comes from secretion from the germinal layer and is a layer of semitransparent, elastic, thick membrane, which can be separated from pericyst. The laminated membrane plays the role of protecting echinococcus by preventing hazardous substances, such as enzyme, bile, and bacteria, from entering into the cyst. If the laminated membrane defects or ruptures, the germinal layer may penetrate it and develop into an exogenous daughter cyst. The compression

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of the host tissue around the endocyst produces a fibrous layer called pericyst. At the beginning of the formation of the cyst, pericyst is just a layer of thin fibrous membrane, and then it can reach 1 cm. Pericyst may calcify partially or even totally as the disease progresses. Calcification of pericyst prevents the endocyst from absorbing nutrient substances. Therefore, total calcification leads to the death of echinococcus, but partial calcification does not.

A hydatid cyst is filled with infective protoscoleces that can develop into daughter cysts in the cystic fluid, and the daughter cysts can produce granddaughter cysts in the same way. Some cysts of echinococcus contain thousands of protoscoleces. The cystic fluid is a kind of water-like sterile fluid secreted by the germinal layer under normal conditions. When cysts communicate with the biliary tract, the cystic fluid is dyed yellow by bile. The cystic fluid is purulent if infection occurs. The pressure of fluid within the cyst is very high, especially in a living echinococcus cyst, which can reach 70 cm of water column. For this reason, careful operation is important to prevent the cyst from rupturing, which may lead to spillage of cystic fluid. Spillage of cystic fluid may cause dissemination of protoscoleces in the peritoneal cavity, which develop into new cysts and give rise to secondary echinococcosis.

Hepatic hydatid cyst can develop in any part of the liver, but the pathogenic site is related to the volume of the liver lobe. So most hydatid cysts (65 %) develop in the right lobe of the liver; some cysts (13 %) grow in the left lobe of the liver, and a few cysts occur in both lobes of the liver [7]. The majority of cysts of *E. granulosus* are solitary [8].

Alveolar echinococcosis can be classified into massive type, nodule type, and mixed type. The most common type in the clinic is the massive type. Alveolar echinococcosis develops like slow-growing liver cancer and infiltrates surrounding liver tissue in a similar manner to blastogenesis, forming honeycombed small vesicles [9]. Necrosis can often be seen in the center of the cyst. Necrotic foci sometimes liquefy into jellylike fluid. Advanced alveolar echinococcosis has the ability to metastasize like a malignant tumor. It can erode adjacent organs directly and fall off into the portal vein, leading to intrahepatic metastasis. Metastasis to other organs may even occur through blood flow.

19.3 Clinical Manifestation

Patients usually have no obvious clinical symptoms in the early phase of the disease, which are often discovered by imageological examination. In the later stage of the disease, the enlarged cyst can compress adjacent organs and lead to corresponding symptoms. Sometimes infection and other complications occur, which may cause some symptoms.

19.3.1 Compression Symptoms

In the late stage of the disease, abdominal pain is the most common symptom, which is caused by the compression of adjacent liver tissue and organ by the enlarged cyst [10]. The most common physical signs are hepatomegaly and abdominal mass caused by the enlarged cyst [11]. If the biliary tract is obstructed by a hydatid cyst, patients will have the symptoms of obstructive jaundice. Symptoms and signs of portal hypertension, such as splenomegaly, ascites, and lower esophageal varices, will appear when the cyst compresses the portal vein. Compression of inferior vena cava will lead to Budd–Chiari syndrome complex [12]. Sometimes a large cyst can oppress intestinal tract, which results in intestinal obstruction [13]. If the diaphragm is compressed by an enlarged cyst, respiration will be influenced.

19.3.2 Cyst Infection

A hepatic hydatid cyst may sometimes be infected by bacterium, especially when the cyst has communication with the biliary tract. If the cyst gets infected, patients will display the same symptoms as hepatic abscess, such as liver area pain, chill, and hyperpyrexia.

19.3.3 Manifestations of Complications

19.3.3.1 Cyst Ruptures into Biliary Tract

Cyst ruptures into biliary tract are the most common complication of hepatic hydatid disease, which accounts for 5–25 % of all the patients [14]. A small communication between cyst and biliary duct usually displays no symptoms and is discovered after an operation for bile leakage. A large communication would cause biliary obstruction. The contents of cyst could enter into biliary tract, which causes jaundice and biliary colic; sometimes it can even cause cholangitis.

19.3.3.2 Cyst Ruptures into Abdominal Cavity

Cyst ruptures into the abdominal cavity are not common in clinic, but are a fatal complication [15]. Generally, the cyst ruptures spontaneously in resting state. Sometimes blunt trauma on the abdomen also can lead to rupture of a cyst. Common symptoms in clinic are abdominal pain, nausea, vomiting, and symptoms of peritonitis. Sometimes an anaphylactic reaction may occur if a large amount of cystic fluid and protoscoleces enters into abdominal cavity [16], which may even develop into anaphylactic shock. Infective protoscoleces entering into abdominal cavity can cause implantation metastasis, which creates secondary abdominal echinococcus cysts.

19.3.3.3 Cyst Rupture into Thoracic Cavity

Cysts located at the top of the liver may rupture into the thoracic cavity. The most common symptoms are sudden severe chest pain, cough, and expiratory dyspnea. A lung abscess will be formed if the contents of cysts rupture into lung tissue. Protoscoleces in thoracic cavity may cause anaphylactic reaction and induce asthma. Some severe patients even develop asphyxiation.

19.3.3.4 Cyst Rupture into Other Organs

Echinococcus cysts can rupture into the pericardial cavity. Daldoul reported that hydatid cysts could burst into the duodenum [17]. Sometimes, cysts can even rupture into inferior vena cava and induce pulmonary embolism [18].

19.3.4 Manifestation of Alveolar Echinococcosis

Clinical symptoms of alveolar echinococcosis are similar to those of slow-growing liver cancer. Patients usually have no obvious manifestation in the early course of the disease. About one-third of patients are discovered by accident when they receive a medical examination as a result of fatigue and emaciation. Initial symptoms of advanced patients are upper abdominal pain, dyspepsia, anemia, and emaciation. The symptoms and signs of portal hypertension, such as splenomegaly, ascites, and lower esophageal varices, will appear when the entire liver is involved. Some patients may manifest symptoms of obstructive jaundice.

19.3.5 Physical Examination

The most common signs of hepatic hydatid disease are abdominal mass and hepatomegaly. Round cystic mass can usually be palpated in the right upper abdomen, which has a distinct boundary and no tenderness. When pressing a little harder on the cyst, the facies palmaris of right-hand finger can feel a kind of special tremor, which is called liver tremor. This is a characteristic sign of hepatic hydatid disease.

19.4 Laboratory Examination

19.4.1 Liver Function Test

Patients generally have no obvious change in liver function. The values of ALT and AST are normal. Sometimes ALP and GGT have slight elevation among a few patients. If ALP and GGT elevation are accompanied by a rise of bilirubin, communication between cyst and biliary duct is possible [19]. When the value of bilirubin in blood increases dramatically, complications associated with biliary duct should be taken into consideration, such as cyst ruptures into bile duct.

19.4.2 Eosinophilic Granulocyte Test

Elevation of eosinophilic granulocyte will happen in 25–45 % of patients. Elevation may be obvious in cases who have complications. However, an eosinophilic granulocyte test has no specificity in epidemic areas.

19.4.3 Casoni Intracutaneous Test

The Casoni test is a highly sensitive examination for hepatic hydatid disease. The positive rate of patients with *E. granulosus* can reach 90 %, and the positive rate of alveolar echinococcosis patients is much higher. However, this test is not applicable to a follow-up visit after an operation, because the antibody to echinococcus can exist in the body for a long time. The Casoni test may be still positive for a long period after an operation. Sometimes it can last for 20 years after the operation. Furthermore, the specificity of the Casoni test is not so high as its sensitivity, which is about 47 % [20]. It may give a false-positive reading when a patient is infected with other kinds of tapeworms.

19.4.4 Enzyme Immunoassay Test (ELISA)

When applying the ELISA test to the diagnosis of *E. granulosus*, its sensitivity can reach 85–98 % [21–23]. The test can be completed easily and has good stability. But some patients do not produce antibodies during their whole life, so the test is false negative in 10–20 % of patients. It needs to be pointed out that the ELISA test may have a cross-reaction with other kinds of diseases, such as other species of tapeworms, gastrointestinal worm, liver cirrhosis, and malignant tumor. For this reason, specificity of the test is only 60 % [24, 25]. It has been reported that the ELISA test was still positive after hydatid disease had been cured for 11 years, under the condition that the result of imageological examination was negative [26]. This is because there were IgG antibodies existing in body. So the ELISA test is suitable for large-scale epidemiological investigation, but not suitable for follow-up visit and reexamination after treatment.

Applying this test to diagnosis of alveolar echinococcosis can obtain a great effect. Its reliability is much higher than for cystic echinococcosis, and its sensitivity may be up to 95–100 %. If the antigen is specific and purified, the specificity can be also very high [27].

19.4.5 Western Blotting Analysis

Western blotting can be used to conduct quantitative analysis for antigens of echinococcus in serum at molecular level. If antigens of echinococcus can be purified, Western blotting analysis is an excellent measure for diagnosis, and it is also a good means for a follow-up visit after treatment. However, the procedure of Western blotting is complicated, in which antigen should be purified. For this reason, it is more useful in fundamental research than in clinical diagnosis.

19.5 Radiographic Assessment

Imageological examination plays an important role in the diagnosis and preoperative assessment of hepatic hydatid disease. The advantage of imageological examination in diagnosis of hepatic hydatid disease is not only its high sensitivity; its reliability is also much better than that of serological examination. The result of imageological examination is not affected by antibody, and it is commonly used for follow-up visit after operation.

19.5.1 Abdominal Ultrasound (US)

It is the easy operation and the low price that make abdominal ultrasound the first choice for diagnosis of hepatic hydatid disease. And its sensitivity can reach 92 %. The ultrasonic manifestation of cystic echinococcosis is a cystic liquid dark area, clear boundary, and thick cyst wall. Sometimes cyst wall is calcified, so the ultrasonic image will show strong echoes and rear acoustic shadow. Floating echogenic mass can be seen in the cyst, and the echogenic mass moves with change of posture, which is the characteristic of cystic echinococcosis. The ultrasonic manifestation of alveolar echinococcosis is a dense echogenic mass which has no obvious boundary with surrounding liver tissue. The internal echo of alveolar echinococcosis is always irregular and a liquid dark area can be usually seen in the central part, which is difficult to distinguish from liver cancer. Because the ultrasound device is cheap and easy to operate, this examination is used for the screening of an epidemic area and inspection after operation.

19.5.2 Computed Tomography (CT)

CT scan is also a common method for diagnosis of hepatic hydatid disease. It can not only reveal the morphology and location of cyst but also can obtain other morphological information including number, volume, and density of hydatid cysts and the relationship between blood vessels and surrounding organs. At the same time, we can also discover whether there are cysts in any other organs through CT scan. In addition, the information provided by CT image is objective and has no operator dependence. Therefore, using CT to conduct preoperative assessment is much preferable to ultrasound.

19.5.3 Magnetic Resonance Imaging (MRI)

MRI has better specificity than CT scan, and it can display the morphology and density of cysts more clearly. When biliary complications of a cyst are doubted, MRCP can show the intrahepatic and extrahepatic bile duct very well; this gives surgeons information concerning the relationship between cysts and biliary tract. For radiographic assessment of alveolar echinococcosis, MRI is superior to CT, because there is always central necrosis in cysts of alveolar echinococcosis, and alveolar echinococcosis has the ability to infiltrate into hepatic vein, inferior vena cava, and surrounding liver tissue.

19.6 Classification and Stage

In 2003, the WHO Informal Working Group on Echinococcosis (WHO/IWGE) classified echinococcosis disease into six types according to the US image [28]. The classification is summarized in Table 19.1:

1. Type CL: early-stage echinococcosis disease, unilocular, cystic lesion with uniform anechoic content, not clearly delimited by an hyperechoic rim, cyst wall not visible.
2. Type CE1: unilocular, simple cyst with uniform anechoic content. Cyst may exhibit fine echoes due to shifting of brood capsules which is often called hydatid sand (snow flake sign). Cyst wall is visible.
3. Type CE2: multivesicular, multiseptated cyst in which the daughter cysts may partly or completely fill the unilocular mother cyst. Cyst septations may produce “wheel-like” structure, or the contained daughter cysts may produce a “rosette-like” or “honeycomb-like” structure. Cyst wall is normally visible.
4. Type CE3: anechoic content with detachment of laminated membrane from the cyst wall visible as floating membrane or as “water-lily sign” which is indicative of wavy membranes floating on top of remaining cyst fluid. Unilocular cyst may contain daughter cyst. These cysts appear at US as a “complex mass.”
5. Type CE4: heterogeneous hypoechoic or dyshomogeneous degenerative contents. No daughter cysts. It may show a “ball of wool” sign which is indicative of degenerating membranes.
6. Type CE5: cysts characterized by thick calcified wall which is arch-shaped, producing a cone-shaped shadow. Degree of calcification varies from partial to complete.

Table 19.1 WHO classification of echinococcosis cyst

Type	Image features and remarks
CL	Status: active
	Image features: unilocular; not clearly delimited by a hyperechoic rim; cyst wall not visible
	Remarks: generally early-stage and non-proliferative cyst
CE1	Status: active
	Image features: visible cyst wall; hydatid sand (snow flake sign)
	Remarks: generally active proliferative cyst
CE2	Status: active
	Image features: multivesicular cyst; "wheel-like," "rosette-like," or "honeycomb-like" structure
	Remarks: generally active proliferative cyst
CE3	Status: transitional
	Image features: detachment of laminated membrane; double wall sign; water-lily sign or wavy membrane
	Remarks: start to degenerate and produce daughter cysts
CE4	Status: inactive
	Image features: Heterogeneous hypoechoic or dyshomogeneous degenerative contents. No daughter cysts
	Remarks: there is no living protoscoleces
CE5	Status: inactive
	Image features: thick calcified wall which is arch-shaped, producing a cone-shaped shadow. Degree of calcification varies from partial to complete
	Remarks: there is no living protoscoleces

Types CL, CE1, and CE2 are identified as active proliferative cysts. Type CE3 is identified as transitional cyst. Type CE4 is degenerative cyst. Type CE5 is inactive cyst.

The growth pattern of alveolar echinococcosis is similar to slow-growing liver cancer, so alveolar echinococcosis also has its PNM classification system [29]. This classification is summarized in Tables 19.2 and 19.3.

19.7 Surgical Indication and Preoperative Preparation

Now, drug therapy, percutaneous puncture treatment, and operation are the three principal treatments for hepatic hydatid disease. Operation is the most effective treatment for hepatic hydatid disease, and it is the only way to cure echinococcosis radically.

No Surgical Indication

1. Patients with type CL cyst who have no clinical symptoms, and the diameter is less than 5 cm.
2. Totally calcified cyst is generally inactive cyst.

Preoperative Preparation At present, there is still no exact conclusion as to whether there is a need to use chemotherapy before operation. Albendazole is the most effective drug for the treatment of hepatic hydatid disease in clinic. A small sample retrospective study shows that there were only 28 % hydatid cysts still living during the operation if the patient took albendazole for a month before operation. If chemotherapy using albendazole lasted 3 months, the activity of cysts decreases to 8 % [30]. Therefore, albendazole is an effective added therapy before operation. To date, there is no study showing the exact usage of albendazole during the perioperative period. We advise starting to take albendazole at least 2 days before operation.

19.8 Selection of Operation

The principle of surgical treatment for CE is to remove all parasite groups, prevent capsule contents overflowing, close pipes connected with the cyst, and deal with residual cavity [31–33]. Removing as much parasitic tissue as possible is the key to treating and preventing recurrence. Removing parasitic tissue more thoroughly leads to a lower recurrence rate, but the operation risks increase, and vice versa [34]. Laparoscopic operation for the treatment of hepatic cystic echinococcosis has characteristics of small trauma and quick recovery, but the high risk of recurrence and planting of this method limits its application [35]. Operating methods used at present are the following:

19.8.1 Excision of Internal Capsule

This type of operation in the treatment of hydatid disease is the most classic, clinical application of more than 100 years

Table 19.2 The PNM classification of alveolar echinococcosis

P—Parasitic location in the liver	
P_x	Primary lesion can't be estimated
P_0	No lesion in the liver
P_1	Peripheral lesion without biliary or proximal vessel invasion
P_2	Central lesion with biliary or proximal vessel invasion in one lobe of the liver
P_3	Central lesion with biliary or proximal vessel invasion in two lobes of the liver and/or invasion to two hepatic veins
P_4	Any lesion grows along portal vein, inferior vena cava, or hepatic vein
N—Neighboring organs	
N_x	Can't be estimated
N_0	No infiltration to surrounding tissue
N_1	Infiltration to neighboring tissue and organs
M—Metastasis	
M_x	Can't be estimated
M_0	No metastasis by chest X-ray and brain CT
M_1	No metastasis

Table 19.3 Stage of alveolar echinococcosis based on PNM classification

Staging	P	N	M
I	P_1	N_0	M_0
II	P_2	N_0	M_0
IIIa	P_3	N_0	M_0
IIIb	$P_{1\sim3}$	N_1	M_0
IV	P_4	N_0	M_0
	P_4	N_1	M_0
	Any P	Any N	M_1

of history; the operating method is simple and feasible, doctors and medical equipment requirements are relatively low, and it is easy for all levels of hospital, but the operative complications (2.6–10 %) and the rate of recurrence (4.5–20.2 %) are higher [36–40].

Figure 19.1 shows the lesion site and lesion position containing 20 % NaCl solution gauze, preventing extravasation of the cystic fluid and allergic reaction. Two stitches hanging in the cyst wall, diagnostic puncture in two lines, pumping out the cystic fluid, preliminary judgment without infection or biliary fistula occurred, if the cyst fluid cool, no infection; suctioning clean of the cystic content, reinjection of slightly less than the protoscolex reagent kill suction quantity, currently recommend the use of 20 % NaCl solution [42], for 15 min, once again suction clean the cystic content. (see below)

Cut the cystic wall, see Fig. 19.2 below

Bluntly dissect and remove the jellylike endocyst (see Fig. 19.3) below

had been soaked in 20 %NaCl solution gauze wipe repeatedly external capsule wall, note there is no bile leakage, carefully and find out the external capsule wall fistula, for by the cystic duct injection of methylene blue check without biliary fistula wound. See below as found in the fistula with thread or 4–0 vascular suture closure of the fistula routine abdominal drainage tube; the wound larger when necessary feasible "T" tube drainage of common bile duct. See Figs. 19.4 and 19.5 below.

19.8.2 Total Cystectomy

Cyst enucleation takes place along the gap between the internal and external capsule of the cyst; the operation wound is small in liver resection, but the process of stripping of echinococcosis rupture spreads risk, and there is also the risk of biliary fistula.

Revealed lesions (Fig. 19.6)

Incise the liver capsule; find out the space between external capsule and outer cystic membrane; (Fig. 19.7)

along the gap spiral turn to deep stripping external capsule, until the whole external capsule is completely stripped (Fig. 19.8);

in the stripping process, should be carefully distinguished by the outer bag oppression of intrahepatic duct system, the membrane and the pipeline system integrity retained in the liver parenchyma on one side, the pipeline system to the outer sac ligation of membrane (Fig. 19.9);

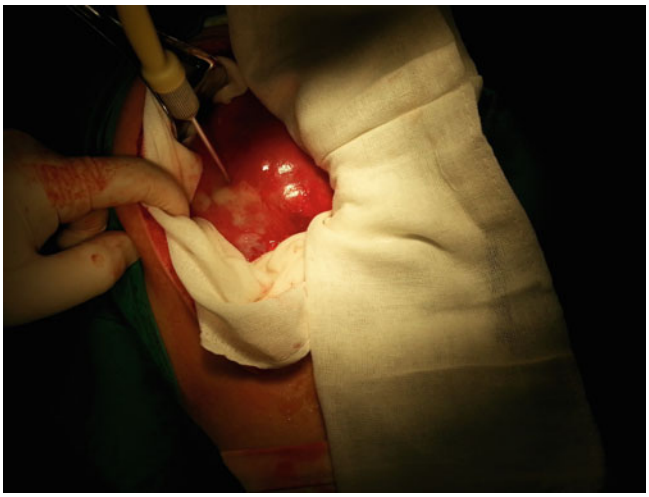

Fig. 19.1 Showing the lesion site

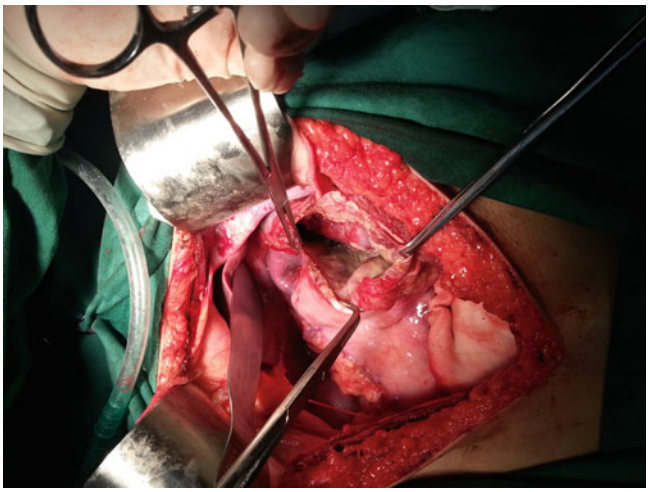

Fig. 19.3 Bluntly dissect and remove the jellylike endocyst

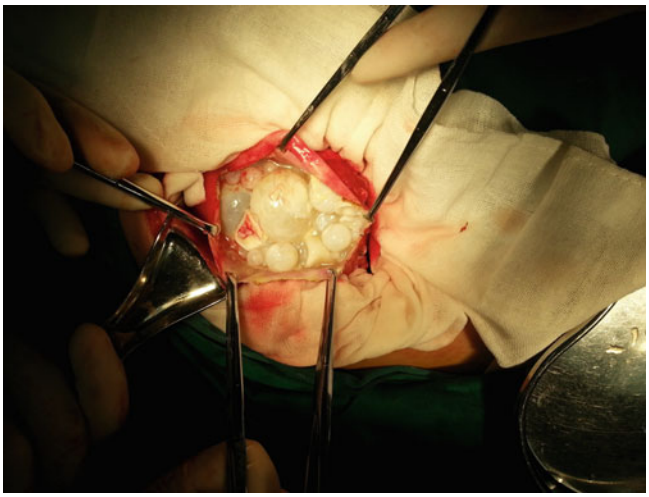

Fig. 19.2 Cut the cystic wall

check whether the biliary fistula and bleeding, the full treatment, plasma layer placed drainage tube after abdominal closure.

19.8.3 Liver Resection

The cyst along with normal liver tissue around a certain range is resected. The operating method is thoroughly reliable [41], and there is no residual cavity, so this method can effect a radical cure to problems, depending on the site selection of the cyst for anatomical liver resection or non-anatomical liver resection.

For hepatic hydatid, whether cystic or alveolar, hepatectomy is a radical method. Liver resection can be divided into anatomical liver resection and non-anatomical liver resection. Operating methods can be divided into hepatic segment resection, lobectomy of liver, hemihepatectomy and trisegmentectomy. Earlier, the operating method for liver resection was described in detail. Here, the emphasis is on the resection of liver hydatid.

In view of the clinical characteristics of alveolar hydatid disease, the difficulty of treatment is higher than that of cystic echinococcosis. Radical resection is the first choice for hydatid disease of the liver [43, 44]. In the whole operation for resection of the lesion, the process for malignant tumor treatment follows the "tumor-free principle." Operation excision grades are as follows: (1) R0 resection (parasitic tissue is excised completely, without any residue), (2) R1 resection (the parasitic tissues are excised; microscopic examination shows positive margin), (3) R2 resection (the parasitic tissue is not completely removed, but the gross margin is positive). The R0 resection is regarded as radical resection; the other two approaches are considered palliative resection [45, 46]. Although radical resection is the first choice, if the lesion is larger, with invasion of the portal vein or inferior vena cava, then palliative resection combined with drug treatment can obtain good clinical efficacy [47]. The selection of a bubble-type liver resection as an example:

Alveolar hydatid showing a lesion (Fig. 19.10)

Alveolar hydatid showing invasive growth, invasion of the surrounding organs, as shown in Fig. 19.11.

Separation, organ and resection of hydatid violations such as graph (Fig. 19.12);

Anatomy of hepatic portal (Fig. 19.13);

If the hydatid invades more than half of liver, it's helpful to preset a blocking tape encircling the hepatoduodenal ligament, suprahepatic inferior vena cava and infrahepatic inferior vena cava, respectively (see Fig. 19.14).

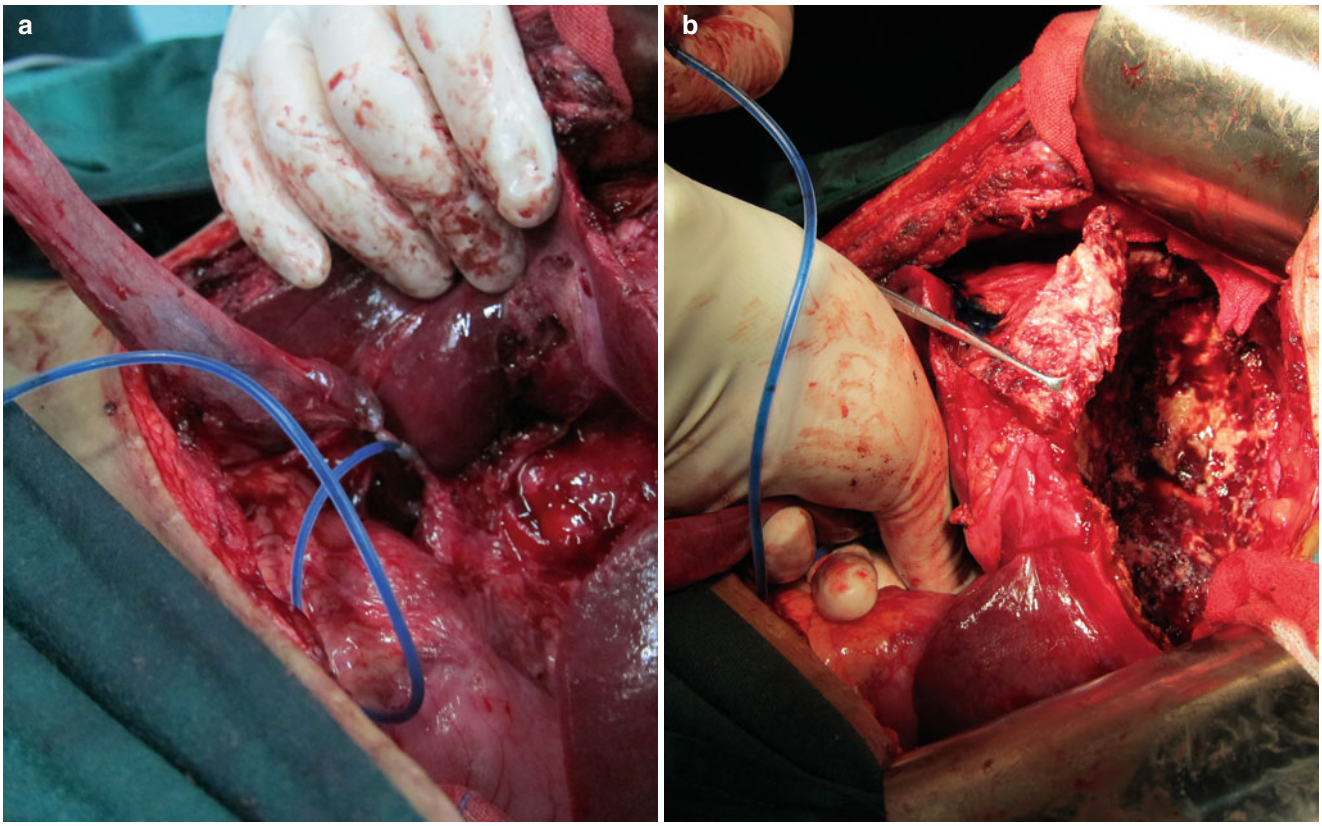

Fig. 19.4 Check bile leakage

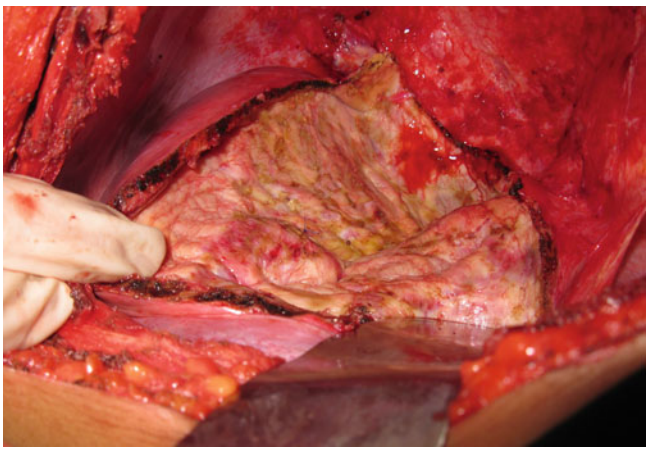

Fig. 19.5 Closure of the fistula

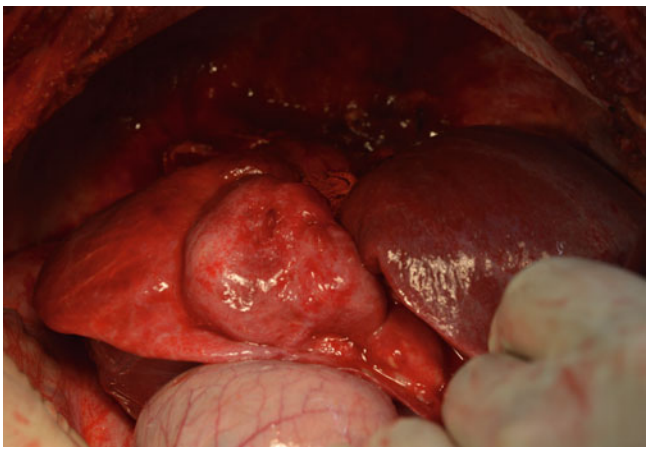

Fig. 19.6 Revealed lesions

If the lesion is localized in the hepatic segment, it is generally not necessary to block the hepatic portal, bleeding, temporary blocking of the hepatoduodenal ligament; if the lesion is localized to within half the liver, hemihepatectomy would be applicative with hemi-hepatic flow occlusion or directly cutting off the right hepatic artery and portal vein.

Cut off the right hepatic artery (Fig. 19.15);

Cut off the right branch of portal vein (Fig. 19.16).

Dissect the perihepatic ligaments from the areas without lesions, as shown in Fig. 19.17.

Hydatid disease generally shows invasive growth, especially in the bubble. And peripheral hepatic ligaments are dense adhesions, as shown in Fig. 19.18.

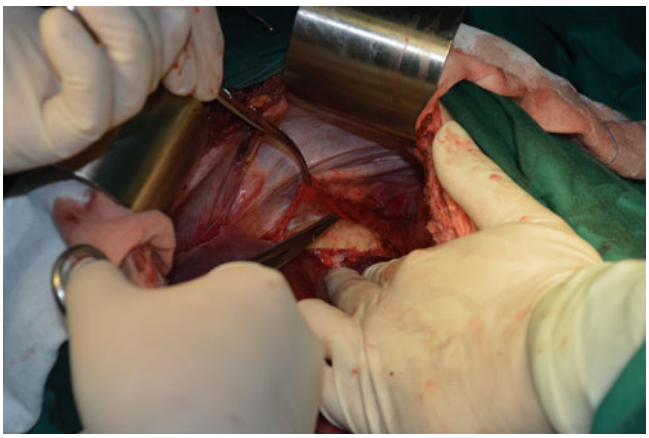

Fig. 19.7 Find out the space between external capsule and outer cystic membrane

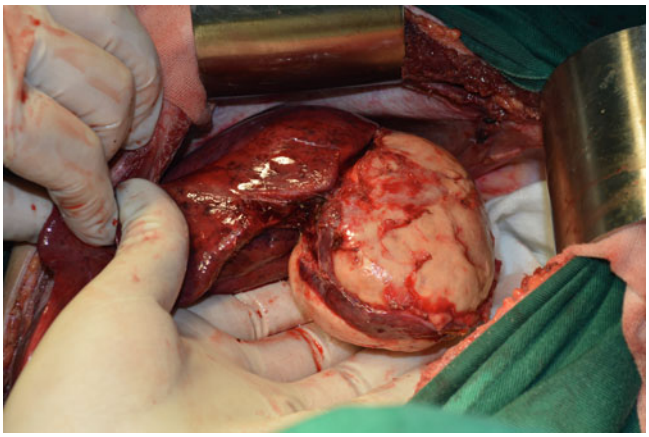

Fig. 19.8 Stripping external capsule

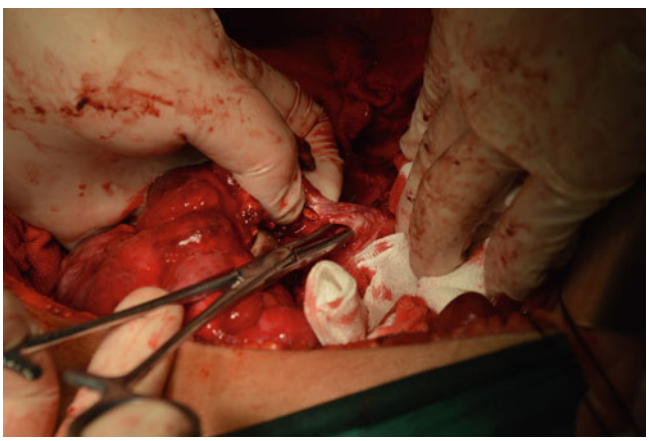

Fig. 19.9 The pipeline system to the outer sac ligation of membrane

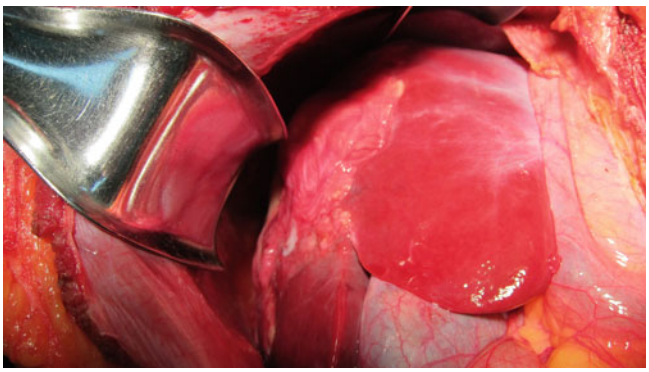

Fig. 19.10 Showed a lesion

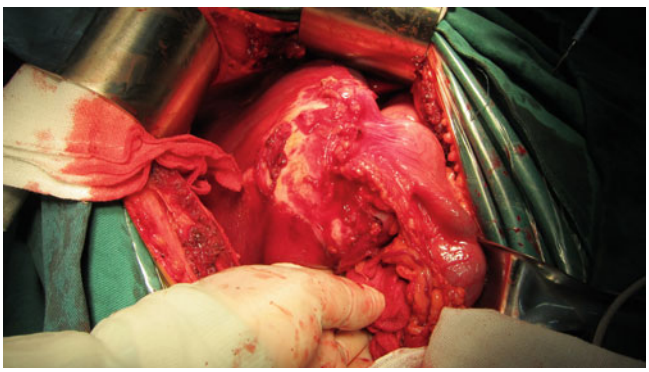

Fig. 19.11 Invasion of the surrounding organs

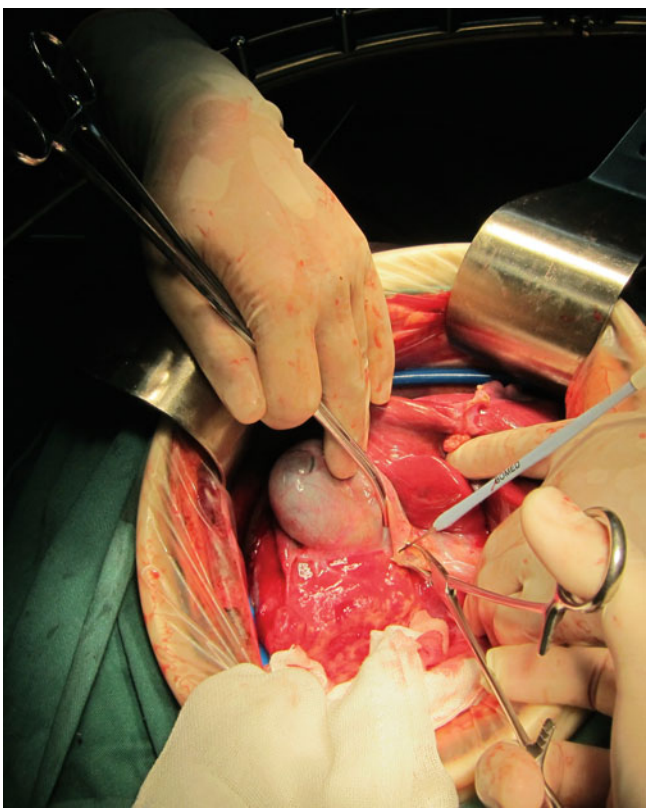

Fig. 19.12 Separation, organ and resection of hydatid violations such as graph

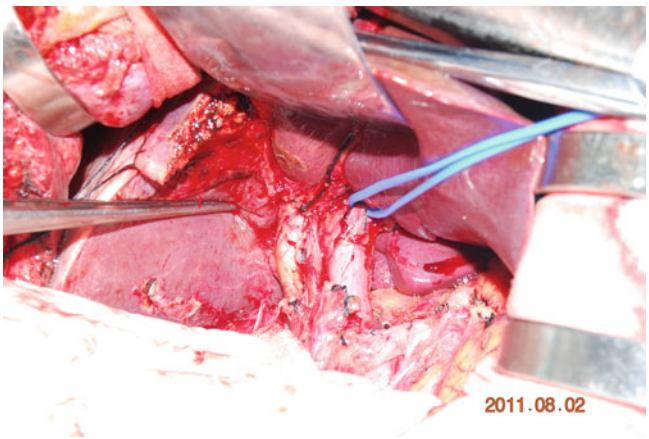

Fig. 19.13 Anatomy of hepatic portal

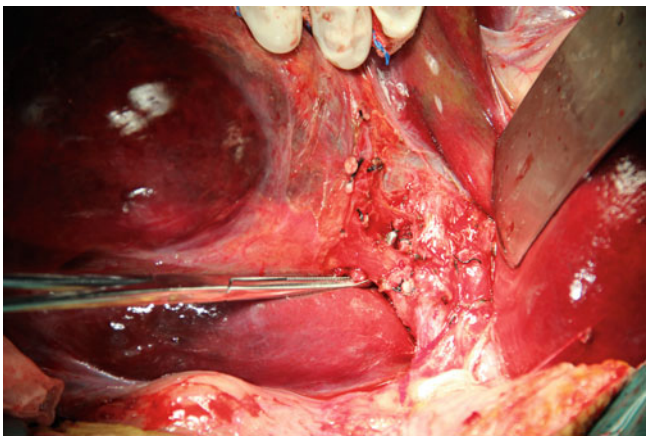

Fig. 19.16 Cut off the right branch of portal vein

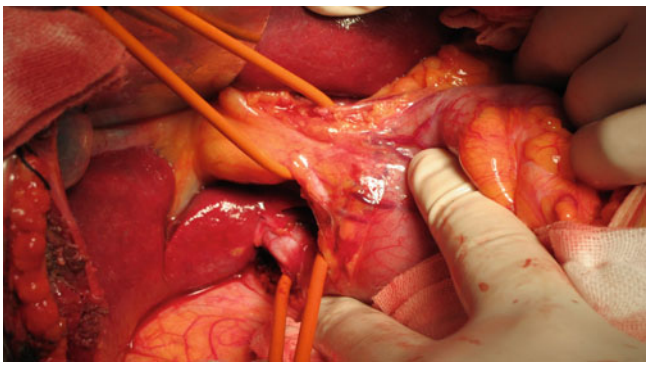

Fig. 19.14 Preset a blocking tape encircling the hepatoduodenal ligament, suprahepatic inferior vena cava and infrahepatic inferior vena cava, respectively

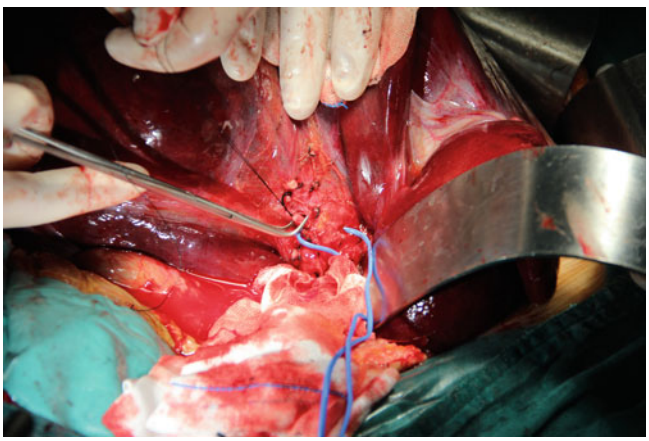

Fig. 19.15 Cut off the right hepatic artery

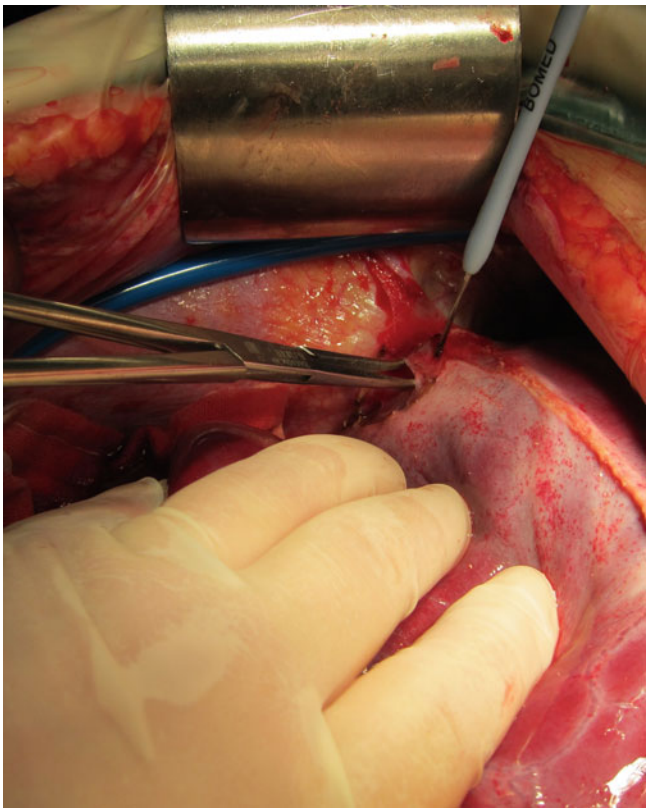

Fig. 19.17 Dissect the perihepatic ligaments from the areas without lesions

Anatomy of third hepatic portal, with ligation cutting short hepatic blood vessels, generally in the hepatic artery 3 – eight short, ligation cut off one by one. See Fig. 19.19

Reveal third hepatic portal, as shown in Fig. 19.20.

(see Fig. 19.21)

In both sides of traction line tangent suture, and began to cut off; A lot of Broken Liver way; can use CUSA, water jet, ultrasonic scalpel, or clamp can be applied. Figure 19.22 shows starting position of liver.

When blood vessels (including hepatic arteries, portal veins and hepatic veins) exposed, they need to be ligated and cut off (Fig. 19.23)

Disarticulation, ligation of right hepatic duct (Fig. 19.24)

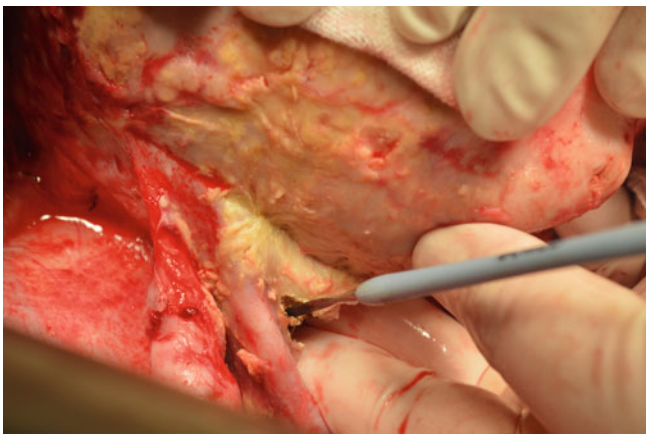

Fig. 19.18 Peripheral hepatic ligaments are dense adhesions

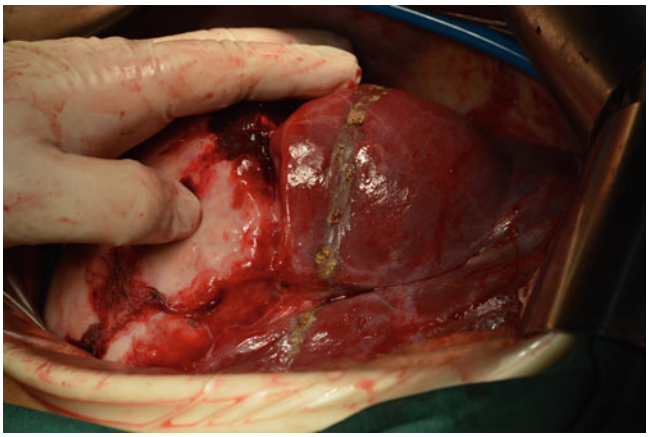

Fig. 19.21 Determine the liver tangent, generally more than 1-2 cm

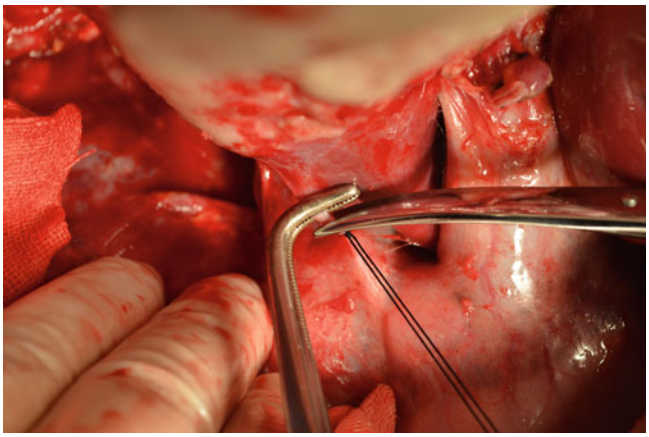

Fig. 19.19 Anatomy of third hepatic portal

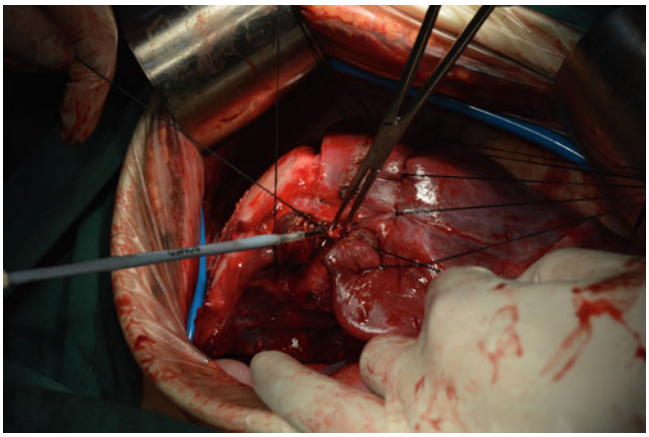

Fig. 19.22 Begin to cut off

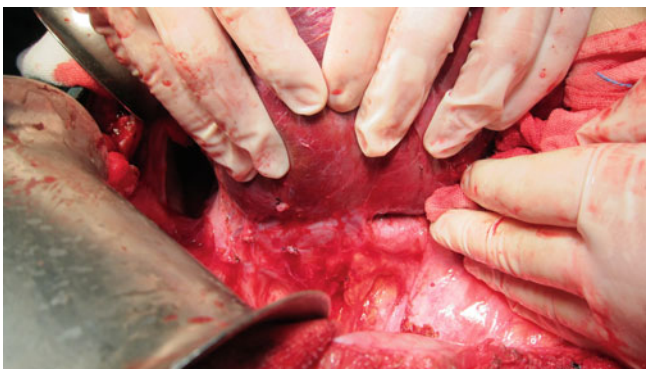

Fig. 19.20 Anatomy of third hepatic portal

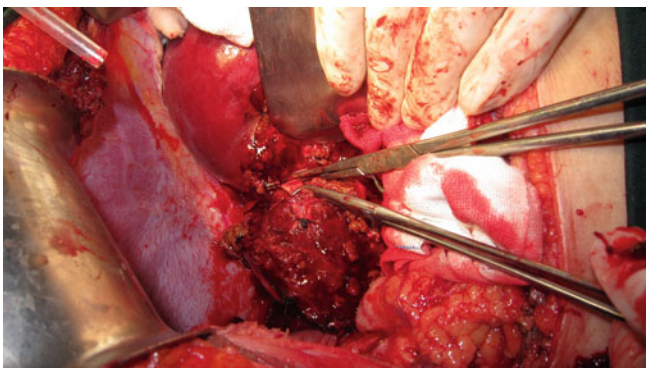

Fig. 19.23 When blood vessels (including hepatic arteries, portal veins and hepatic veins) exposed, they need to be ligated and cut off

In the liver from breaking short hepatic branch (Fig. 19.25)

Cut off the right hepatic vein, and suture the retained end of right hepatic vein with 5-0 prolene (Fig. 19.26)

Remove the specimen (Fig. 19.27)

Carefully stop bleeding at the surface of surgical resection, rule out the biliary fistula, place a drainage tube at the surgical area and close up abdominal cavity. See Fig. 19.28

Notes: for larger cysts, along the liver resection anatomic plane, part of the outer wall remains; in this case, it is necessary to remain outside the wall for full hemostatic and biliary fistula closure, and take care not to leave parasitic tissue residue. Non-complete resection, leaving the residual part of the outer wall in the main blood vessels and bile duct, also can be thought of as a received radical operation. This is shown in Fig. 19.29.

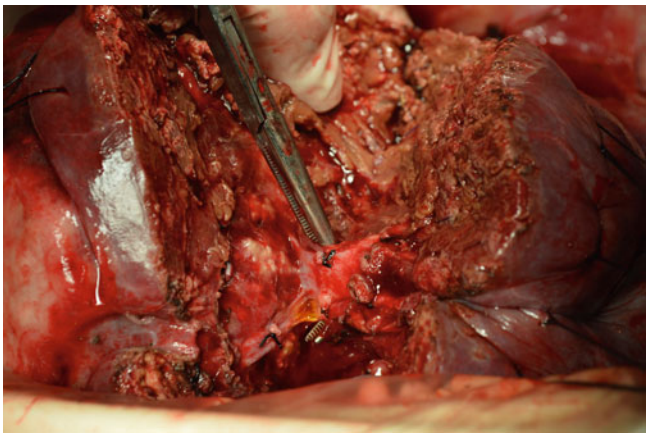

Fig. 19.24 Disarticulation, ligation of right hepatic duct

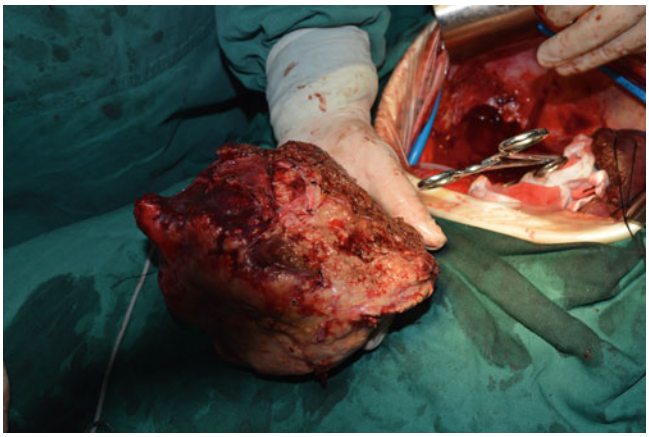

Fig. 19.27 Remove the specimen

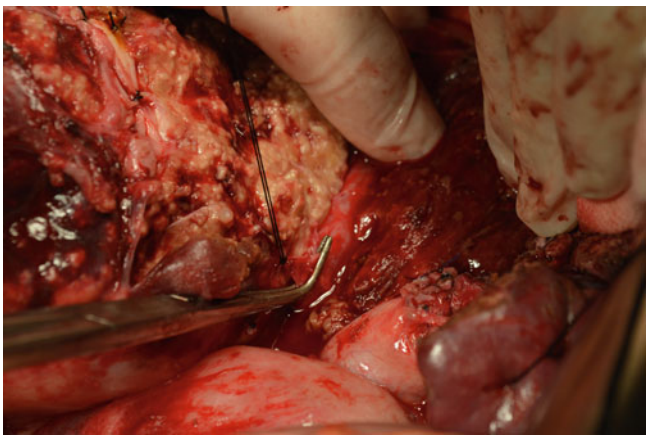

Fig. 19.25 In the liver from breaking short hepatic branch

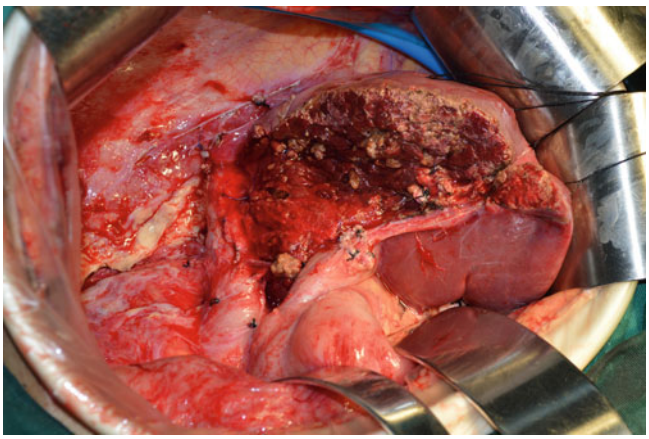

Fig. 19.28 Carefully stop bleeding at the surface of surgical resection, rule out the biliary fistula, place a drainage tube at the surgical area and close up abdominal cavity

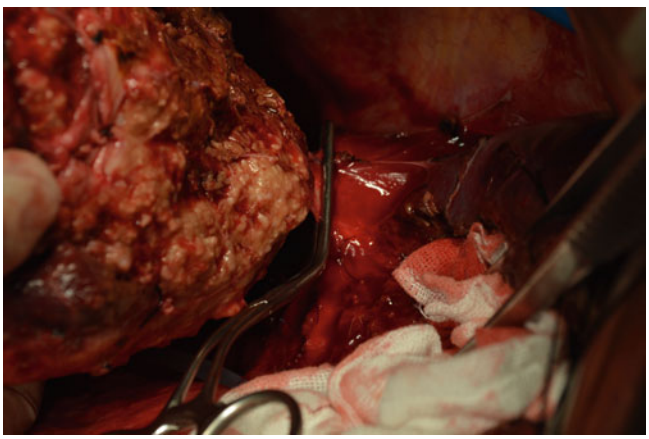

Fig. 19.26 Cut off the right hepatic vein, and suture the retained end of right hepatic vein with 5-0 prolene

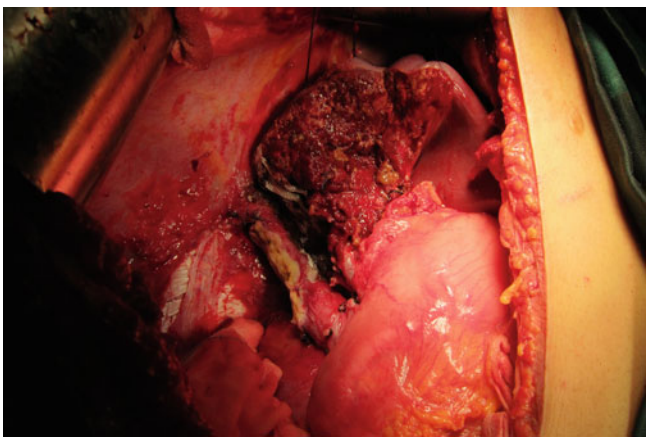

Fig. 19.29 For not complete resection, and the residual part of the outer wall in the main blood vessels and bile duct, also can be thought of as received radical operation

19.8.4 Liver Transplantation

When resection cannot be carried out, especially with liver failure, liver transplantation can be used as salvage therapy [48]. Immunosuppression after liver transplantation may lead to disease recurrence and may encourage residual parasites in tissue and metastatic and undiscovered metastasis proliferation [49]. The patient must be treated with albendazole for relapse prevention after liver transplantation. In recent years, the clinical technique of autologous liver transplantation has been applied; this has not only solved the

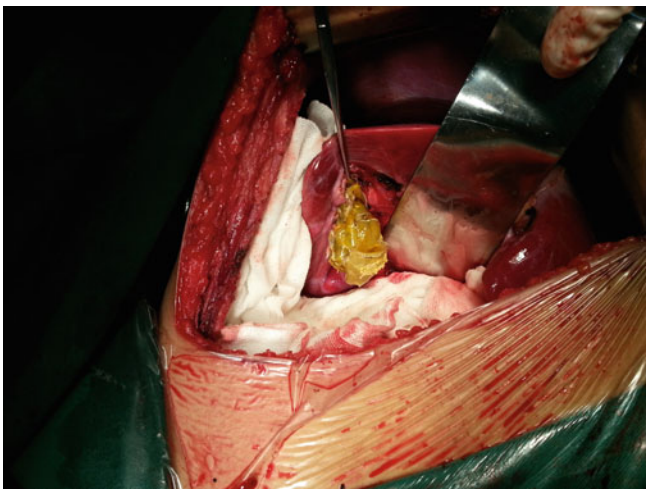

Fig. 19.30 Visible cystic contents stained yellow

problem of shortage of donors, it is a very good solution to the application of immunosuppressant-produced complications after transplantation, but due to the lack of clinical data about its advantages and disadvantages, this technique still needs further verification [50, 51].

19.9 Complications and Treatment

19.9.1 Cyst Rupture

Including hydatid liver resection: the most common complications are cyst rupture into the bile duct, abdominal, pericardial, pleural, or lung [52].

19.9.1.1 Cyst Rupture into the Biliary Tract

When performing excision of the cyst, there should be a careful check whether the cyst biliary fistula. Fistula formation may occur before or during operation. Intraoperative visible capsule wall yellow dye and the cystic content clear, this may be due to the break of cystic duct opening to the outside, external capsule wall inner surface, which are communicated between the bile duct and external capsule, also visible cystic contents stained yellow, cyst and biliary interlinked. This is shown in Fig. 19.30.

A clean gauze pad should be put inside the cyst, gently squeeze the gallbladder, judging whether a channel is formed. If the channel is suspicious, use intraoperative cholangiography to clarify the situation. During resection of the cyst, inject methylene blue into the cyst biliary fistula to check if there is no small bile duct fistula. If cholangiography suggests a choledochal inner filling defect, this should be treated with common bile duct exploration, repeated washing with physiological saline, and thorough removal of the cyst contents in the biliary tract; biliary endoscopy may help to clean the cyst contents, and finally put in "T" tube drainage.

The radical operation is the best choice in treatment of large cystic biliary fistula; this can shorten the length of hospital stay and reduce the rate of complications. But the radical operation requires that the doctor performing the operation has a certain level of experience in a department of hepatobiliary surgery. A simple fistula may be closed with absorbable suture material. If there is calcification of the cyst wall, with hard texture, resection of the fistula should be carried out around the calcified tissue, exposing fresh liver tissue, and the fistula then closed. For a large fistula, the closure should not be central or lateral; it is necessary to perform biliary enteric anastomosis or insert a drainage tube.

19.9.1.2 Cyst Rupture into the Peritoneal Cavity

If cyst fluid bursts into the abdominal cavity, this can cause severe abdominal pain, severe peritonitis, and allergic shock. Emergency rescue from anaphylactic shock by application of glucocorticoid should be carried out, maintaining the stability of blood pressure. At laparotomy, thoroughly remove the cyst contents into the abdominal cavity, excise the cyst, carry out warm, repeatedly irrigate the peritoneal cavity with saline, and insert abdominal cavity drainage. Postoperatively, carry out systemic use of anti-echinococcosis drugs and antibiotics.

19.9.1.3 Cyst Rupture into the Pericardial Cavity

Cyst rupture into the pericardial cavity may lead to cardiac tamponade, circulatory system disorders, and change in blood pressure. Emergency laparotomy should be carried out through the cavity at the end of the pericardium, to clear cyst fluid, with repeated washing, decompression, and drainage of the pericardial cavity. At the same time, the lesion should be resected.

19.9.1.4 Cyst Rupture into the Pleural or Lung

Abdominal thoracic incision should be performed, then open the side the chest and cut the diaphragm and clean the cyst fluid. Bronchial fistula should be closed. After flushing thoracoabdominal cavity and repairing the diaphragm, closed thoracic drainge should be performed. The drainge tube may be taken out after drainage volume less than 10 ml every day [53].

19.9.2 Biliary Fistula

Pipe outflow of bile for bile leakage after drainage operation, more than 10 days continuous bile out, regardless of the quantity many, were diagnosed as bile fistula. Endoscopic treatment with simple sphincter incision, nasobiliary drainage, and stent is the main method for treatment of biliary fistula, but the best treatment has not yet been defined [54, 55].

19.9.3 Biliary Stricture

This complication is uncommon, but once it occurs, the clinical prognosis for treatment is complex, as it can result in secondary biliary cirrhosis and portal hypertension. Because placing reagents for killing protoscolex into the biliary tract may cause complications, it is recommended to use 20 % NaCl, where complications are rare. It is common to use other corrosive reagents for killing protoscolex. Also common in biliary fistula closure method is undeserved, caused by bile duct injury. Usually the placement of stents in the treatment of endoscopic [56], such as invalid consider enterohepatic anastomosis.

19.9.4 Recurrence

Intrahepatic or extrahepatic lesions after treatment show recurrence of cysts or new activity. Cysts becoming active in the original treatment site are called local recurrence, and cysts in other parts are called metastasis and recurrence. Overflow of cyst, capsular tissue residue, small cyst omissions and reagent for killing protoscolex with low efficiency are the main reasons for recurrence. A radical operation is the preferred treatment for recurrence, especially applicable to many local recurrences and peritoneal metastases.

19.10 Long-Term Prognosis

Hepatic hydatid disease and operation mortality rate is between 0.5 and 4 %; if the medical technology is relatively backward, these figures are higher [57, 58].

Hepatic echinococcosis treated by operation can achieve a long-term survival rate. If hepatic alveolar echinococcosis is supplemented after operation with benzene and albendazole treatment, a good long-term survival rate can also be achieved. In cases of alveolar hydatid disease after liver transplantation, 5 years disease free survival rate was 58 %, 5 years survival rate was 71 % [58, 59].

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Hepatolithiasis Hepatectomy

20

Zheyu Chen and Qing Wang

20.1 Epidemiology

Hepatolithiasis is also known as Oriental biliary hepatitis. As its name implies, this disease occurs primarily in the East Asian region, including mainland China, Hong Kong, China, Taiwan, and Japan. In contrast, this disease is rare in the west, and the hepatolithiasis morbidity rate is 0.6–1.3 % in western countries [1, 2]. However, the morbidity rate in Asian is very high, 2.1 % in Japan, 11.7 % in Malaysia, 17.0 % in South Korea, 38.8 % in mainland China, and 47.3 % in Taiwan [3]. The incidence in Latin America is also as high as approximately 2 %, especially in Brazil [4]. Additionally, with the increasing mobility of the population, the morbidity rate of this disease in western countries has recently increased.

Hepatolithiasis is characterized by brown bilirubin stones (also known as bilirubin calcium stones), cholesterol stones, and other types of stones [5]. Some districts have reported cases of cholesterol gallstone [6, 7]. However, these reports account for only a small number of hepatolithiasis cases (approximately 5.8–13.1 %). The chemical composition of intrahepatic brown bilirubin stones differs from extrahepatic stones. The former contain more cholesterol, less bilirubin and bile acid, and a small amount of bile acid metabolized by bacteria [8]. Bacteria, which produce β-glucuronidase, play an important role in the formation of hepatolithiasis. Additionally, biliary tract parasite infections are uncommon in the context of the intrahepatic bile duct stone lesions that require hepatectomies. Recent research has shown that biliary tract worm infections are possible risk factors for hepatolithiasis [9]. Variation in the intrahepatic bile duct is not thought to affect the pathogenesis of hepatolithiasis [10]. Intrahepatic brown bilirubin stones are dark brown and soft and have a crisp, lamellar structure in sections.

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20.2 Anatomy and Classification

By definition, hepatolithiasis occurs in the intrahepatic bile duct, regardless of whether cholecystolithiasis is present within the extrahepatic bile duct. The intrahepatic bile duct generally refers to the left and right hepatic ducts above the confluence of the bile duct. There is no universal standard regarding the types of hepatolithiasis. The Chinese Medical Association Surgery Branch biliary surgery group proposed a new classification session in 2003 at Xiamen. In this scheme, the intrahepatic bile duct stones are divided into the following types: type I, localized; type II, regional; type III, diffuse stones that are subdivided into subtypes IIIa (no regional damage) and IIIb (regional damage); and type IV, diffuse with biliary cirrhosis. In Japan, hepatolithiasis is divided into two categories according to the site of stones: type I (intrahepatic bile duct) and type II (intrahepatic and extrahepatic bile duct). According to the distribution site, the condition is also divided into type R (right), type L (left), type LR (left and right side), and type C (caudate lobe). In clinical practice, classification of the anatomical type is more practical and significant with respect to selecting the type of operation. The main basis for classification includes the following: (1) whether the extrahepatic bile duct is involved, (2) whether the stones are located in the left lobe and/or the right lobe of the liver, (3) whether the gallstones have combined, (4) which portion of the intrahepatic bile duct exhibits stenosis, (5) the presence or absence of symptom, and (6) the presence or absence of complications. In patients with intrahepatic stones in East Asia, intrahepatic bile duct stones combine with extrahepatic bile duct stones in 69 % of cases. The stone is located in the left lobe of the liver, and this lobe contains the main lesions in 78 % of cases (stones only on one side account for 45 %). Stones combined with cholecystolithiasis

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account for 48 % of the cases, and the rate of biliary stricture is 76 % [11].

20.3 Diagnosis

There is no specific method for the diagnosis of hepatolithiasis. Given its clinical manifestations, the symptoms and the results of auxiliary examination are both necessary for diagnosis.

20.3.1 Symptoms

The symptoms of hepatolithiasis include abdominal pain, fever, jaundice, vomiting, and abdominal discomfort. Abdominal pain primarily occurs in the right upper quadrant or upper abdomen. It is the most common initial symptom of hepatolithiasis. Intrahepatic bile duct stones result in nonspecific symptoms. The corresponding symptoms are often due to inflammation caused by the stones, biliary obstruction, and hepatocellular damage. Suppurative cholangitis caused by hepatolithiasis and bile duct stricture can easily relapse, and secondary liver abscess is common. Chronic cholangitis and resulting septicemia are the typical symptoms of hepatolithiasis. A study on 303 patients who underwent operation treatment for 10 years confirmed that 12 % of the postoperative patients had fever or abdominal pain symptoms. In this study, patient deaths reached 30 %, with 25 % patient deaths occurring due to cholangiocarcinoma [12]. Hepatolithiasis in combination with biliary carcinoma accounted for 5.2 %; among these cases, intrahepatic cholangiocarcinoma was the most common carcinoma observed [13]. In Japan, cholangiocarcinoma combined with hepatolithiasis accounted for 5.7–17.5 % of cases [14].

20.3.2 Ultrasound

The use of ultrasound examination avoids the requirement for ionizing radiation and is a noninvasive, simple, and easy means of inspection. Thus, ultrasound has been widely used in the diagnosis of hepatolithiasis. This technique can show hepatolithiasis and bile duct dilation very well [15, 16]. When considering hepatolithiasis, ultrasound is a very suitable first choice, showing a high echo with an acoustic shadow. Higher calcium content in the stone leads to a more obvious, high echo of the stone's surface. For stones with lower calcium content, it is easier to observe the entire stone.

It is very difficult to distinguish between gas and stone with ultrasound. In these cases, the mobilization of hyperechoic nodules is helpful in the diagnosis. In the supine and knee-chest positions, gas will always move up. However, when the dilated bile ducts wrap around the lesions, it is difficult to distinguish between gas and stones. Due to the existence of the stone, it is very difficult to accurately display the stenosis of the biliary tract. With advances in ultrasonic technology, higher tissue resolution can show anatomical structures very well. However, all of these techniques have certain requirements, such as ultrasound equipment and operators.

20.3.3 CT

CT can simultaneously provide the size of the liver, the degree of bile duct dilatation, and the location of the stones, and this information is helpful for the treatment plan. Although the latest CT cannot be used to identify the distal bile duct, bile duct dilatation and stenosis can be identified. It is difficult to distinguish stones from the liver parenchyma with enhanced CT. Expansion of the bile duct is observed as a tubular low-density shadow with a curved branching structure on enhanced CT [17–19]. CT cholangiography makes use of a slow intravenous injection of contrast agent, which travels with fluid excreted from the bile duct, allowing the duct system to be visualized [20]. The sensitivity of this technique in detecting intrahepatic bile duct stones is higher than that of unenhanced CT. However, in the context of diagnosing hepatolithiasis, the excretion of contrast agents may not be sufficient due to reduced liver function in the lesioned portion to distinguish between bile duct and stones. Additionally, in cases of liver atrophy caused by long-term hepatolithiasis, contrast agents can only show the lack of a bile duct system.

Acute suppurative cholangitis secondary to hepatolithiasis can cause liver abscesses, which can contain a necrotic cystic mass on CT [21].

20.3.4 MRI

MRI technology has improved in recent years, especially the application of MRCP, and this technique performs the same function as an endoscopic retrograde cholangiopancreatography (ERCP). Moreover, it is a noninvasive examination, making it an excellent contribution with respect to the diagnosis of hepatolithiasis. MRCP can be very effective for locating the stone and examining the intrahepatic bile duct obstruction [22, 23]. MRI examination avoids ionizing radiation and can provide an accurate image with the use of an auxiliary contrast agent. A commonly used contrast agent is gadolinium chelate [24]. The application of MRCP in gallstone disease is often compared to ERCP. In one study of MRCP examination for intrahepatic bile duct stones, the positioning sensitivity, specificity, and accuracy were 97 %, 99 %, and 98 %, respectively. MRCP examination for intrahepatic bile duct stricture and its

position revealed a sensitivity, specificity, and accuracy of 93 %, 97 %, and 97 % [25], respectively. MRCP can accurately display the hepatolithiasis and resulting bile duct stenosis. MRI cannot be used for specific groups, such as claustrophobic patients or those with pacemakers. Moreover, MRCP can help only to a small extent in resolving bile duct cell carcinoma and intrahepatic bile duct stones.

20.3.5 ERCP and Percutaneous Transhepatic Cholangiography (PTC)

Cholangiography is still the best method for identifying tiny biliary lesions and small stones. ERCP is now performed more commonly than PTC. As invasive examination methods, complications related to ERCP and PTC are 1–7 % and 3–5 %, respectively. ERCP also has a 3–10 % failure rate. From the perspective of hepatolithiasis diagnosis, the noninvasive MRCP examination has considerable value and can replace ERCP. However, ERCP can directly remove calculus and perform biopsies; thus, the importance of this procedure cannot be ignored.

20.4 Surgical Indications and Contraindications

For lesions that are confined to one side of the liver and associated with liver atrophy and biliary stricture, the treatment option is resecting the strictured biliary tract and the damaged liver [26–28]. Liver resection should be avoided in the acute phase of acute hepatolithiasis, especially in patients with suppurative cholangitis and septicemia. This procedure relieves the obstruction of the biliary tract, and unobstructed biliary drainage is the most important factor in this condition.

The following factors contraindicate hepatectomy: (1) poor body condition that is unable to tolerate the operation; (2) hepatolithiasis that is not associated with bile duct strictures, in which the intrahepatic stones can be depleted; and (3) the presence of diffuse lesions, with stones distributed throughout the liver.

20.5 Preoperative Preparation

Combined with imaging examination, a detailed operation plan should be formulated. The stone location should be determined preoperatively, and whether the bile duct is obstructed and whether liver atrophy has occurred should be ascertained. If bile duct obstruction is observed in combination with severe dilatation or with obstructive jaundice, preoperative puncture drainage should be performed. This procedure will improve liver function and blood clotting status.

20.6 Selection of Operation

In 1958, the resection of hepatic lobes for the treatment of intrahepatic bile duct stones was first reported by Huang Zhiqiang. This procedure has since become the main method for treating hepatolithiasis. When hepatolithiasis is associated with liver atrophy, hepatic abscess, and biliary stenosis, hepatic resection is the best treatment choice. Compared with other diseases requiring liver resection, hepatectomy for hepatolithiasis has its own unique characteristics. To achieve a thorough treatment, a choledochoscope is often used intra- and postoperatively [29]. The mode of operation may be a segmental liver resection, hepatolobectomy, hemihepatectomy, or clover hepatectomy. For patients with secondary biliary cirrhosis caused by hepatolithiasis, it is difficult to use hepatolobectomy, biliary intestinal anastomosis, and choledochoscope for treating the hepatolithiasis which are widely distributed. Liver transplantation can provide the ultimate final treatment plan [30]. As mentioned, hepatolithiasis hepatectomy has its own characteristics; the following case description is for left hepatolithiasis (Figs. 20.1, 20.2, 20.3, 20.4, 20.5, 20.6, 20.7, 20.8, 20.9, 20.10, 20.11, 20.12, 20.13, 20.14, 20.15, 20.16, 20.17, 20.18, 20.19, 20.20, 20.21, and 20.22).

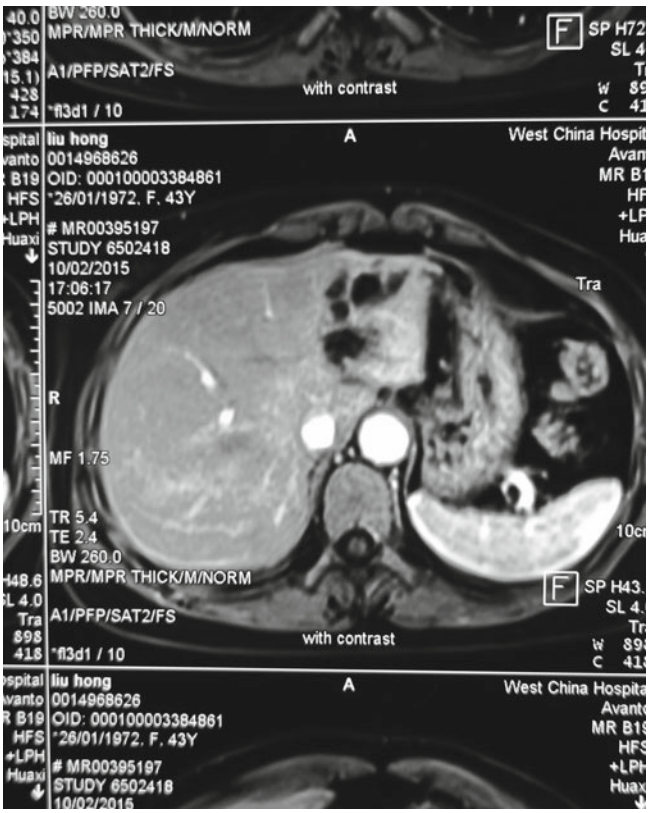

Fig. 20.1 Lesions are primarily concentrated in the left lateral lobe, as in the following MRI image

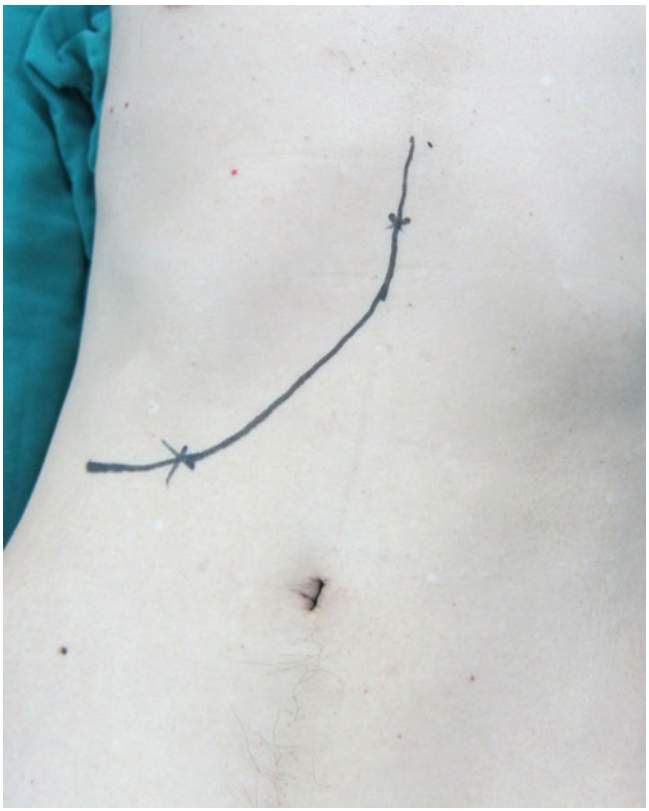

Fig. 20.2 Generally select a right costal margin incision for left lobe hepatectomy

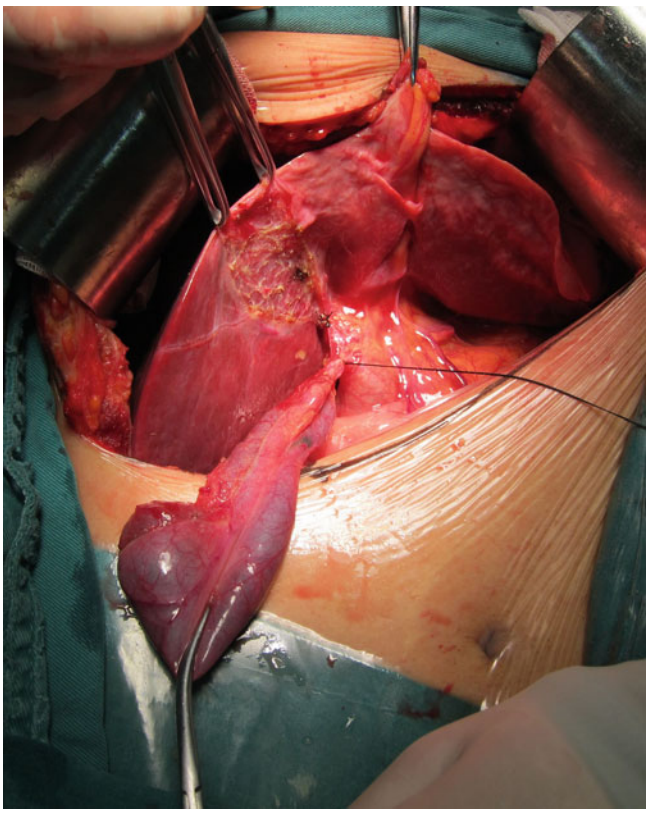

Fig. 20.4 Perform a cholecystectomy first

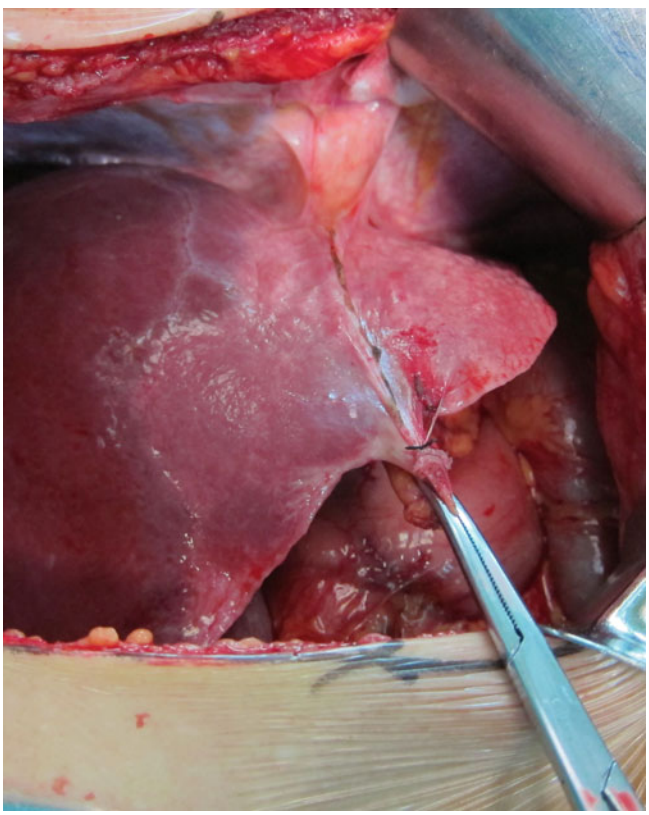

Fig. 20.3 Expose the lesion

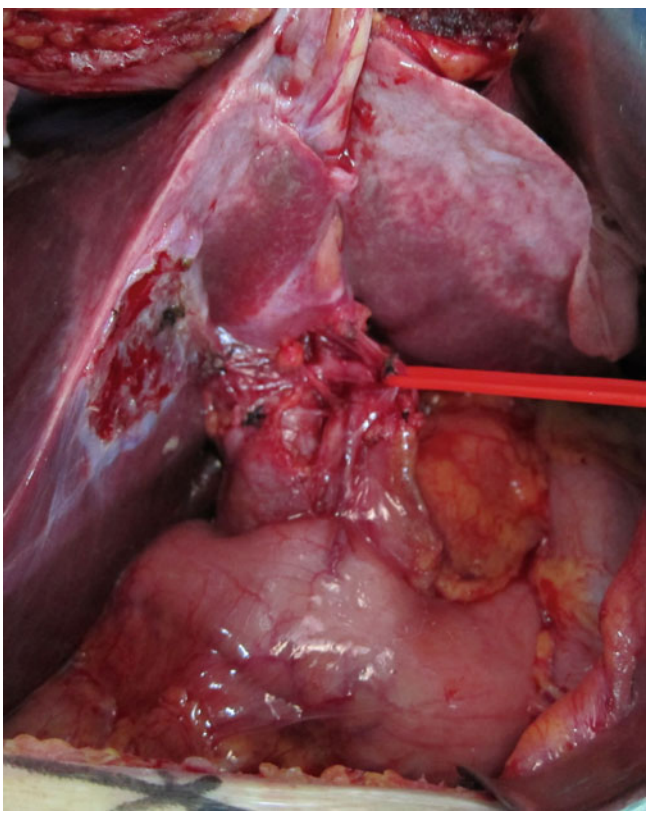

Fig. 20.5 Expose the hepatoduodenal ligament

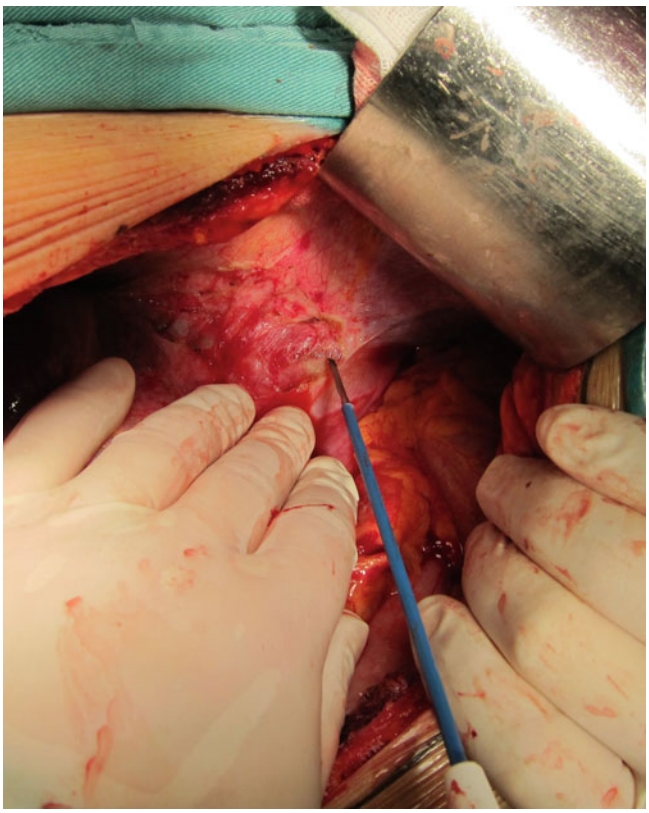

Fig. 20.6 Free the perihepatic ligaments, such as the left coronary ligament

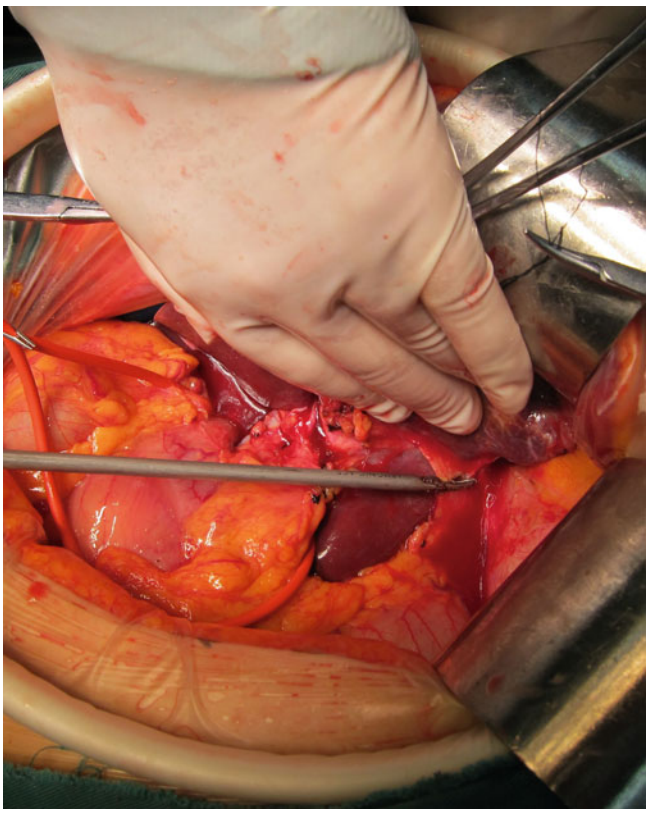

Fig. 20.8 Free and cut the hepatogastric ligament

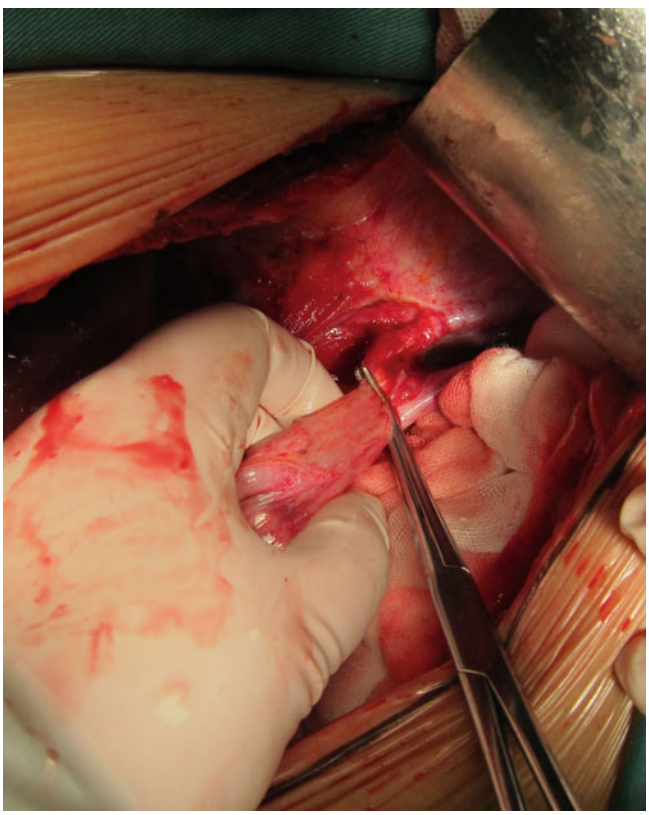

Fig. 20.7 Transection of the left triangular ligament

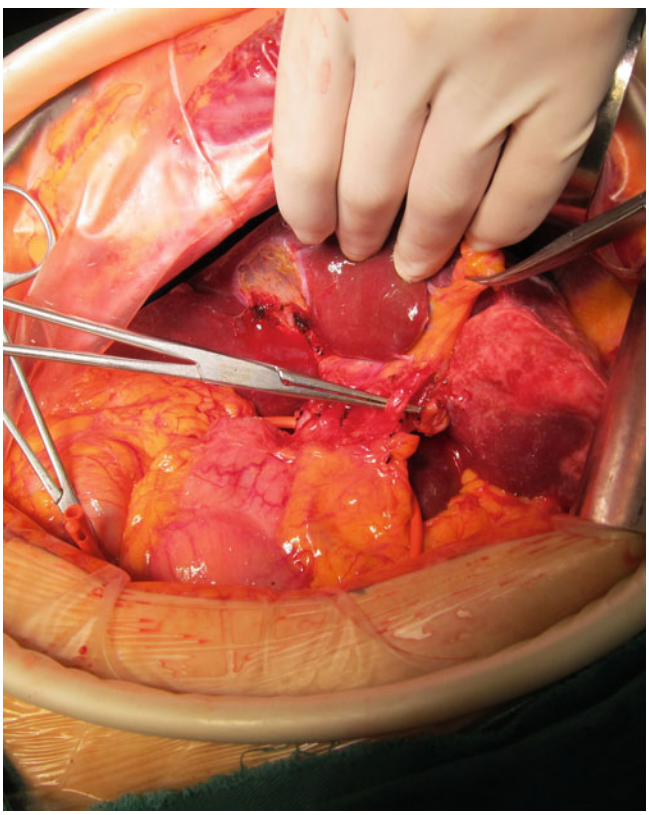

Fig. 20.9 Isolate and cut the left hepatic artery

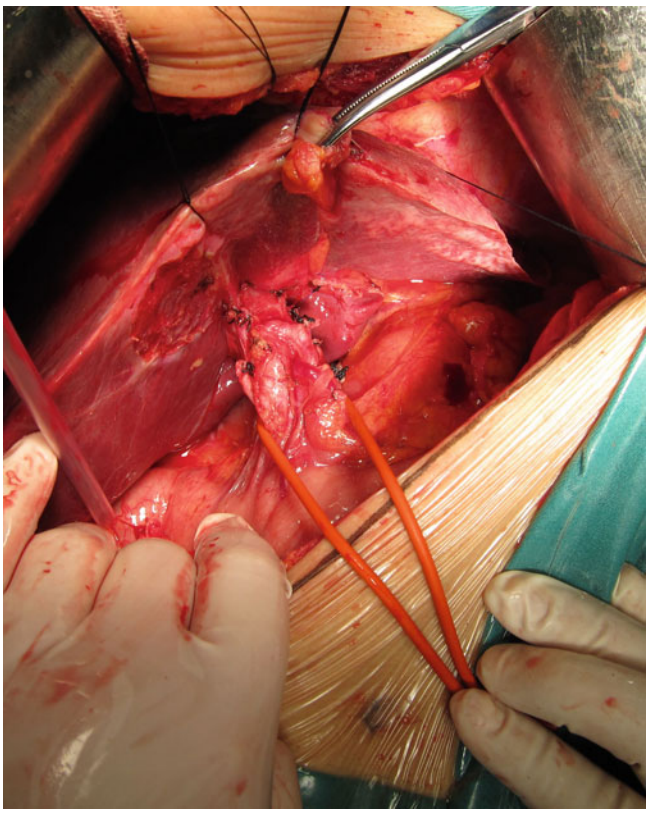

Fig. 20.10 Pre-blockage of the hepatoduodenal ligament

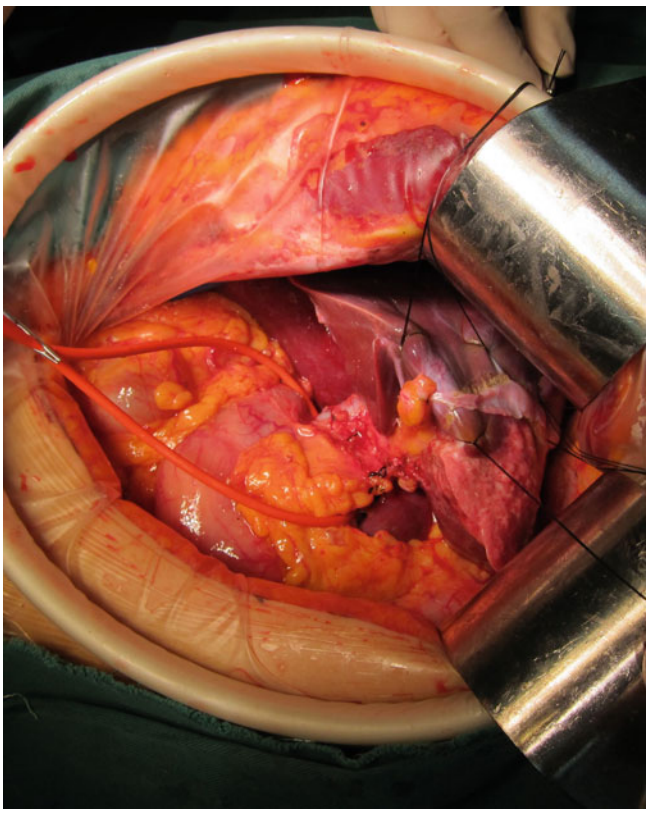

Fig. 20.12 Suture the traction line on both sides of the tangent line

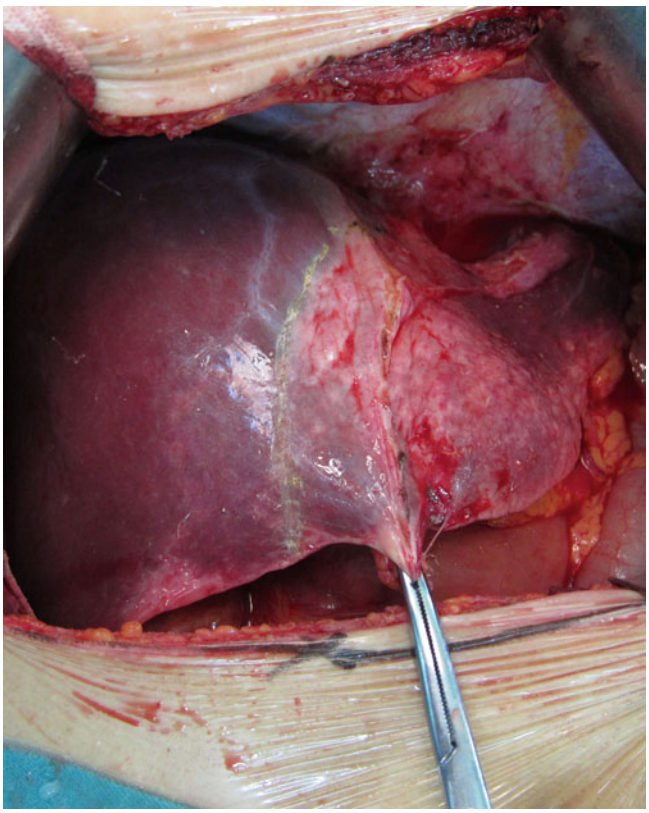

Fig. 20.11 Identify the liver tangent line

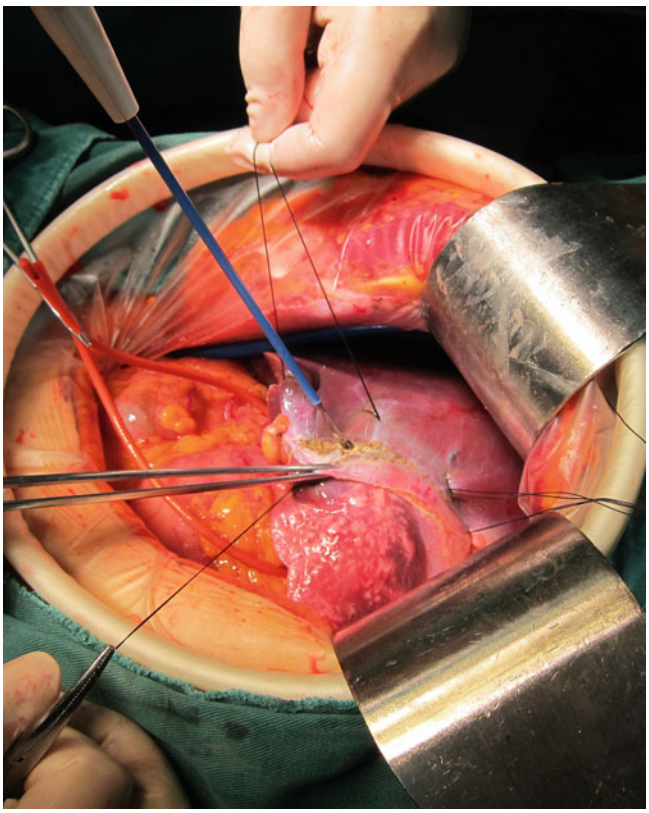

Fig. 20.13 Cut the liver capsule with an electric knife

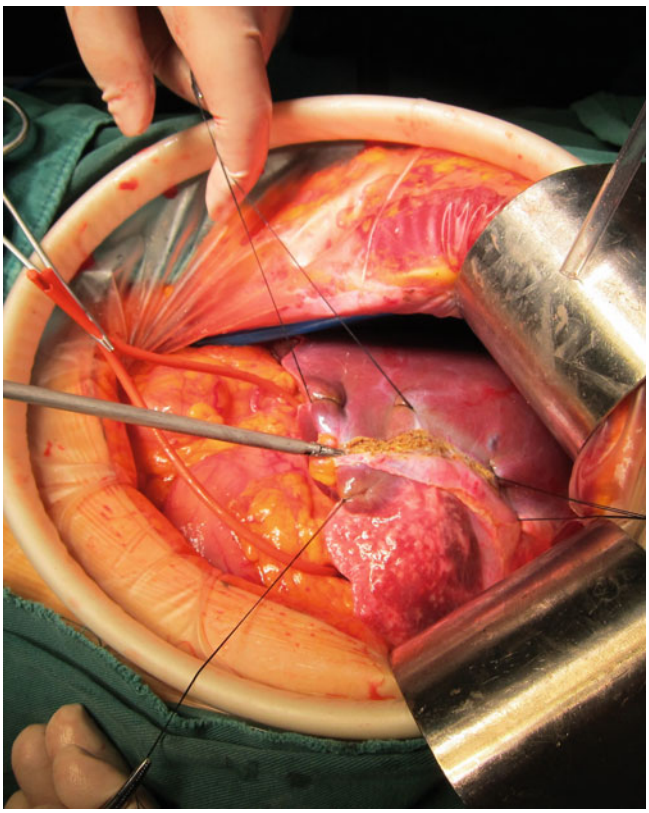

Fig. 20.14 Perform a hepatectomy with an ultrasonic scalpel with a small tube (e.g., artery, vein, and bile duct, with ultrasonic scalpel in direct contact)

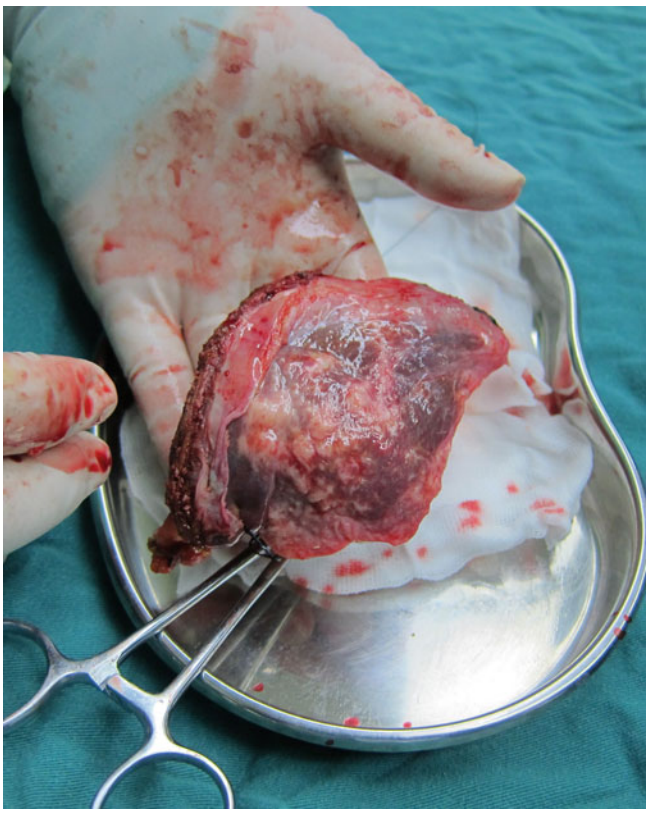

Fig. 20.16 Transect the specimen

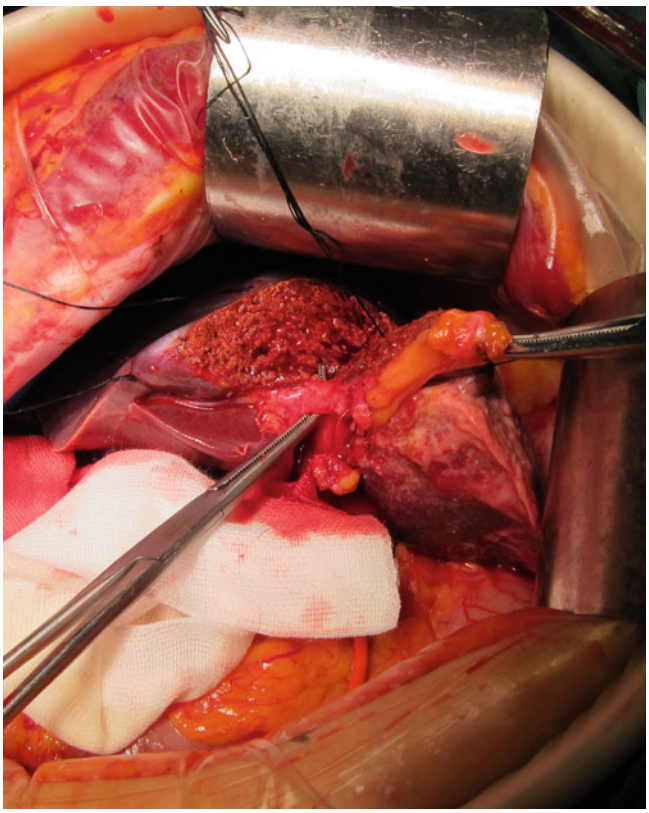

Fig. 20.15 Transect the left branch of the portal vein and left hepatic vein; expose and remove the left hepatic duct

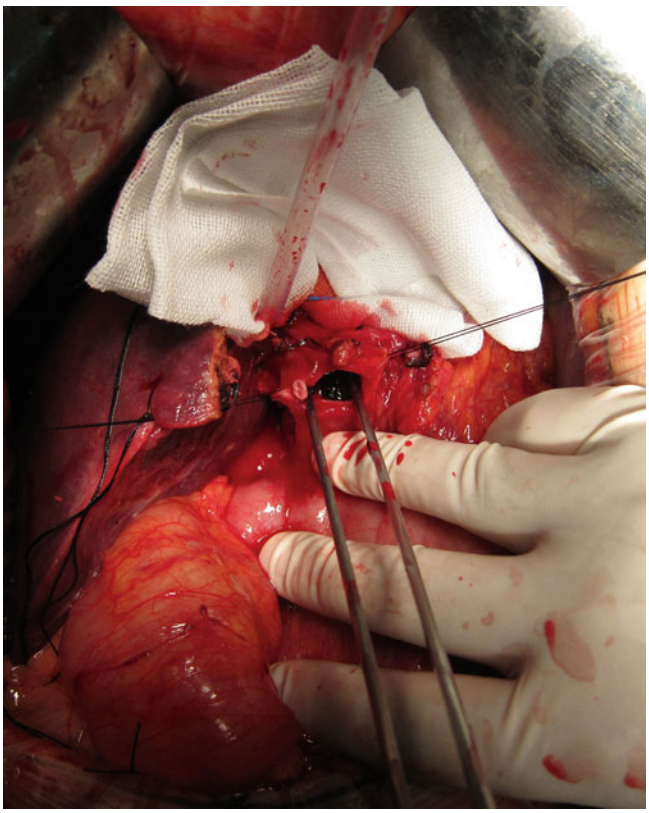

Fig. 20.17 Expose the common bile duct and remove the extrahepatic bile duct stones

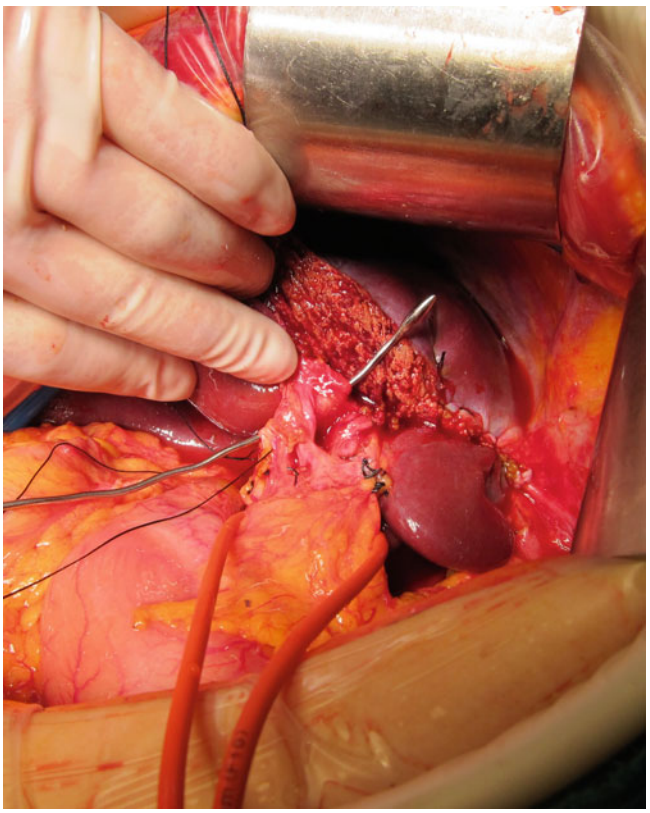

Fig. 20.18 Use a biliary bougie to explore for residual stones

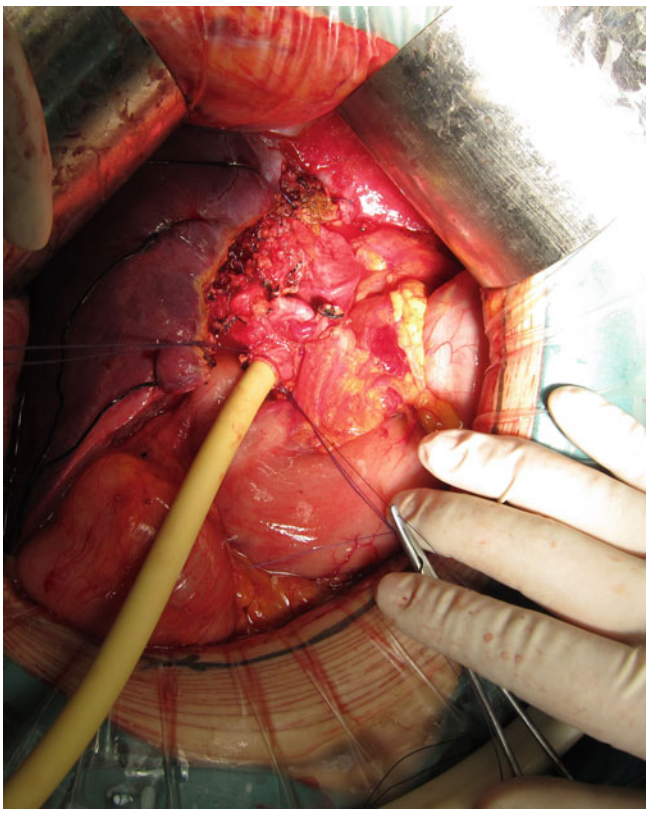

Fig. 20.20 After confirming that there are no residual stones, place a T-drainage tube in the common bile duct

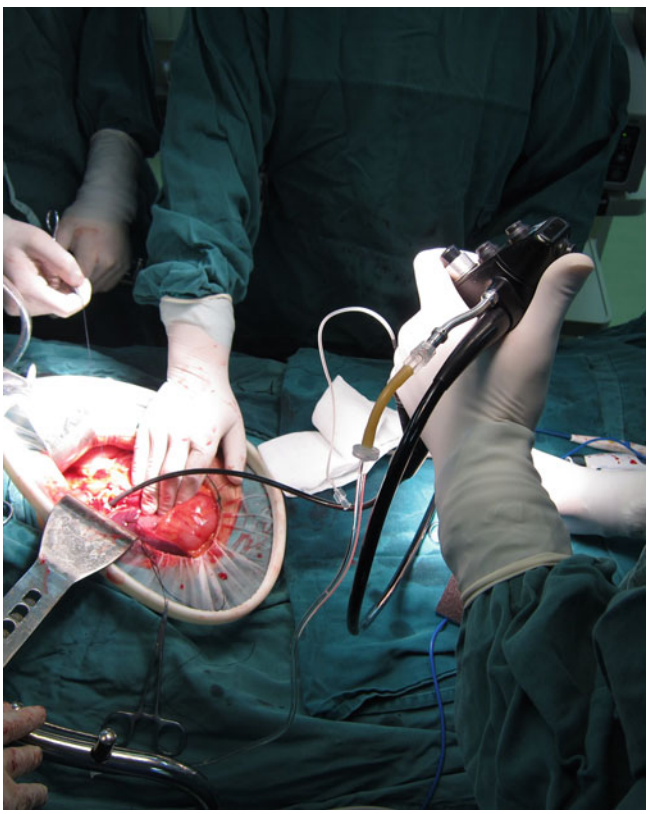

Fig. 20.19 Perform an intraoperative re-exploration with concomitant use of choledochoscope to check for residual stones

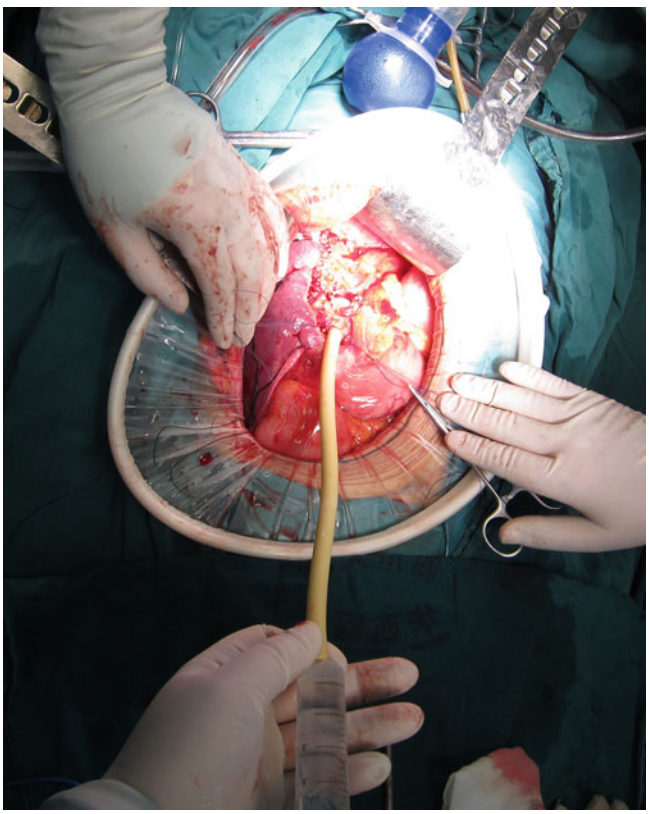

Fig. 20.21 Examine the bile ducts for bile leakage and hemorrhage. The drainage tube and the T tube are placed together, leading out of the body

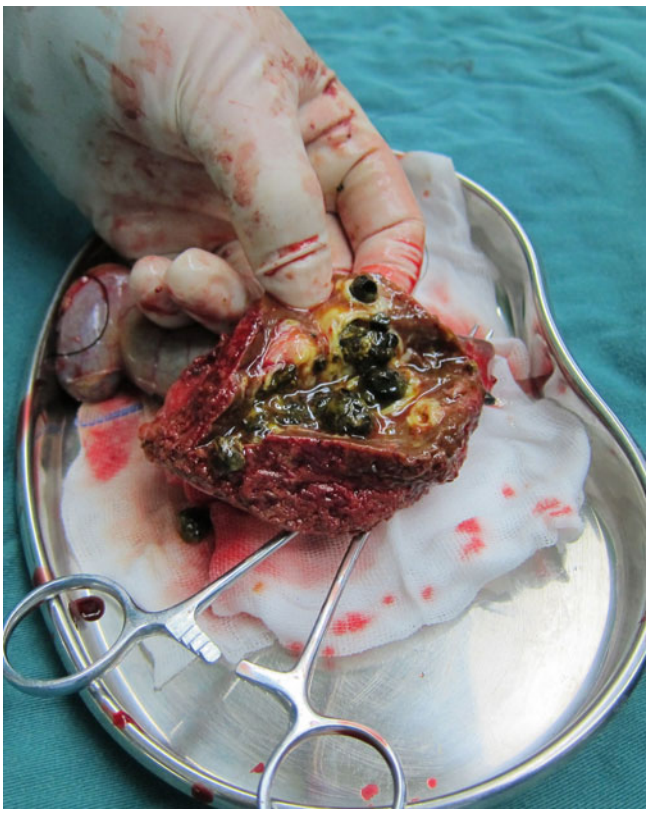

Fig. 20.22 After closing the incision, examine the specimens; here, numerous stones are visible

20.7 Postoperative Complications and Treatment

Complications for this procedure are roughly in line with other liver resections for the treatment of hepatolithiasis. The difference is to pay attention that the T tube remains unobstructed and to prevent its loss. In addition, because the clinical manifestations of the hepatolithiasis are varied, the operation can be more complex, resulting in more surgical complications. The incidences of various complications are as follows: incision infection, 22 %; pulmonary infection, 6 %; bile leakage, 5 %; hemorrhage, 3 %; and hematosepsis, 1 % [31]. If intrahepatic duct bile leakage is observed, percutaneous drainage is the most effective method [32].

20.8 Long-Term Prognosis

The clinical manifestations of hepatolithiasis are diverse and complex, with varying disease locations and associated lesions. These variations result in a high degree of difficulty with respect to diagnosis and treatment. Moreover, hepatolithiasis has a high postoperative recurrence rate. According to previous reports, surgical complications for one- and two-sided hepatolithiasis are 20.4 % and 38.5 %, respectively. The recurrence rates for these conditions after 5 years are 6.2 % and 16.7 %, respectively. Perioperative mortality is 0.4 %, and the overall survival rate 10 years after hepatic resection is 80.3 % [33, 34].

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Liver Resection for Hilar Cholangiocarcinoma

21

Lunan Yan and Yan Zhong

21.1 Milestones in the History of Surgery in Hilar Cholangiocarcinoma

In 1965, Klatskin initially reported 13 cases of hilar cholangiocarcinoma and described their pathological and clinical indications; thus, this type of tumor was subsequently referred to as a Klatskin tumor [1].

In the 1970s, the major treatment for hilar cholangiocarcinoma was palliative surgery to relieve jaundice and prolong life. These surgeries mainly involved T-tube drainage, the placement of biliary stents, and internal and external percutaneous transhepatic biliary drainage (BD) [2, 3].

In 1975, Bismuth, a French surgeon, first proposed a staging system to determine the scope of surgical resection for hilar cholangiocarcinoma based on tumor location and the extent of tumor invasion [4]; this system laid a foundation for the surgical resection of these types of tumors.

In the 1980s, the treatment of hilar cholangiocarcinoma by local resection and hepaticojejunostomy began to be implemented [4, 5]. However, these surgeries produced a low radical resection rate, and high postoperative recurrence and mortality rates were observed [6].

In the 1990s, bile duct resection combined with hepatectomy gradually came to be utilized for the treatment of hilar cholangiocarcinoma [7, 8]. In addition, because the caudate lobe bile duct enters the common hepatic duct close to the bifurcation of the left and right hepatic ducts, 40–98 % of hilar carcinoma cases involve the caudate lobe; therefore, the combined resection of the entire caudate lobe is frequently recommended [9, 10].

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In 1997, Klempuauer first reported the treatment of hilar cholangiocarcinoma using extended right hemihepatectomy combined with portal vein resection [11].

In 1999, Neuhans utilized the "no tache" technique to perform conventional resection of the portal vein bifurcation [12].

For nearly 20 years, conclusions from an extensive body of literature have indicated that hepatoduodenal lymphadenectomy, bile duct resection combined with hepatectomy, and caudate lobe resection should be used as the primary surgical procedures for the treatment of hilar cholangiocarcinoma; the use of these approaches as opposed to other alternatives can increase radical resection rates, improve cancer-free survival rates, and reduce recurrence rates [10, 13, 14]. Using these procedures, 5-year survival rates of up to 25–40 % can be attained [15]. Local resection has produced 5-year survival rates of 0 % even for cases involving tumors of Bismuth types I and II [12]; thus, this approach has been abandoned by most medical centers.

21.2 Several Specific Anatomical Features Related to Hilar Cholangiocarcinoma Surgery

21.2.1 The Hjortsjo Crook

The right posterior hepatic duct and the right anterior hepatic duct converge to form the right hepatic duct. The right posterior hepatic duct is located on the dorsal side of the right portal vein prior to this convergence; it winds around to the front of the right portal vein to converge with the left hepatic duct, forming the Hjortsjo crook (Fig. 21.1).

Therefore, during the resection of segments 5 and 8, the cutting surface should not be overly close to the site where the right anterior branch separates from the portal vein; otherwise, the right posterior hepatic duct will be damaged and will cause difficulties during the reconstruction process.

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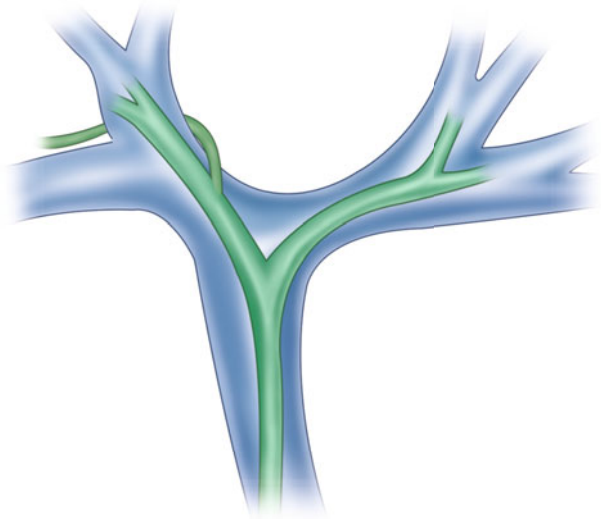

Fig. 21.1 Hjortsjo crook

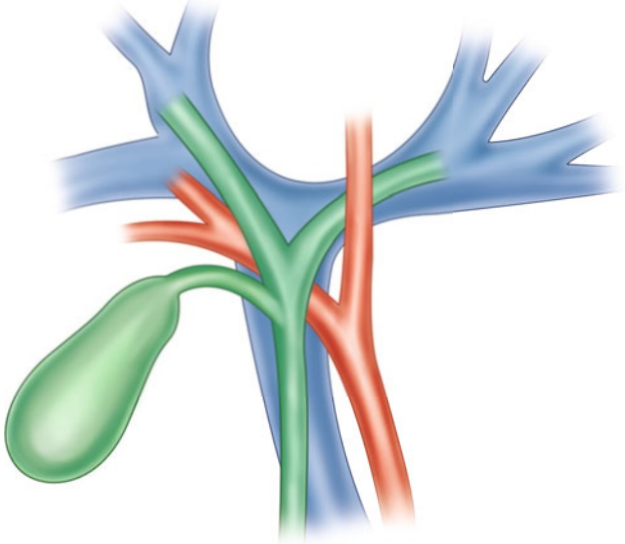

Fig. 21.2 The right hepatic artery typically runs behind the common hepatic duct

21.2.2 Bile Ducts That Drain the Caudate Lobe

The caudate lobe is divided into the following three parts: (a) the spigelian lobe; which is located at the left side of the venous ligament and has one to two bile duct branches; (b) the paracaval portion, which is located in front of the vena cava and has one to two bile duct branches coming from the right posterior lobe; and (c) the caudate process, which is a small projection located between the vena cava and the right side of the portal vein into which one to two bile duct branches enter.

Because the site from where the caudate lobe bile duct issues is very close to the hilar confluence, hilar cholangiocarcinoma can readily invade this duct at early stages; accordingly, this duct should be resected.

The right hepatic artery typically runs behind the common hepatic duct, that is, beneath this duct after the confluence of the right and left hepatic ducts. This artery is often subjected to tumor invasion in cases of hilar cholangiocarcinoma (Fig. 21.2).

The right anterior branch of the right hepatic artery travels along the inner anterior side of the right branch of the portal vein, whereas the right posterior branch crosses the inner anterior side of the right branch of the portal vein and runs in Rouviere's sulcus behind the gallbladder neck. These branches are easily freed and not particularly susceptible to tumor invasion; these characteristics facilitate the reconstruction of the right hepatic artery (Fig. 21.3).

21.2.3 Hepatic Hilar Plate System

Glisson's sheath and the connective tissue sheath surrounding the bile ducts and blood vessels below the liver fuse together to form the hilar plate system, which includes the hilar plate above the bile duct confluence, the cystic plate at the gallbladder fossa, the umbilical plate above the umbilical portion of the portal vein, and the Arantion plate covering the venous ligament (Fig. 21.4).

In 1956, Hepp and Couinaud introduced the following approach: segment 4 of the liver was pulled upward to cut the bottom of Glisson's sheath at its base, clearly revealing the hilar structure and indicating that vascular communication may only occur among 1 % of branches. However, in hilar cholangiocarcinoma, because the tumor readily invades adjacent hilar plate tissues and segment 1 of the liver, the hilar plate should not be dissected. Instead, en bloc resection of the bile duct confluence, the hilar plate, and the caudate lobe should be performed.

21.2.4 Lymphatic Drainage

The following two routes of lymphatic drainage are involved in hilar cholangiocarcinoma.

The left route travels through lymphatic vessels and lymph nodes (LN) along the cystic duct, the hepatic artery, and the anteromedial side of the portal vein to the celiac trunk; in other words, this route travels along LN #12a → 8 → 9 → 16.

The right route travels through lymphatic vessels and LN along the cystic duct and the anterolateral side of the portal vein, behind the pancreas, along the aorta, between the left side of the aorta and the vena cava, and below the left renal vein; in other words, this route travels along LN #12b → 13a → 16.

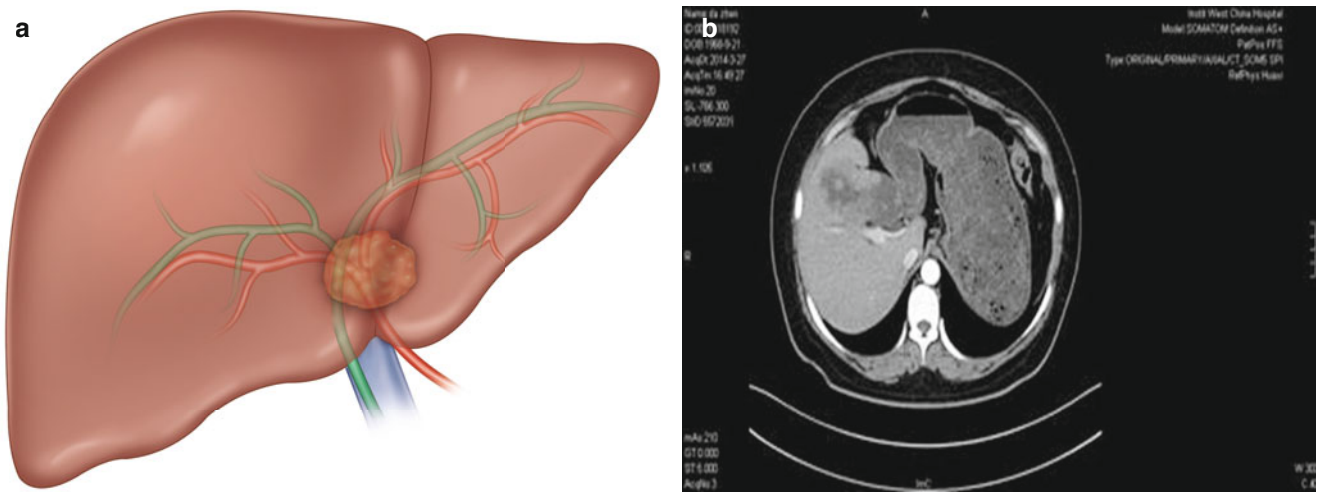

Fig. 21.3 (**a**, **b**) The right anterior branch of the right hepatic artery travels along Rouviere's sulcus behind the gallbladder neck

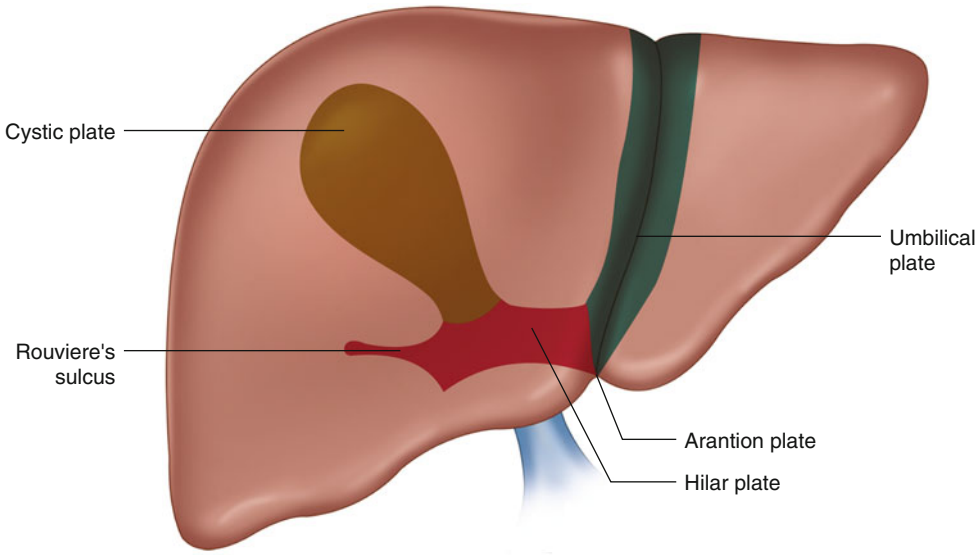

Fig. 21.4 Hepatic hilar plate system: *a*. cystic plate; *b*. hilar plate; *c*. umbilical plate; *d*. Arantion plate; *e*. Rouviere's sulcus

Therefore, regions that should be included in lymphadenectomy include the common hepatic artery, the celiac trunk, and behind the pancreatic head, although complete lymphadenectomy is difficult to accomplish.

21.3 Staging Systems

The seventh edition of the TNM (tumor, nodes, metastasis) staging criteria issued by the American Joint Committee on Cancer (AJCC) supplement the Bismuth classification system by considering tumor-related difficulties associated with the liver parenchyma, vascular structure, and invasion of the lymphatic system. Thus, this staging system provides information regarding tumor resectability based on pathological criteria.

☆ TNM classification (the AJCC stage 7th edition)	
Primary tumor (T)	
Tx	The primary tumor cannot be assessed
T0	No evidence of a primary tumor
Tis	Carcinoma in situ
T1	The tumor is confined to the bile duct histologically
T2a	The tumor invades the surrounding adipose tissue beyond the wall of the bile duct
T2b	The tumor invades the adjacent hepatic parenchyma
T3	The tumor invades unilateral branches of the portal vein or hepatic artery
T4	The tumor invades the main portal vein or its branches bilaterally, the common hepatic artery, the second-order biliary radicals bilaterally, or the unilateral second-order biliary radicals with contralateral portal vein or hepatic vein involvement

(continued)

☆ TNM classification (the AJCC stage 7th edition)			
Regional lymph nodes (N)			
Nx	Regional lymph nodes cannot be assessed		
N0	No regional lymph node metastasis		
N1	Regional lymph node metastasis (cystic duct, common bile duct, hepatic artery, and portal vein)		
N2	Metastasis to periaortic, pericaval, superior mesentery artery, and/or celiac artery nodes		
Distant metastasis (M)			
M0	No distant metastasis		
M1	Distant metastasis		
Stage group			
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2a-T2b	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T1-T3	N1	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	N2	M0
	Any T	Any N	M1

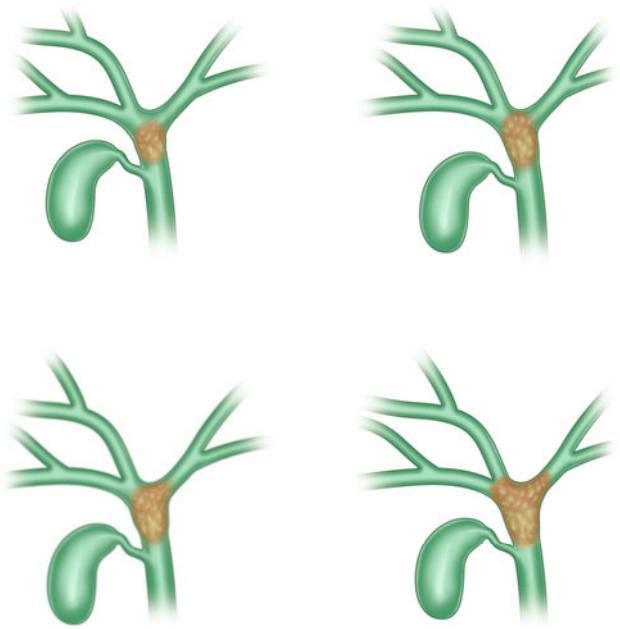

Fig. 21.5 Bismuth-Corlette classification

21.3.1 Bismuth-Corlette Classification (Fig. 21.5)

This classification system was proposed by Bismuth and Corlette of France in 1975. In this system, tumors are categorized based on assessments of tumor location and the degree of longitudinal invasion along the biliary system; therefore, Bismuth-Corlette classification facilitates the clinical determination of the scope of surgical resection. This classification approach is simple and practical and has therefore become widely respected.

Type I: the tumor is below the confluence of the right and left hepatic ducts.
Type II: the tumor has reached the confluence of the right and left hepatic ducts.
Type IIIa and IIIb: the tumor has caused the embolization of the common hepatic duct and the left and/or right hepatic ducts.
Type IV: the tumor has invaded the confluence and the left and right hepatic ducts.

21.3.2 The Anatomical Classification of Hilar Cholangiocarcinoma [16, 17]

Intrahepatic bile duct tumors (5–10 %)
Perihilar tumors (60–70 %)
Extrahepatic bile duct tumors (20–30 %)

21.4 Preoperative Evaluation

21.4.1 Radiological Evaluation

Ultrasonography (US) is the preferred approach when jaundice is present because US can confirm biliary dilatation, locate obstruction sites, and exclude the possibility of stones [15]. Color Doppler is helpful for discovering portal vein and hepatic artery compression as well as tumor encapsulation [18].

Endoscopic US (EUS) can be utilized to assess local LN and vascular invasion [19, 20].

Percutaneous transhepatic cholangiography (PTC) can display intrahepatic and hilar lesions.

Endoscopic retrograde cholangiopancreatography (ERCP) can reveal extrahepatic lesions. Although ERCP has limited application in cases of hilar cholangiocarcinoma, this technique is helpful for assessing drainage and stent placement.

Multidetector-row computed tomography (MDCT) can be used to not only examine tumor size, blockage levels, and hepatatrophia but also to evaluate resectability.

Magnetic resonance imaging (MRI) or magnetic resonance cholangiopancreatography (MRCP) can contribute to the assessment of biliary tumors, the determination of resectability, and the evaluation of the extent to which the tumor has invaded bile ducts, blood vessels, and the surrounding liver parenchyma [21].

21.4.2 Three-Dimensional (3D) Image Reconstruction

Hilar cholangiocarcinoma surgery now makes use of 3D imaging techniques [22–26]. With 3D imaging, the scope of

patients' tumors can be accurately determined, and 360° imaging of the biliary system can be performed to display each bile duct branch. This approach can be used to not only determine a tumor's Bismuth type and whether a tumor has invaded the hepatic arteries and portal veins in its vicinity but also to assess the anatomical changes in the blood flow of hepatic vessels as well as the remnant liver volume. Thus, the use of 3D imaging can allow surgeries to be more precisely planned, which can reduce intraoperative blood loss and complications.

However, many unresolved difficulties remain.

21.4.3 Assessments of Hepatic Function

Hepatic function will be compromised in patients who suffer from obstructive jaundice. Hepatic function can be evaluated using the Child-Pugh scoring system, the model for end-stage liver disease (MELD), and the indocyanine green (ICG) clearance test.

Computed tomography (CT) is used to assess remnant liver volume, and CT and MRI are used to measure the extent of steatosis in patients' livers. Typically, the remnant volume of a normal liver should be >25 %; in patients with hepatic dysfunction, remnant liver volume should be >40 % [27].

The regenerative capacity of the liver has been investigated using embolism of the right branch of the portal vein to induce left liver hyperplasia; this approach has shown that non-embolized hepatic tissues can typically increase in size by 30 % in patients with normal regenerative capacities.

21.4.4 Preoperative Assessment

Hilar cholangiocarcinomas can exhibit exophytic, infiltrating, polypoid, or mixed types of growth. Periductal-infiltrating tumors account for 70 % of hilar cholangiocarcinomas [28, 29]. Radiological evaluation is first performed to determine a tumor's scope, hepatic parenchymal invasion status, vascular invasion status, the extent to which liver lobes have atrophied, the number of metastatic lesions, and the extent to which LN metastasis and distant metastasis have occurred.

Cases involving any of the following conditions are typically unresectable [20, 30]: ① extensive invasion at the confluence of the left and right hepatic ducts; ② invasion of the main trunk of the portal vein; ③ concurrent invasion of the left and right branches of the portal vein; ④ invasion of the left or right portal vein, combined with extensive invasion of the bile ducts on the opposite side; ⑤ extensive LN metastasis; and ⑥ distant metastasis.

However, surgical evaluation is ultimately necessary to determine resectability.

21.4.5 Laparoscopic Assessment

CT and MRI can typically confirm the extent of portal vein involvement in cases of hilar cholangiocarcinoma. However, metastatic lesions in the liver, the greater omentum, and the peritoneum are difficult to discover. Therefore, in recent years, many researchers have recommended performing an initial laparoscopic procedure to detect small metastatic lesions and thereby avoid unnecessary laparotomies [31].

Furthermore, laparoscopic US (LUS) can discover intrahepatic metastatic lesions and local vascular invasion that cannot be detected through imaging examinations; thus, LUS can contribute to the determination of resectability.

21.5 Preoperative Preparation

Hilar cholangiocarcinoma usually manifests as jaundice and leads to liver damage. In addition, these tumors frequently invade portal veins, hepatic arteries, and peripheral hepatic parenchyma; as a result, resection is difficult, with operative mortality rates of up to 20 % and complication rates of up to 67 %. Therefore, accurate preoperative evaluation and careful preparation are extremely important [32–34].

21.5.1 Preoperative Biliary Drainage (BD)

The objectives of BD are as follows: ① reduce bilirubin levels, ② treat biliary tract infections, and ③ allow for explicit radiographic confirmation of the extent to which a tumor has spread.

The risks of BD are as follows: ① implantation of approximately 5 % of tumors, ② infection, and ③ bleeding.

The modes of BD are as follows: ① endoscopic nasobiliary drainage (ENBD) and ② percutaneous transhepatic biliary drainage (PTBD). Typically, unilateral drainage is sufficient, and drainage should continue for 4–6 weeks until a patient's total bilirubin level has decreased to 2–3 times the upper limit of the normal range [35]. Because BD has risks and most jaundice patients can tolerate extended hepatectomy [36], many medical centers do not recommend preoperative BD.

21.5.2 Preoperative Portal Vein Embolization (PVE)

The purpose of PVE is to induce the regeneration of the future liver remnant (FLR) and thereby reduce postoperative liver failure and death.

Indications: ① patients with liver remnants of <40 % and ② patients who will undergo extended hepatectomy, particularly patients with possible revascularization [37].

Methods: BD is first performed for 4–6 weeks; when the total bilirubin has decreased to 50 u, PVE is performed. Hepatectomy can be performed 2–3 weeks after PVE.

21.5.3 Two-Stage Resection Approach

A two-stage resection approach may be utilized for patients with indications for PVE. The first stage involves the surgical transection of the liver parenchyma and the concurrent ligation of bile duct and portal vein branches without the transection of hepatic arteries or hepatic veins. After 1 week, when the liver remnant exhibits hyperplasia, the second stage of the liver resection can be performed [38].

The advantage of this method is that this approach can significantly shorten preoperative preparation time.

21.5.4 Preoperative Laparoscopic Staging

An initial laparoscopic exploration is recommended for hilar cholangiocarcinoma patients whose tumors have been confirmed to be resectable by preoperative CT, MRI, or other approaches and who will undergo PVE. If this laparoscopic examination detects peritoneal and/or omental metastatic lesions or extensive small intrahepatic metastatic lesions, then surgical resection should be abandoned, and palliative treatments, such as the placement of biliary stents, should be performed to shorten the patient's hospital stay. LUS can be performed to further determine a patient's situation with respect to intrahepatic metastatic lesions and portal vein invasion. Thus, laparoscopic staging should be performed to avoid unnecessary laparotomies.

21.6 Consideration of the Surgical Procedure for Hilar Cholangiocarcinoma

Numerous clinical reports have indicated that only radical resection with histologically negative surgical margins (R0) is required to achieve radical resection of cholangiocarcinomas [39, 40]. Therefore, there is a broad spectrum of hilar cholangiocarcinoma surgeries, which range from local hilar resection or limited hepatectomy to mesohepatectomy, extended left and right hepatectomy, and caudate lobe resection [41, 42]. To achieve R0 resection, for certain patients with advanced-stage hilar cholangiocarcinoma or with relatively widespread invasion, an extended hemihepatectomy with vascular resection and reconstruction [43, 44] or a comprehensive hepatopancreatoduodenectomy (HPD) [43, 44] should be performed. Thus, the current surgical options for hilar cholangiocarcinoma include the following approaches:

1. Mesohepatectomy – suitable for Bismuth types I, II, and III
2. Extended right hemihepatectomy – suitable for patients with Bismuth type IIIa or IV tumors and invasion of the right branch of the portal vein
3. Extended left hemihepatectomy – suitable for patients with Bismuth type IIIb or IV tumors and invasion of the left branch of the portal vein
4. Extended right hemihepatectomy with portal vein resection – suitable for patients with Bismuth type III or IV tumors and invasion of the main trunk or bifurcation of the portal vein
5. Combined hepatic artery resection and reconstruction – suitable for patients with hepatic artery invasion
6. Combined HPD – suitable for patients with lower common bile duct and pancreatic head invasion

21.7 Mesohepatectomy (Resection of Segments IVb, V, and I)

1. Separation is performed at the superior edge of the pancreas and the left edge of the hepatoduodenal ligament. Lymphadenectomy is performed upward along the hepatic artery and portal vein to skeletonize this region (Fig. 21.6).
2. Separation is performed along the superior margin of the pancreas to the right edge of the hepatoduodenal ligament. The common bile duct is transected upward to free the extrahepatic bile duct and the posterior wall of the gallbladder until the posterior side of the hilar tumor is reached. Surgeons then confirm that the main trunk and

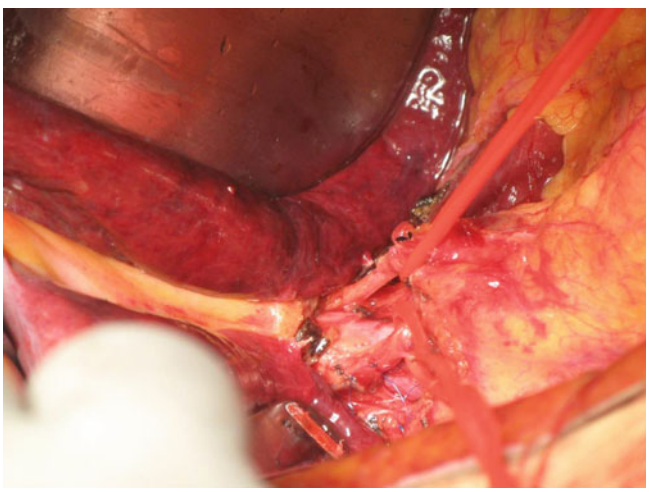

Fig. 21.6 Separation is performed at the superior edge of the pancreas and the left edge of the hepatoduodenal ligament

bifurcation of the portal vein have not been invaded. If the right hepatic artery has been invaded by the tumor, then this artery can be transected (Fig. 21.7).
3. The caudate lobe of the liver is freed from the lower vena cava (LVC).
4. Under the guidance of baseline US (BUS), the liver parenchyma and hilar bile duct are transected 1 cm from the edge of the tumor. The bile duct stump is then frozen.
5. The entire affected hepatic tissue is resected, together with the extrahepatic bile duct, the gallbladder, and the caudate lobe.
6. The liver remnant has three to five right hepatic duct openings and two to four left hepatic duct openings. The openings are sutured to <2 mm, leaving two to four openings for anastomosis.
7. Hepaticojejunostomy:

All bile duct openings are integrated as much as possible by choledochoplasty to reduce the number of anastomosis procedures that must be performed.

Bilioenteric anastomosis is performed using Roux-en-Y choledochojejunostomy. During the anastomosis, the posterior wall is first anastomotized using continuous and interrupted 5/0 Prolene sutures. For the anastomosis of two or more biliary openings, the posterior wall of all such openings should be sutured first.

For support, one or two stents 1.0–1.5 cm in length are placed at the anastomotic openings and fixed to the intestinal wall with a needle. These stents will not need to be surgically removed from the body but will instead be automatically eliminated from the body through the intestinal tract. The anterior walls of anastomotic openings are then closed with interrupted sutures.

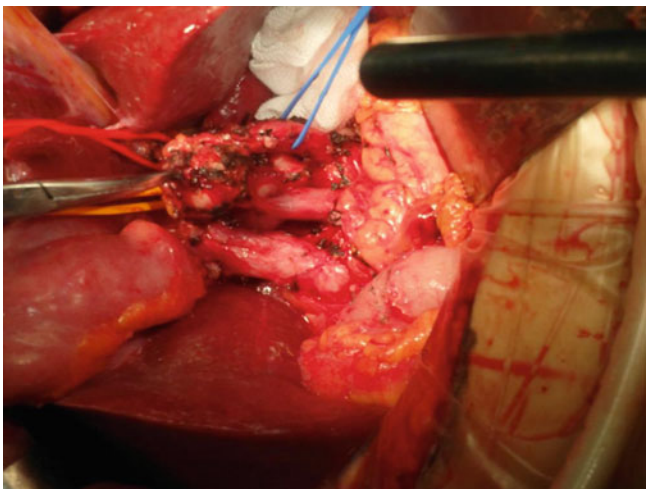

Fig. 21.7 Separation is performed along the superior margin of the pancreas to the right edge of the hepatoduodenal ligament

21.8 Extended Right Hemihepatectomy

1. Separation is performed along the proper hepatic artery and the common hepatic artery until the celiac trunk is reached. The beginning portion of the right hepatic artery is then ligated and transected (Fig. 21.8).
2. The bridge tissues connecting segments III and IV of the liver are separated (Fig. 21.9). The hepatic round ligament is dissected (Fig. 21.10), and the left hepatic artery and the left branch of the portal vein are transected (Fig. 21.11).
3. The branch of the hepatic artery that connects to segment IV of the liver is transected (Fig. 21.12).
4. The left branch of portal vein is separated until the umbilical fissure is reached (Fig. 21.13).

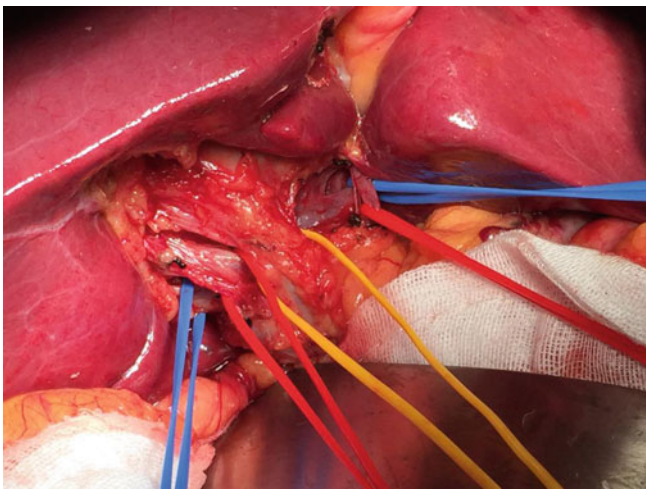

Fig. 21.8 Separation is performed along the proper hepatic artery and the common hepatic artery

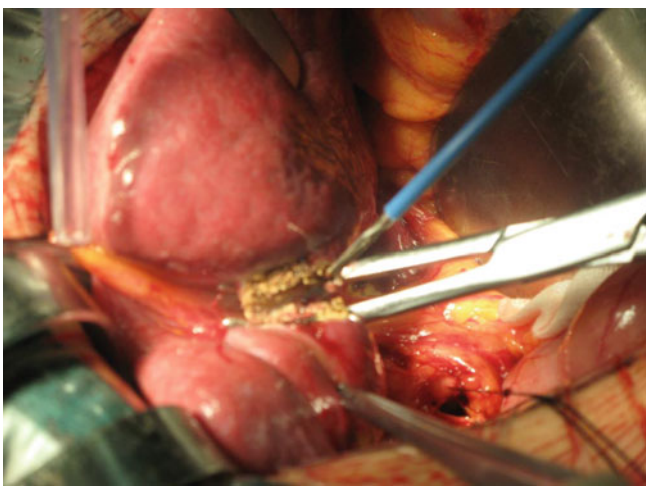

Fig. 21.9 Bridge tissues connecting segments III and IV of the liver are separated

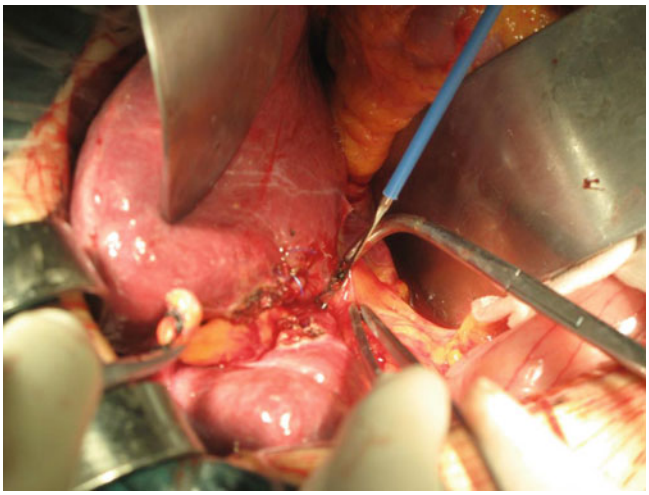

Fig. 21.10 The hepatic round ligament is dissected

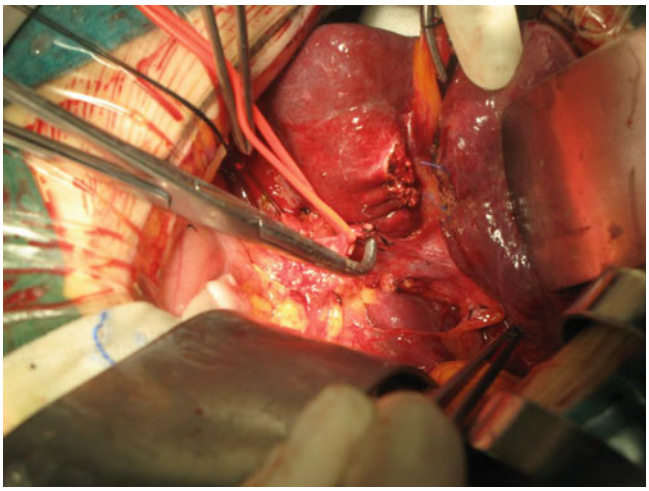

Fig. 21.12 The branch of the hepatic artery that connects to segment IV of the liver is transected

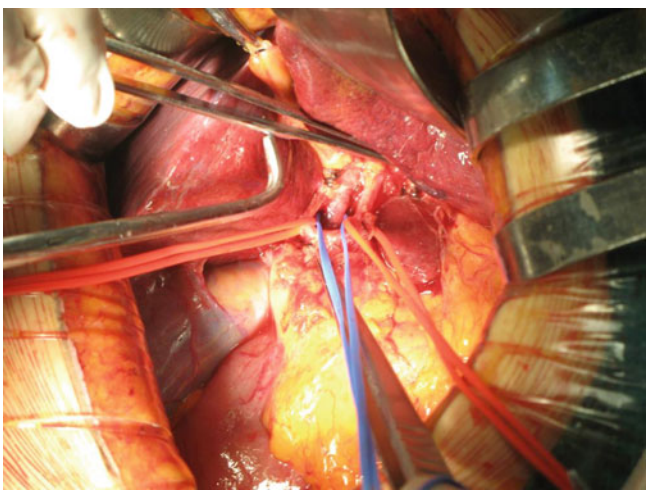

Fig. 21.11 The left hepatic artery and the left branch of the portal vein are transected

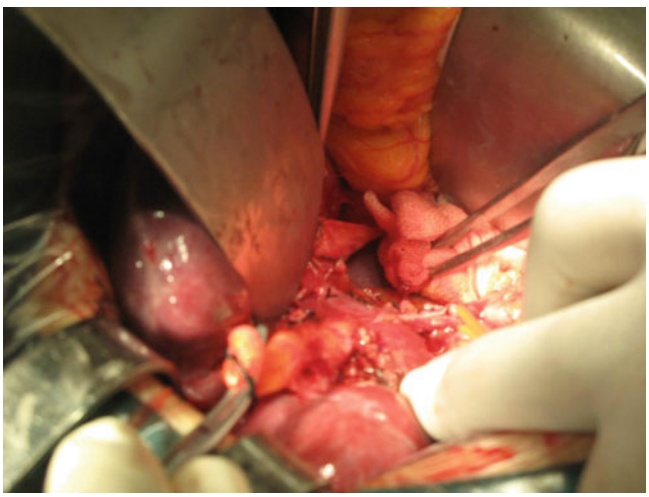

Fig. 21.13 The left branch of portal vein is separated until the umbilical fissure is reached

5. The branch of the portal vein that goes to the caudate lobe is separated and transected to facilitate caudate lobe resection.
6. The portal vein is separated until the bifurcation is reached, and the portal vein bifurcation is completely freed from the bile duct and the posterior wall of the tumor.
7. A Kocher incision is used to dissect the LN behind the pancreatic head and expose the right edge of the portal vein.
8. The common bile duct is transected from behind the duodenum and separated upward until the portal vein bifurcation is reached.
9. The right branch of the portal vein is transected and ligated.
10. The coronary ligament, triangular ligament, and hepatorenal ligament of the liver are freed to free the right liver to the LVC (Fig. 21.14).
11. The right liver resection line is confirmed, and the extended right hemihepatectomy is performed. Segment IVa of the liver is preserved, the remaining section is ligated, and the middle hepatic vein is transected (Fig. 21.15).
12. The remaining section contains two to four left hepatic duct openings (Fig. 21.16).
13. Hepaticojejunostomy is performed as described above.

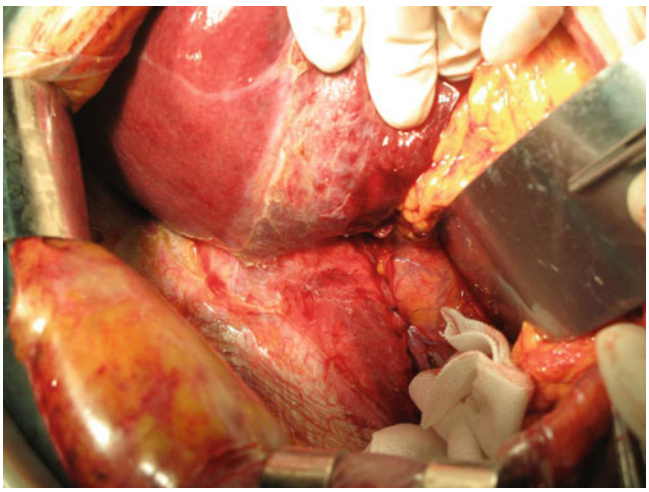

Fig. 21.14 Free the right liver to the IVC

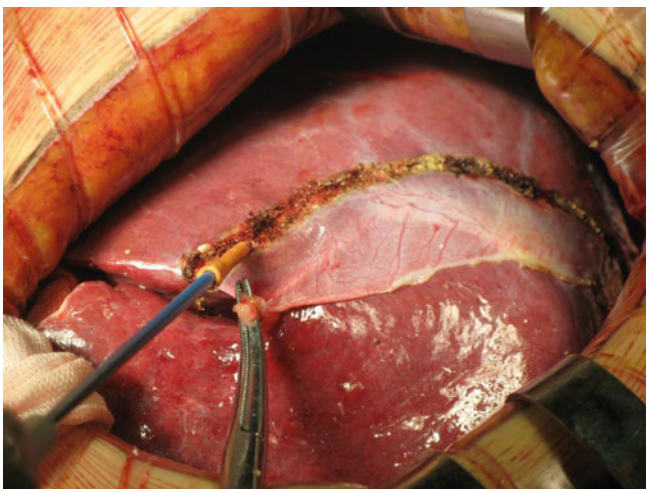

Fig. 21.15 The right liver resection line is confirmed

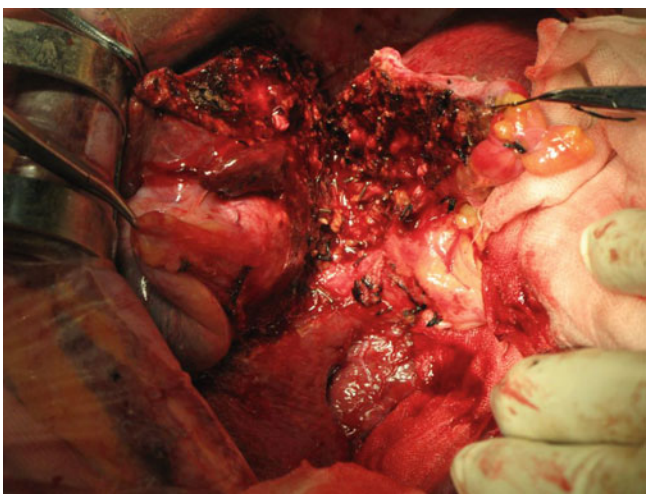

Fig. 21.16 The remaining section contains two to four left hepatic duct openings

21.9 Extended Left Hemihepatectomy

1. The freeing begins at the right side of the hepatoduodenal ligament. The gallbladder is freed starting from the fundus of the gallbladder; the cystic duct is not transected, but the left hepatic artery and its branch are exposed behind the hilar plate.
2. The right branch of the portal vein behind the right hepatic artery is freed.
3. After confirming that the right hepatic artery and the right branch of the portal vein have not been invaded and that the proximal bile duct tumor boundaries satisfy resection requirements, the freeing can continue.
4. The separation of the portal vein bifurcation and the main trunk continues. LN on the right edge of and behind the portal vein is dissected. A Kocher incision is used to dissect the LN behind the pancreatic head.
5. LN along the left side of the hepatoduodenal ligament is dissected. The common hepatic artery and the proper hepatic artery are freed until the separation of the left and right hepatic arteries is reached. The left edge of the portal vein is exposed.
6. The common bile duct is transected at the superior margin of the duodenum. The freeing process continues upward to separate the right hepatic artery. The beginning of the left hepatic artery is ligated, and this artery is transected.
7. The left branch of the portal vein and two to three branches of the caudate lobe are exposed. The branches of the caudate lobe are transected and ligated. Finally, the left branch of the portal vein is transected and ligated.
8. If the portal vein bifurcation has been invaded, the liver should ultimately be split. The right hepatic duct is transected, followed by the resection of the portal vein bifurcation. Repair or anastomosis is then performed.
9. If the hepatic artery has been invaded, part of the hepatic artery can be resected, and hepatic artery reconstruction can be performed. An autologous graft from the great saphenous vein can be used for this reconstruction.
10. The left perihepatic ligament is freed, and short hepatic blood vessels in the caudate lobe are ligated to free the caudate lobe from the LVC.
11. The liver is transected along Cantler's line. The tumor's scope is used as a basis to determine which part of segment V will be transected. The middle and left hepatic veins are transected when the liver is transected.

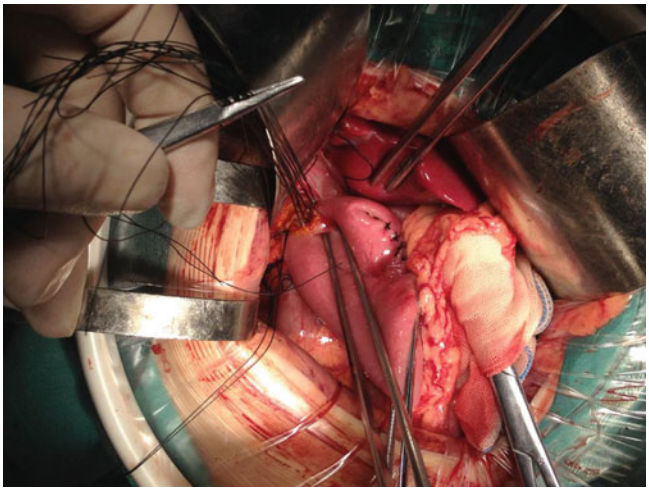

Fig. 21.17 Two to four hepatic ducts require reconstruction

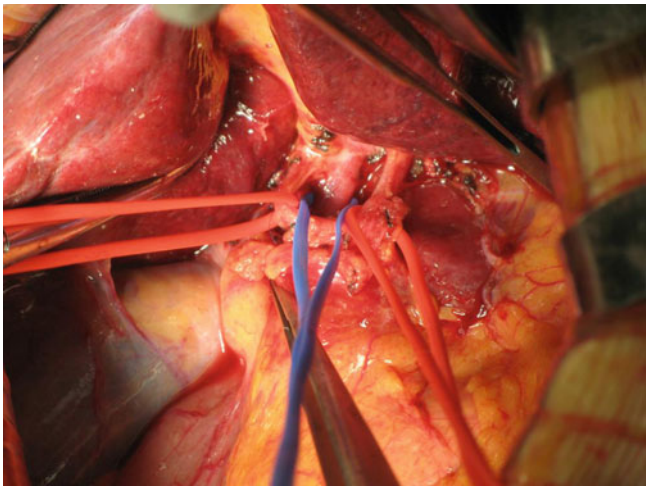

Fig. 21.18 1.5–2-cm segment of the left branch of the portal vein is freed

12. After the left hemihepatectomy or the extended left hemihepatectomy is performed, two to four hepatic ducts require reconstruction (Fig. 21.17).
13. In approximately 80 % of patients, the right posterior lobe bile duct branch travels behind the superior side of the right branch of the portal vein to the inferior side of the right branch of the portal vein (the Hjortsjo crook). Therefore, attention must be devoted to the transection of the right branch of the bile duct; otherwise, difficulties with anastomosis and bile leakage may result.
14. Bile duct reconstruction is performed as described above.

21.10 Extended Right Hemihepatectomy Combined with Portal Vein Resection

1. The first steps are the same as steps one to four for an extended right hemihepatectomy.
2. A 1.5–2-cm segment of the left branch of the portal vein is freed, and vascular ribbons are placed in preparation for clamping and anastomosis (Fig. 21.18).
3. The next steps are the same as steps seven to eight for an extended right hemihepatectomy.
4. The main trunk of the portal vein is completely exposed. Vascular ribbons are placed in preparation for clamping and anastomosis (Fig. 21.19).
5. At this point, it should be confirmed that the tumor has not invaded the common hepatic artery, the left hepatic artery, the left branch of portal vein, or the proximal end of the portal vein. The combined portal vein resection can then proceed.
6. The main trunk and left branch of the portal vein are clamped using vessel forceps. The bifurcation is excised. End-to-end anastomosis is performed using 6/0 or 7/0 Prolene sutures. The paths associated with the two broken ends should be monitored to avoid creating angular stress or reversals (Fig. 21.20).

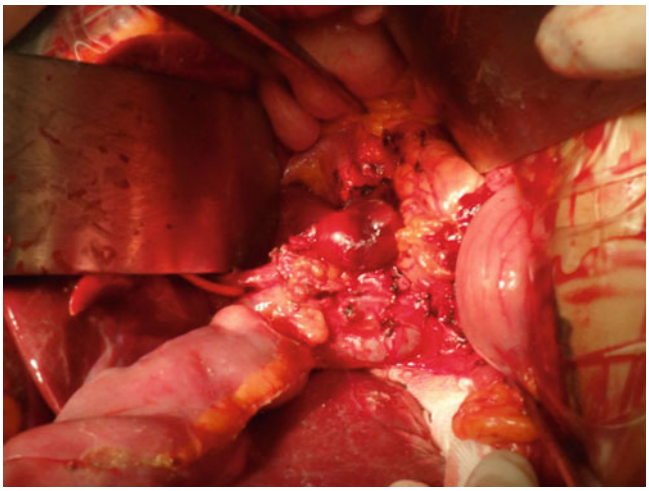

Fig. 21.19 Main trunk of the portal vein is completely exposed

When performing anastomosis, the two sides of the broken ends are sutured first. The posterior wall is sutured from the inside, whereas the anterior wall is sutured from the outside. Both walls are continuously sutured. Growth factors are administered to prevent stenosis. After opening, blood in the portal vein should travel in a straight line. If necessary, the external iliac vein or cryopreserved iliac vessels can be used for bypass.

7. Parenchymal resection:

Because the right hepatic artery and the right branch of portal vein have been transected, an ischemic line on the liver surface can be produced. Parenchymal resection occurs along this ischemic line. The liver can be transected using the hook ligature method or a water knife. The middle hepatic vein and the right hepatic vein are transected

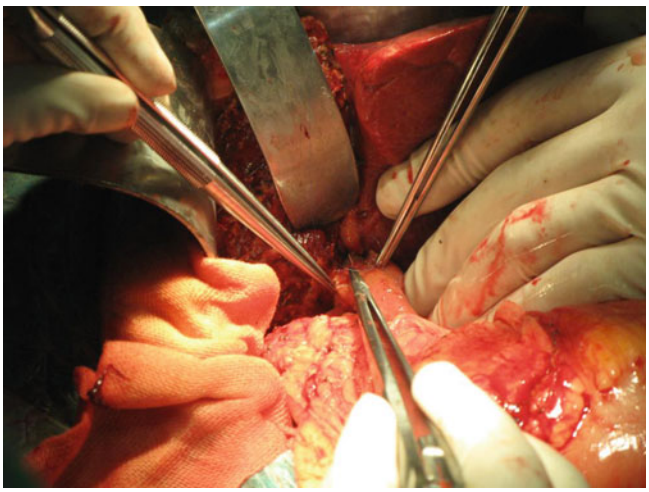

Fig. 21.20 End-to-end anastomosis is performed

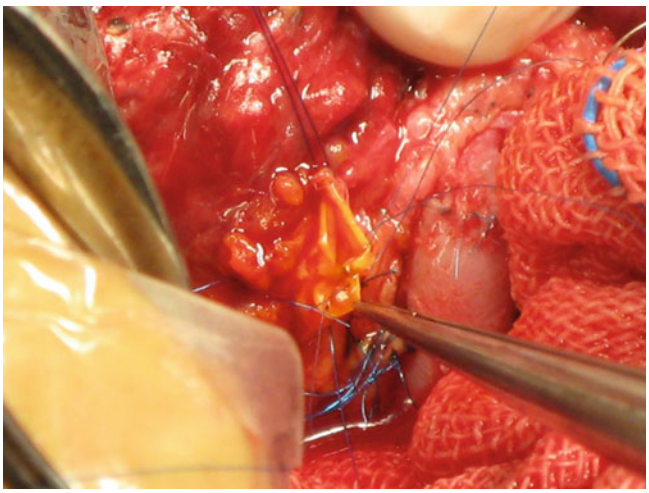

Fig. 21.21 The IVa segment may have one to two bile duct branches

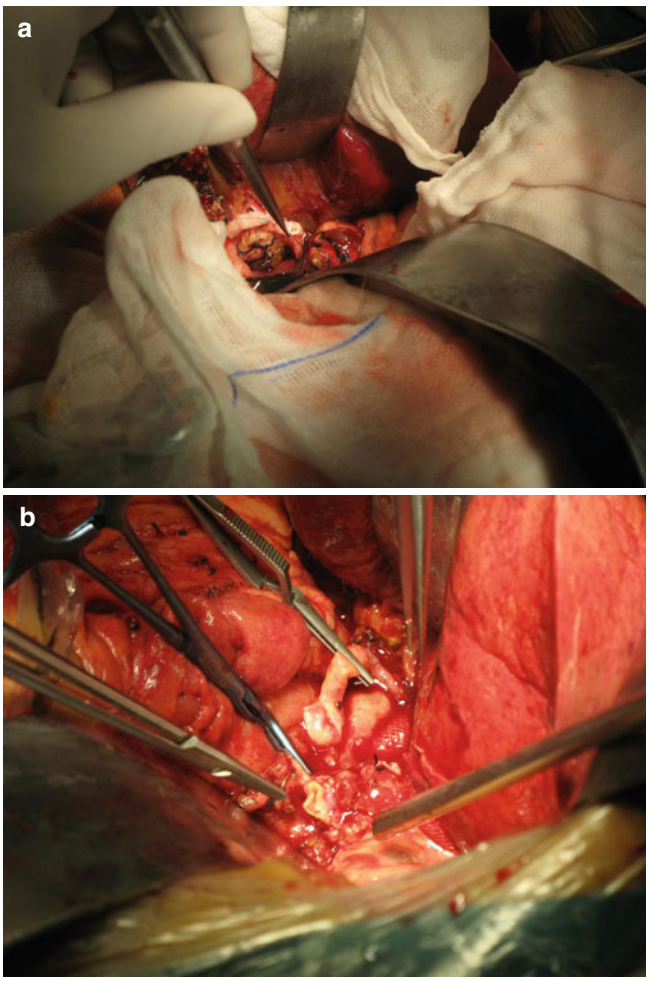

Fig. 21.22 (**a**, **b**) Right hepatic artery resection and reconstruction

during the transection of the parenchyma. Due to preoperative jaundice and impairment of liver function, we tend to retain a portion of segment IV of liver tissue that is as large as possible to reduce the risk of postoperative liver failure.

8. After extended hepatectomy, the IVa segment may have one to two bile duct branches, and the left lateral lobe has one to two bile duct branches; therefore, there may be a total of three to four bile duct branches that require anastomosis (Fig. 21.21).

21.11 Combined Hepatic Artery Reconstruction Surgery

1. This surgery is mainly suitable for Bismuth types IIIb and IV hilar cholangiocarcinomas with left-side invasion. A feasible procedure in these cases is extended left hemihepatectomy combined with right hepatic artery resection and reconstruction, and if necessary, these procedures combined with portal vein resection and reconstruction.
2. The whole left hepatic artery is freed as far as possible toward the left liver to obtain sufficient length for reconstruction with the end of the right posterior hepatic artery in Rouviere's sulcus. Our hospital typically uses a portion of the autologous great saphenous vein for bypass purposes (Fig. 21.22).
3. The left branch of the portal vein is transected, and the liver parenchyma is resected (an extended left hemihepatectomy).
4. Hepatic artery reconstruction can be performed before or after the resection of the liver parenchyma. Anastomosis is performed under a microscope, and end-to-end anastomosis is performed under a 2.5× surgical loupe.

21.12 In Situ Hepatectomy and Autologous Liver Transplantation

No indications

21.13 Liver Transplantation

The early results of liver transplantation were disappointing; in particular, early postoperative tumor recurrence occurred, and 5-year survival rates were as low as 28–30 % [45, 46].

The "Mayo regimen" proposed in recent years recommends that after patients receive a new radiochemotherapy regimen, laparotomy should be performed for tumor staging. Liver transplantation can then be performed after excluding LN and extrahepatic metastasis [47, 48]. However, liver transplantation is not an appropriate treatment for resectable hilar cholangiocarcinomas.

The 1-, 3-, and 5-year survival rates after liver transplantation have reached 92 %, 82 %, and 82 %, respectively.

21.14 Complications and Treatment

The postoperative complication rate is 20–50 %, and the hospital mortality rate is 5–10 %. Common complications include the following:

(1) Hepatic failure, which is associated with an overly small remnant liver volume, postoperative infections, vascular complications, and hemorrhage; (2) vascular complications (such as hepatic artery embolization and portal vein torsion, among other complications); (3) biliary complications, with biliary fistulas occurring in approximately 25 % of patients; and (4) infections, which cause cholangitis in 10 % of patients and abdominal or intrahepatic abscesses in 10 % of patients.

21.15 The Results of Long-Term Follow-Up

The 5-year survival rate for palliative resection (R1) was 0 [49, 50].

After R0 resection (i.e., extended hepatectomy), 5-year survival rates of 20–40 % were observed, and the median survival time was 20–25 months [14, 41].

Univariate analysis has indicated that long-term survival is correlated with tumor stage, left hemihepatectomy, a lack of postoperative chemotherapy, gross tumor type (papillary or diffuse infiltrative), vascular invasion, positive LN (specifically, positive LN in the celiac trunk), poorly differentiated tumors (G3), unresectable or incompletely resected (R1, R2) tumors, and distant metastasis.

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Hepatectomy for Gallbladder Carcinoma

22

Mingqing Xu and Haipeng Meng

22.1 Incidence of Gallbladder Carcinoma

According to pathological research, gallbladder carcinoma (GBC) is the most common malignant tumor of the bile duct system, with its incidence accounting for 80–95 % [1], ranking sixth, of all gastrointestinal malignant tumors. Every year, 2.2 out of every 100,000 people are diagnosed with GBC [2]. This carcinoma has a high malignancy and poor prognosis, with an average expected lifespan of 6 months after diagnosis; the 5-year survival is 5%, and the median survival time is 8–10 months [3–5]. The anatomical features of the gallbladder are partially responsible for the high mortality of GBC. There is no serosa between the gallbladder and liver, and the connective tissue of these two organs makes it easy for GBC to metastasize to the liver.

The risk factors associated with GBC include cholelithiasis and other causes of chronic inflammation, such as salmonella or helicobacter, Amerindian ethnicity, female gender, obesity, smoking, and low socioeconomic status [6].

22.2 Anatomical Features Associated with GBC Resection

22.2.1 Anomaly of the Extrahepatic Bile Duct

Anomaly of the extrahepatic bile duct: the most common form of bile duct is the bile duct of segment I that enters the right bile duct, common hepatic duct, cystic duct, or common bile duct. If this bile duct is dissected, more than 500 mL of bile will flow out daily. Thus, Longmire and Tompkins suggest that the dissected bile duct be sutured.

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22.2.2 Artery of the Gallbladder

An anomaly of the cystic artery is frequently encountered. It is critical to know the origin and path of the cystic artery, as well as the path of the right hepatic artery, to avoid arterial damage.

The classic distribution of the cystic artery is as follows: One cystic artery originates from the right hepatic artery behind the common hepatic duct and traverses Calot's Triangle. It then divides into the deep branch division in the gallbladder bed and the shallow branches to the free gallbladder surface. Approximately 2/3 of the population have the typical distribution. Another one third of the population, regardless of the depth of the two cystic arteries, have a single artery leading into the gallbladder wall and subsequently divided into small irregular branches.

Cystic artery variation: The cystic artery may originate in the left hepatic artery, hepatic artery, gastroduodenal artery, superior mesenteric artery, or celiac artery. Some individuals may have a double cystic artery or a cystic artery in front of part of the common bile duct.

22.2.3 Gallbladder Lymphatic Drainage

The gallbladder wall has extensive lymphatic drainage. The lymphatic plexus in the gallbladder is formed on both sides of the rear wall, extending mainly to the left side of the neck of the gallbladder and into the common bile duct lymph nodes. The plexus then divides into two: ① lymph nodes behind pancreatic head and duodenum → mesenteric artery lymph nodes → lymph nodes between abdominal aorta and inferior vena cava and ② lymph nodes behind portal vein → the celiac artery lymph nodes → lymph nodes between abdominal aorta and inferior vena cava.

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22.3 Primary Gallbladder Cancer Staging

The most widely used primary gallbladder cancer staging tools include the Nevin staging and UICC TNM staging systems. In 1976, Nevin first proposed the clinical staging of primary gallbladder cancer (referred to as Nevin staging), basing on the infiltration and diffusion range of gallbladder cancer. Nevin staging is divided into five stages:

Stage I: carcinoma in situ within the mucosa
Stage II: invasion of gallbladder mucosa and the muscle
Stage III: invasion of the full-thickness of the gallbladder wall, i.e., mucosa, muscle, and serosa
Stage IV: invasion of the full-thickness of the gallbladder wall with lymph node metastasis
Stage V: a direct invasion of liver tissue or liver metastases or metastasis to any organ

TNM staging is jointly published by the American Joint Committee on Cancer and the International Union Against Cancer and is mainly based on the depth of tumor invasion of the gallbladder wall (T), lymph node metastasis distance (N), and distant metastasis (M). The specifications of the staging of the primary gallbladder cancer (the 7th edition which was started in 2010 [7]) are shown in Table 22.1. T represents the primary tumor: Tx represents primary tumor unable to assess; T0 represents no evidence of primary tumor; Tis represents carcinoma in situ; T1 represents invasion in the lamina propria or muscle; T1a represents lamina propria invasion; Tlb represents tumor invasion of the muscle; T2 represents invasion of the connective tissue around the muscle but no invasion of the serosa or liver; T3 represents tumor invasion through the plasma membrane and/or a direct violation of the liver and/or an adjacent organ or tissue; and T4 represents direct tumor violation of the portal vein or hepatic artery or two or more violations of the liver and other organs or tissues. Lymph node metastasis: Nx represents regional lymph node metastasis unable to assessed; N0 represents no regional lymph node metastasis; N1 represents tumor metastasis to lymph nodes near the cystic duct, common bile duct, hepatic artery, and/or portal vein; and N2 suggests tumor metastasis to lymph nodes near the abdominal aorta, inferior vena cava, superior mesenteric artery, and/or celiac artery (lymph node metastasis by the 7th edition classification standards). Distant metastasis: Mx suggests distant metastasis unable to be assessed; M0 represents no distant metastasis; and M1 suggests distant metastasis.

Table 22.1 AJCC TNM staging gallbladder (5th, 6th, and 7th Editions)

	5th (1997)	6th (2002)	7th (2010)
0	TisN0M0	TisN0M0	TisN0M0
Ia	T1N0M0	T1N0M0	T1N0M0
Ib		T2N0M0	
IIa	T2N0M0	T3N0M0	T2N0M0
IIb		T1-3N1M0	
IIIa	T3N0M0,T1-3N1M0	T4NxM0	T3N0M0
IIIb			T1-3N1M0
IVa	T4N0M0,T4N1M0	TxNxM1	T4N01M0
IVb	TxN2M0,TxNxM1		TxN2M0,TxNxM1

22.4 Hepatectomy for Gallbladder Carcinoma

22.4.1 Surgical Treatment Principles

Gallbladder cancer therapy is divided into curative and palliative treatment. Curative therapy is used to treat early cancer, whereas palliative treatment is for patients with advanced cancer. Because the gallbladder is not sensitive to radiotherapy or chemotherapy, surgical resection is the only effective curative method. Gallbladder cancer is an incurable malignancy. R0 resection margin represents a curative resection. Survival of patient with R1 or R2 resection is similar to that without surgical resection. The T stage of gallbladder cancer has a direct impact on its N and M stages. The cure rate is higher when T stage is in the earlier period [8, 9].

The surgical approach for gallbladder cancer depends on the patient's clinical and pathological staging [10]. We used the American Joint Committee on Cancer Staging Manual, 7th edition, as a guide for the staging of gallbladder cancer [7]. For early gallbladder cancer (Tis and T1a tumors), the prognosis after cholecystectomy is very good and no further treatment is needed for these patients [11]. In recent years, considerable evidence has been published in support of the use of radical cholecystectomy to treat T1b gallbladder cancer [12], but some studies have suggested that extended resection for T1b gallbladder cancer is still debatable [13]. T2 gallbladder cancer should be treated with radical resection methods. Radical cholecystectomy includes resection of gallbladder and adjacent liver tissue + skeletonized hepatoduodenal ligament.

Resection of the gallbladder surrounding liver tissue includes the followings:

1. Wedge cholecystectomy and resection of nearly 2 cm or more liver tissue [14, 15].
2. Conventional 4b/5 segmentectomy: gallbladder vein inflowing into the liver 4b/5 segment, thus, a 2 cm wedge liver resection is not sufficient [16–18].
3. Gallbladder infringement or violation of the right hepatic pedicle deeper into the liver should be treated with an extended right hepatectomy including a 4b section or the entire 4 segment 4 [19, 20].
4. Caudate lobectomy: in Japan, physicians undertake conventional caudate lobe resection [21], but physicians do not routinely remove this section in Western countries [20].

If the left liver volume is <20 % of the total liver volume, a right portal vein thrombosis could be developed prior to right hepatectomy [22]. A case of T3 tumor should undergo

liver resection + near violated organ removal (including the colon, duodenum, stomach, and pancreaticoduodenectomy) [20, 21]. Pancreaticoduodenectomy has a high complication rate and high mortality, with low 2-year survival rates, and as a result, it is not universally accepted [20, 21]. The survival rate of patients with combined portal vein or hepatic artery resection is very poor, so it is not generally carried out even in Japan [22–26]. For T4 tumors, although there are few opportunities for surgical resection, and the survival rate is very poor, a radical resection should be performed as far as possible [27]. A prior laparoscopy is beneficial to know whether a radical cholecystectomy could be carried out. Lymph node dissection remains controversial; the current consensus view is to produce a clean liver ligament, that door vein, and the hepatic artery and its branches [14, 20, 27–30]. Bile duct resection should be performed in the following cases: ① when the cystic duct is invaded by the tumor and ② when extended right hepatectomy is carried out to achieve R0 resection for gallbladder carcinoma with common bile duct invasion [31–33].

22.4.2 Preparations for Hepatectomy of Gallbladder Carcinoma

1. Liver function assessment: Because a considerable number of gallbladder patients have jaundice or need major liver resection, preoperative assessment of liver function is critical.
2. Protection of liver function: When the serum total bilirubin is more than 256.5 μmol/L, PTCD should be used to relieve jaundice; intravenous administration of vitamin K1 and fresh plasma is needed to correct the clotting mechanism; exogenous glutathione can maintain liver cell membrane stability; and the addition of many vitamin C, branched-chain amino acids for the preoperative liver can have a protective effect.
3. Determine whether the tumor is resectable: In addition to considering the general condition and whether the patient's liver function can tolerate surgery, local conditions determine whether the tumor is removable. First, whether there are violations of the liver and the extent of the violations should be clear. If there is only direct tumor invasion of liver without liver metastasis, it is possible that liver wedge resection or 4/5 segmentectomy can be used. Semihepatectomy can be performed if the tumor is confined to the infringement of half of the liver. Surgical resection is not an option if multiple liver metastases exist. Second, determining whether the hilum has been violated is important: whether surgery is not possible if there are hilar lymph node invasion, tumor integration into the metastatic lymph node, class I hepatic buct invasion, and the hilar can not be dissected. Third, it is necessary to evaluate the presence of abdominal lymph nodes and abdominal metastases. It is more difficult to diagnose these issues using the current commonly used imaging method. A diagnostic laparoscopic testing before laparotomy is necessary.

22.4.3 Radical Resection of Early Gallbladder Cancer: Liver Wedge Resection

Surgical procedures include en bloc resection of gallbladder, surrounding liver tissue within the range of 2–4 cm, liver ligament lymph tissue with nerves and adipose tissue, as follows:

1. Open: inverted "L" incision under the right costal margin.
2. Exploration of the peritoneum and abdominal visceral and regional lymph node metastases.
3. Pulling forward on the right rib cage with retractor. Pressuring stomach and small intestine to the lower left side of the abdomen with wet gauze, and then to expose the liver hilar and lower areas (Fig. 22.1).
4. Cutting the peritoneum outside of the duodenum to free descending part of the duodenum and pancreatic head to remove the surrounding lymph nodes.
5. Skeletonization of the hepatoduodenal ligament: skeletonization of the portal vein, proper hepatic artery, hepatic artery, right and left hepatic arteries, and splenic artery should be performed. All the lymph nodes, nerve, fiber and fat tissues in the hepatoduodenal ligament and in the gallbladder triangle should be removed completely with the branch vessels ligated. All lymph nodes of the group 5, 7, 8, 9, and 12 were completely excised (Fig. 22.2).

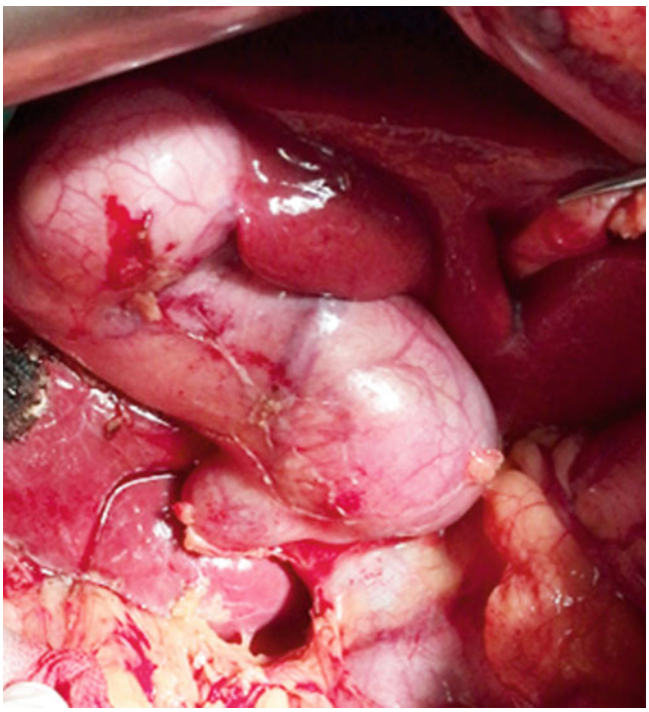

Fig. 22.1 Exposing the hepatic hilum and gallbladder

6. Cystic artery be ligated and cut. Cystic duct excision is performed . Cystic duct margins are routinely submitted to pathological department for evaluating margin free. If there is tumor embolus within the cystic duct, the tumor embolus should be taken out , and even the main bile duct should be opened and probed (Fig. 22.3).
7. Wedge resection of the liver tissue within 2cm of the gallbladder bed is performed. The gallbladder and the wedge resected hepatic tissue within 2 cm of the gallbladder bed as well as all the lymph and fat tissues in the hepatoduodenal ligament be removed by en bloc resection (Fig. 22.4).
9. Electric coagulation and suturing are performed on the remnant surface wound of the liver.
10. Drainage tube is placed under the right liver (Fig. 22.5).

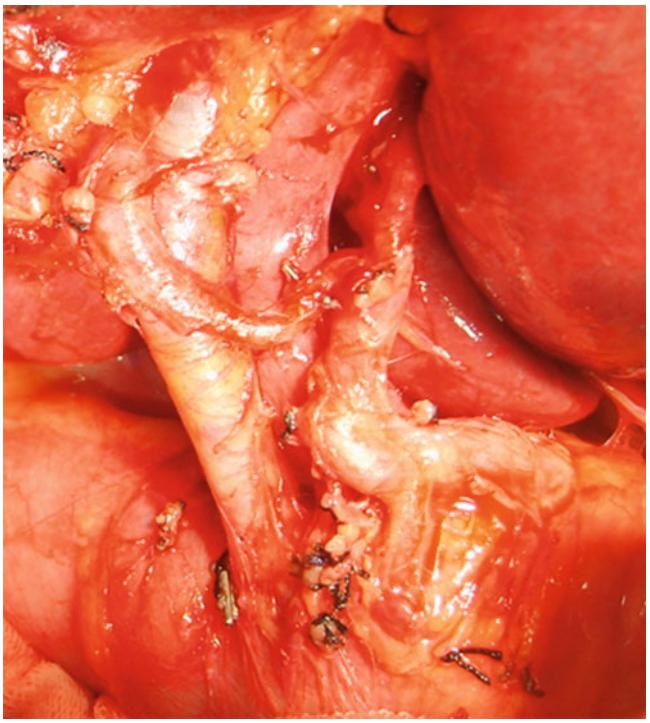

Fig. 22.2 Skeletonization of the hepatoduodenal ligament

22.4.4 Radical Cholecystectomy + Bile Duct Resection for Unsuspected Gallbladder Cancer

Only T1b and T2 gallbladder cancer can be accidentally discovered intraoperatively or postoperatively. It is not easy to have a intraoperative diagnosis of T1b tumor. In this instance, the surgery should be stopped because a second surgery may be the best option. It is very difficult to manage the T2b gallbladder cancer. Because of the possible of tumor cell spreading via cyst duct during laparoscopic cholecystectomy, some surgeons convert surgery to laparotomy for radical resection [34, 35].

In cases of cystic duct invasion by the tumor, radical cholecystectomy as well as bile duct resection + Roux-en-Y hepaticojejunostomy should be performed, with the goal of reaching the R0 resection margin (Figs. 22.6, 22.7, and 22.8).

22.4.5 Segmentectomy

Liver segmentectomy refers to resection of segment IVb and V segment (Fig. 22.9). When the gallbladder cancer invading into the liver parenchyma at a depth >2 cm a segmentectomy

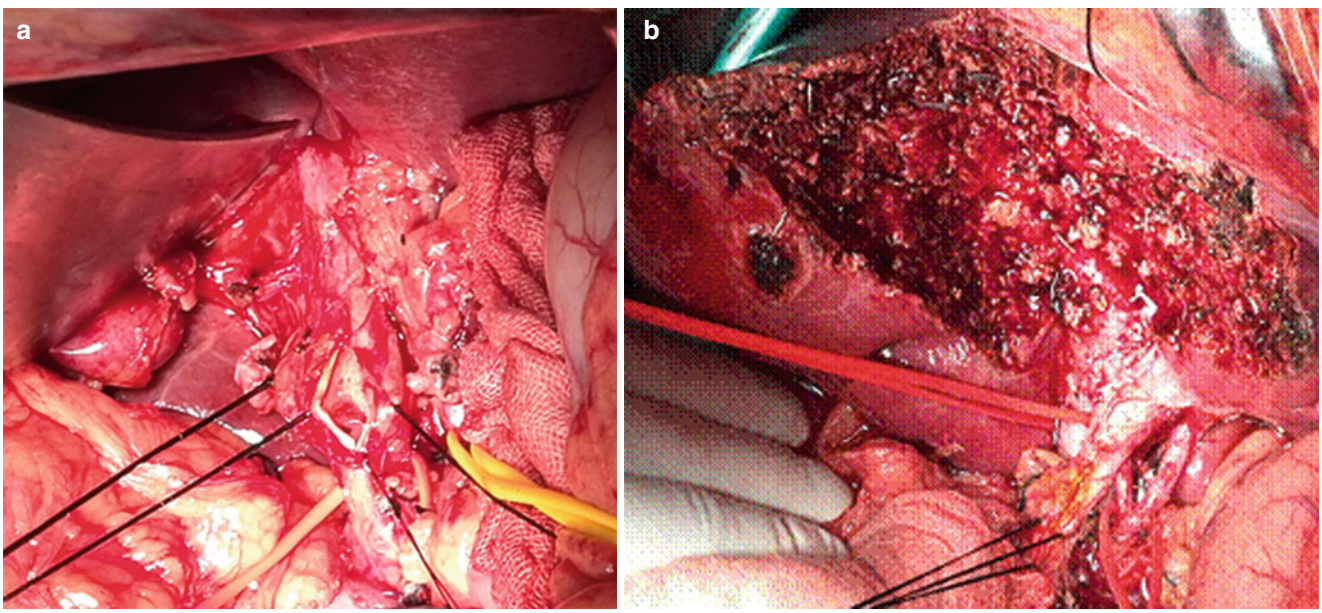

Fig. 22.3 Common bile duct exploration to retract the tumor embolus (**a**). Radical cholecystectomy + common bile duct exploration + skeletonization of the hepatoduodenal ligament as well as the removal of the regional lymph nodes (**b**)

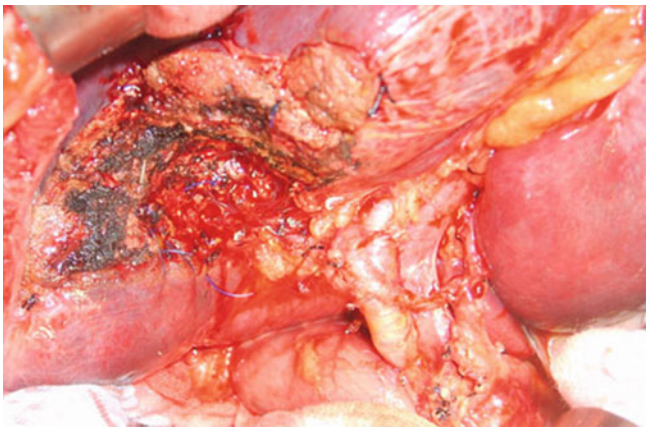

Fig. 22.4 Wedge resection of the liver tissue + skeletonization of the hepatoduodenal ligament

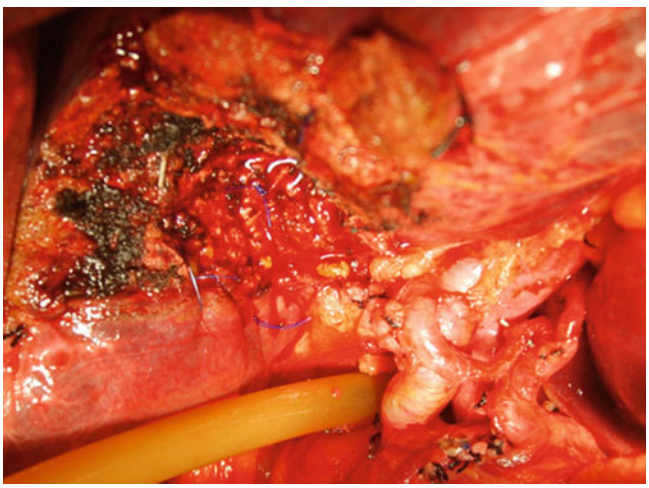

Fig. 22.5 Placement of the drainage tube

should be performed. Surgery key points include regular IVb and V segmentectomy (including gallbladder), skeletonization of the hepatoduodenal ligament, as well as the removal of the regional lymph nodes.

22.4.6 Regular Right Hepatic Lobectomy

A regular right hepatectomy is a suitable option for the followed cases: ① gallbladder cancer infiltration in the liver parenchyma at a invasion depth of more than 2 cm; ② tumor invasion of the right portal vein; ③ multiple metastatic tumors in the right liver. Because the gallbladder neck is anatomically close to the right hepatic duct and the right branch of the portal vein , a regular right hepatectomy should be performed when the tumor is located in the gallbladder neck. Surgery highlights include a regular right hepatectomy (including gallbladder), skeletonization of the hepatoduodenal ligament, as well as the removal of the regional lymph nodes.

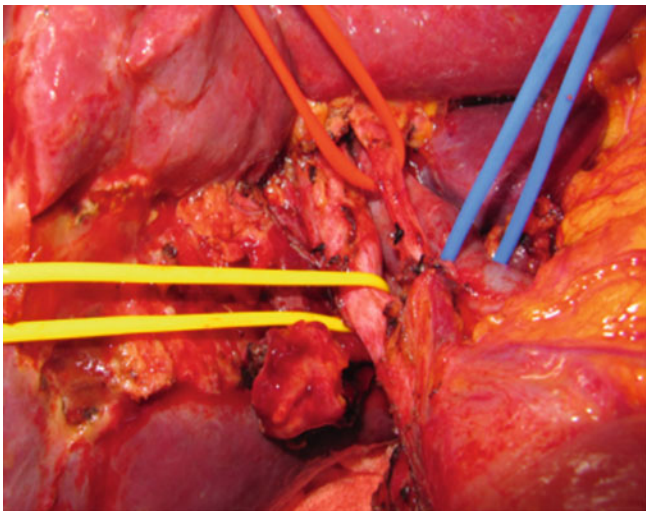

Fig. 22.6 Hepatic bile duct invasion by an unexpected gallbladder cancer (IIIb, T1bN1M0)

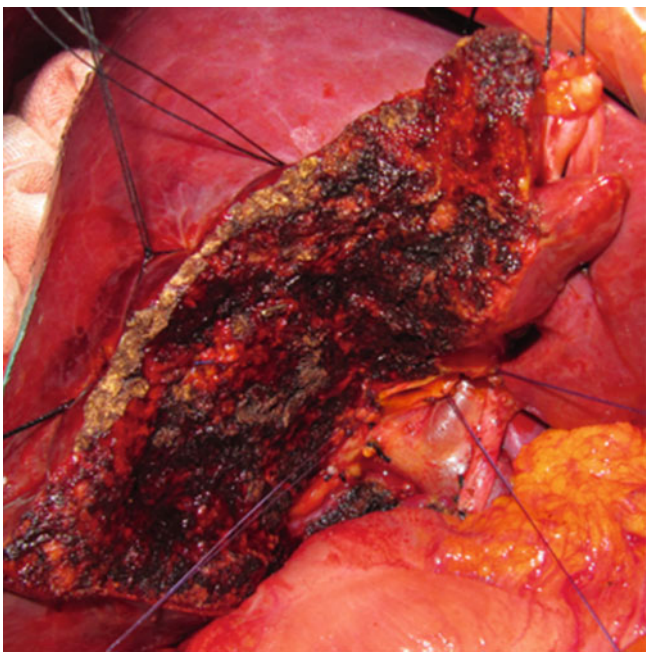

Fig. 22.7 Hepatic bile duct invasion by an unexpected gallbladder cancer (IIIb stage, T1bN1M0). Radical cholecystectomy + extrahepatic bile duct excision + skeletonization of the hepatoduodenal ligament as well as the removal of the regional lymph nodes

Skeletonization of the hepatoduodenal ligament as well as the removal of the regional lymph nodes should be performed at first. And then incision of the cystic artery, cystic duct, right hepatic artery and right portal vein branch are carried out. If the common bile duct has been invaded by tumor, the extrahepatic bile duct must be excised with R0 resection margins, followed by Roux-en-Y hepaticojejunostomy (Figs. 22.10 and 22.11).

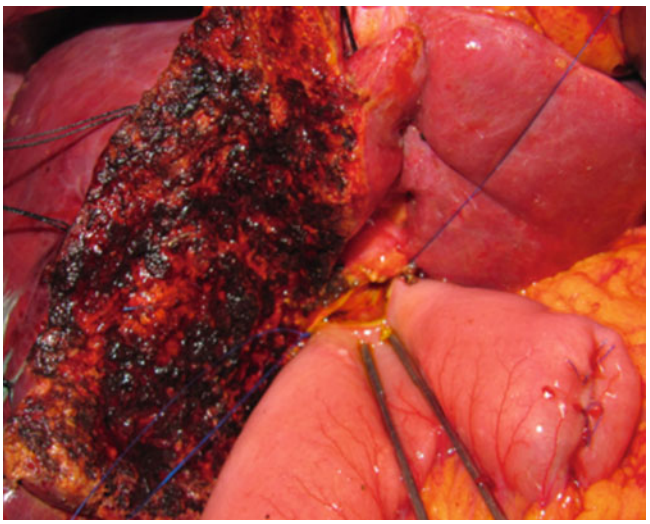

Fig. 22.8 Hepatic bile duct invasion by an unexpected gallbladder cancer (IIIb stage, T1bN1M0). Radical cholecystectomy + Roux-en-Y hepaticojejunostomy (anastomosis of the hilar bile duct and jejunum)

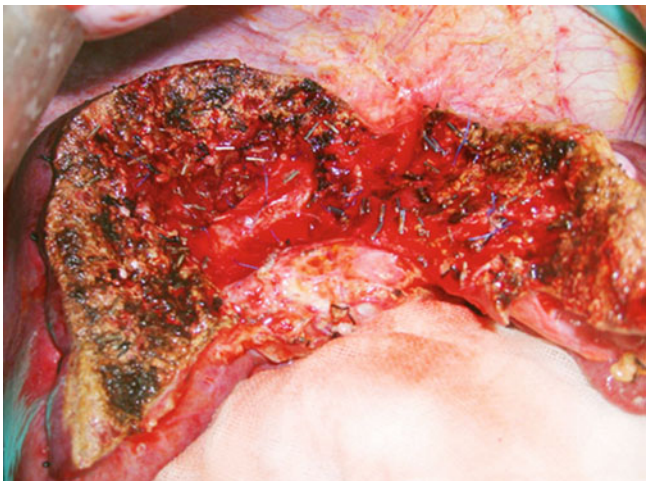

Fig. 22.9 Regular IVb and V segmentectomy (including gallbladder)

22.4.7 Extended Hemihepatectomy

This is suitable for GBC that invades the liver parenchyma beyond S4 or S5; When the presence of metastatic tumor beyond the right lobe but without tumor lesion in the left lateral lobe, an extended right hemihepatectomy can be used. When the metastatic tumor spreading beyond the left lobe but without cancer lesion present in the right inferior lobe, an extended left hemihepatectomy can be used.

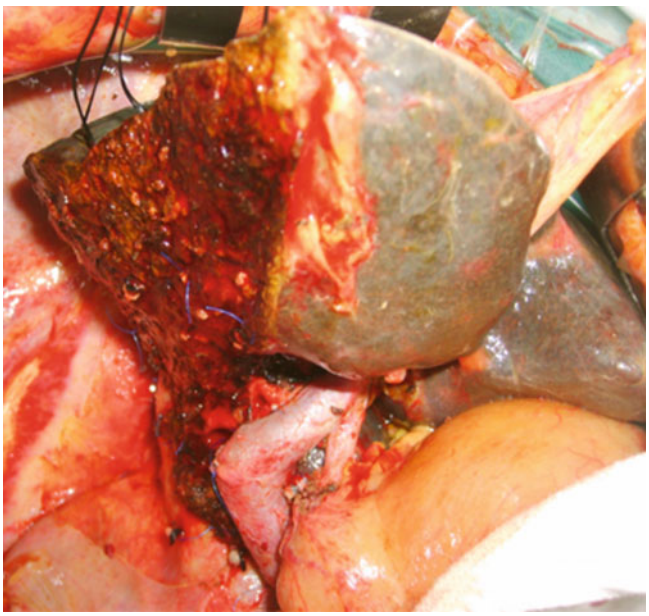

Fig. 22.10 Hepatic duct invasion by gallbladder cancer with obstructive jaundice. Right hepatectomy + extrahepatic bile duct excision + skeletonization of the hepatoduodenal ligament as well as the removal of the regional lymph nodes

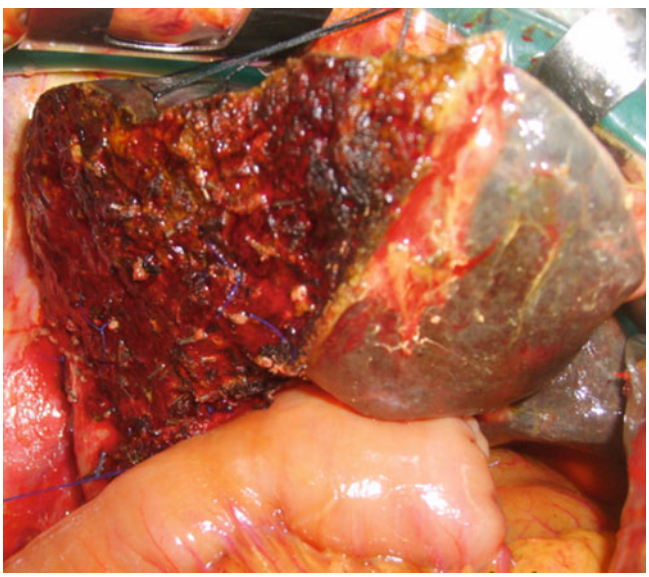

Fig. 22.11 Hepatic duct invasion by gallbladder cancer with obstructive jaundice. Right hepatectomy + extrahepatic bile duct excision + skeletonization of the hepatoduodenal ligament as well as the removal of the regional lymph nodes + Roux-en-Y hepaticojejunostomy (anastomosis of the left hepatic duct and jejunum)

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Liver Resection in Pediatric Patients

23

Mingman Zhang

Liver resection is the most frequently used method to treat hepatocarcinoma in pediatric patients. Approximately 70 % of hepatocarcinomas in children are malignant. In Europe and North America, primary hepatic malignancy is one of the ten most common malignancies in children, although it only accounts for approximately 1.1 % among other primary hepatic malignancies. Hepatoblastoma, the most common primary hepatic malignancy in pediatric patients, accounts for approximately 80 % of primary hepatic malignancies and 43–64 % of hepatocarcinomas in children. Hepatoblastoma is commonly seen in children under 3 years of age, and is rarely observed in those beyond 5 years of age. It is predominantly present in males (male/female ratio 2.5:1); it can also be seen in adults. Hepatocellular carcinoma (HCC) is another common malignancy in children, accounting for approximately 23 % of pediatric hepatocarcinomas. The prevalence distribution of pediatric HCC is bimodal, with the first peak at ages <5 years and a second peak between 13 and 15 years. Surgical removal is important in treating pediatric hepatoblastoma and HCC.

Other hepatic malignancies, such as embryonal sarcoma, leiomyosarcoma, rhabdomyosarcoma, and hemangiosarcoma, should also be considered for operation. Common benign hepatic tumors, such as hemangioma, hemangioendothelioma, and hamartoma, might occasionally require hepatic resection in children. Surgical resection can be considered for hepatic metastases, which commonly originate from a renal embryonal tumor or neuroblastoma, if the primary tumor is under control, the number of metastases is single or limited, and the prospective patient outcome is satisfactory.

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23.1 Anatomy

The liver, which is the largest parenchymatous organ in our body, is located in the right upper abdomen immediately under the diaphragm. Most parts of the liver lie in the right hypochondrium, while the others cross the midline and reach the middle upper abdomen and the left hypochondrium. The liver consists of hepatic parenchyma and has a conduit architecture. Internationally, there are two types of nomenclature for defining the lobes and segments of the liver. The liver is usually divided into 5 lobes and 4 segments according to the branches of the portal vein and the biliary tree in our country, which is similar to the divisions proposed by Hjortsjo and Healey. The liver is divided into 8 regions, each of which is assigned a number, according to Couinaud. This method is also popular in mainland China. Confusion can occur due to disparities in nomenclature; as a result, the International Hepato-Pancreato-Biliary Association (IHPBA) proposed a unanimous terminology of liver anatomy and resections in 2000 (The Brisbane 2000 Terminology of Liver Anatomy and Resections). In this classification scheme, the liver is divided into 9 segments, which are assigned Arabic numerals.

There are two methods for liver resection in pediatric patients. One is anatomic lobectomy, or segmentectomy, which is performed according to anatomical divisions. The other is non-anatomic hepatectomy, which is performed by partial removal of an affected region. The goals of reducing intraoperative bleeding and enhancing safety are pursued in both techniques.

23.2 Staging System

The reserve and regenerating ability of a normally functioning liver are so powerful that a 70 % liver resection can be tolerated in most people. However, in our country, hepatocarcinoma is typically found at a mid or late stage when pediatric patients visit the doctor. At this time, the tumor is so large that assessing liver reserve function before surgery is

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Table 23.1 Child scoring system

	Grade A	Grade B	Grade C
Serum bilirubin (μmol/L)	<34.2	34.2–51.3	>51
Serum albumin (g/L)	>35	30–35	<30
Ascites	(−)	Controllable	Refractory
Hepatic encephalopathy	(−)	Mild	Coma
Nutrition status	Good	Moderate	Poor

Grade A 5–6 points, *Grade B* 7–9 points, *Grade C* ≥10 points

of great importance. In some cases, hepatic resection performed with poor preoperative assessment can result in inadequate remnant liver and subsequently high morbidity and mortality. In other cases, resectable, giant hepatic neoplasms are not removed due to the absence of a quality assessment strategy.

Scholars around the world have been working since the 1960s to develop sensitive indices that can accurately indicate liver reserve function. Having informative indices in place could help evaluate liver reserve before the operation, estimate the maximal volume of the resected liver during the operation, and predict patient outcome.

In 1964, Child and Turcotte first proposed the Child-Turcotte scoring system, which includes ascites, hepatic encephalopathy, and serum bilirubin and serum albumin levels. In 1972, coagulation function (PT or INR) was added by Pugh. Similar scoring systems, such as the Child-Campbell scoring and ANS scoring systems, were subsequently introduced. The Child-Pugh scoring system (Table 23.1) has set standard for methods for liver function evaluation in clinical practice in a considerably long time. When it is used to assess patients before hepatic resection, it is generally thought that grade C is a contraindication, grade A allows resection, and grade B is examined on an individual basis. Although the Child scoring system is useful in assessing the function of the whole liver, it is a poor indicator of a safe volume of resected liver. Furthermore, the five indices included in the Child system can be adjusted by therapeutic intervention.

23.3 Indications

1. Hepatic malignancy: Hepatoblastoma is the most common hepatic malignancy in children, and primary HCC also occurs in older children. Rhabdomyosarcoma, embryonic sarcoma, and leiomyosarcoma can also be diagnosed in pediatric patients. Most commonly originating from the retroperitoneal neuroblastoma or renal blastoma, hepatic metastases are resectable when they are confined within a single lobe with the resectable primary tumor.
2. Hepatic benign tumor: Hemangioma and hemangioendothelioma are common, while teratomas are rare.
3. Traumatic liver rupture: The liver is severely damaged, with over 50 % of the liver parenchyma, the intrahepatic major vessels, and the bile ducts being discontinuous with the uninjured portion. When uncontrolled bleeding after suturing, formation of intrahepatic hematoma, or complicated massive biliary hemorrhage occurs, hepatic lobectomy or hepatectomy should be considered.
4. Chronic infectious lesions: Chronic liver abscess with thick walls, long-lasting fistula leftover from a drained liver abscess, an external fistula of bile duct, or hepatic tuberculosis.
5. Hepatic cyst: Nonparasitic solitary hepatic cyst or follicular hepatic echinococcosis.

23.4 Contraindications

1. Severe damage to multiple organs coexists.
2. Widespread diseased lesions of the liver that are unresectable.
3. Patients with primary hepatic cancer who simultaneously have jaundice, ascites, swelling, bleeding tendency, portal hypertension, or evident liver function damage.

23.5 Preoperative Preparation

1. Whether the hepatic tumor is resectable should be determined, and hepatic metastasis should be excluded before the operation. A CT scan, which is an accurate noninvasive diagnostic method, is helpful in locating the tumor. CTA not only depicts the structure of liver vessels but also displays the features of tumor vessels. Ultrasonography is valuable in assessing the completeness of the inferior vena cava.
2. Hepatectomy itself has a very large impact on metabolism, so careful assessment of homeostasis and electrolyte balance is necessary before the operation. The function of the heart, lungs, and kidneys also requires evaluation, except in emergent hepatectomy. Liver function evaluation is paramount in understanding liver compensation and estimating the volume of resectable liver.
3. A high calorie and protein diet that is rich in fiber is recommended before the operation. An injection of vitamin K is also given. A transfusion of plasma or albumin or whole blood is given to patients with hypoalbuminemia.
4. Oral antibiotics covering Gram-negative bacteria (first-generation cephalosporin) and those covering anaerobic bacteria (metronidazole) are given two days before the operation.
5. Adequate fresh whole blood should be prepared before the operation.

23.6 Principles During Operation

A subcostal incision is sufficient to provide good visibility because children usually have a wide costal angle, a shallow abdominal cavity, and an elastic chest wall. Position: A supine position is used during left hemiliver resection. When right hemiliver resection or right triple segmentectomy is considered, the right side is elevated by 30° using a sandbag cushioned under the right shoulder and waist, with the right upper extremity resting on the headrest. Deep anesthesia is required to eliminate autonomous respiration and prevent air embolism when the liver is dissected, except in thoracotomy. A sufficient blood supply to the liver should be preserved during the operation. Hypothermic anesthesia is advocated in sophisticated hepatectomy to prolong the duration of blood supply blockage.

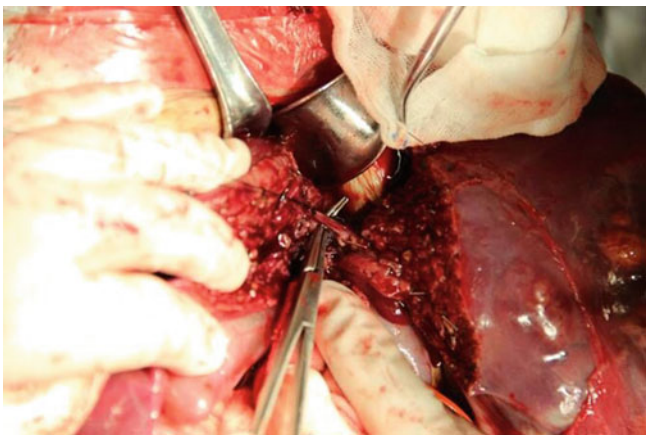

Fig. 23.1 Conduits inside the hepatic parenchyma are closed using suture or metal clips

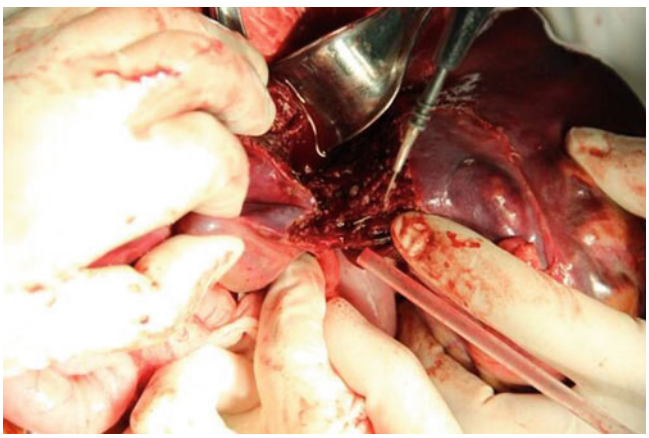

Fig. 23.2 The cutting surface is cauterized for hemostasis

23.7 Surgery Type

23.7.1 Left Hepatolobectomy

1. Incision: An incision across the right rectus abdominis or midline incision is frequently adopted. The incision is extended to the left of the xiphoid process, if necessary, which can be removed for better exposure. An oblique incision under the costal margin in the upper abdomen can be chosen due to the soft costal arch in children. If necessary, the incision can be extended to beneath the left costal margin, and the left rectus abdominis can be cut apart.
2. Mobilization of the left lateral lobe: The left hemiliver requires mobilization before dissecting the hepatic hilum. The ligamentum teres hepatis is ligated and removed. The liver is pulled caudally using a clamp on the end of ligamentum teres hepatis. The hepatic falciform ligament has better exposure after the liver is pressed toward the vertebrae. The hepatic falciform ligament is cut apart along the anterior abdominal wall to the left coronary ligament, which is then removed. The superficial branches of the left hepatic vein and diaphragmatic vessels should be preserved. Better visualization can be obtained by pushing the stomach to the left lower side with a saline-soaked gauze pad. The left triangular ligament is occluded using two long-curved clamps, cut off and ligated close to the diaphragm.

   During mobilization, over-traction of the left lateral lobe should be avoided, or the left hepatic vein might be lacerated. Finger pressure is used to stop bleeding once the left hepatic vein is lacerated where it is then clamped and sutured.
3. Ligature of the left hepatic vein: The left hepatic vein is exposed and ligated when the liver parenchyma is cut apart left to the cranial end of the falciform ligament. The left hepatic and middle hepatic vein often meet and form a common trunk, which then joins the inferior vena cava (IVC). The posterior upper margin of the left hepatic vein, which is usually lying in the left coronary ligament, may directly join the IVC or merge with the middle hepatic vein before joining the IVC at the superficial surface of the left lateral lobe. Attention should be given so the middle hepatic vein and IVC are conserved. The left hepatic vein on the left wall of the IVC can also be separated following separation of the IVC. Then, the liver parenchyma should be bluntly dissected and separated along the left hepatic vein; the left hepatic vein is ligated inside the liver.
4. Left lateral lobectomy: The liver capsule is cut open 1–2 cm left of the falciform ligament after the blood supply to the left lateral lobe is occluded. The hepatic parenchyma is bluntly divided using a scalpel handle or forceps; vessels and bile duct are ligated if encountered (Fig. 23.1).
5. Management of hepatic cutting surface: Every vessel and bile duct termination along the cutting surface requires ligature with number 0 suture (Figs. 23.2 and 23.3). The bleeding points on the liver capsule are electrocauterized

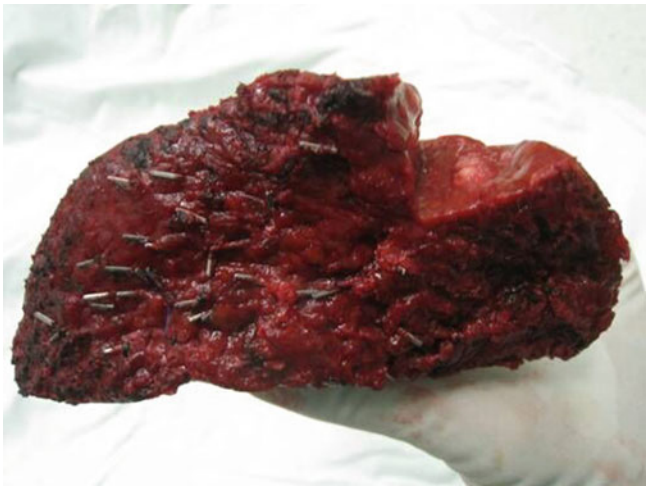

Fig. 23.3 Conduits closed with metal clips are found on the cutting surface

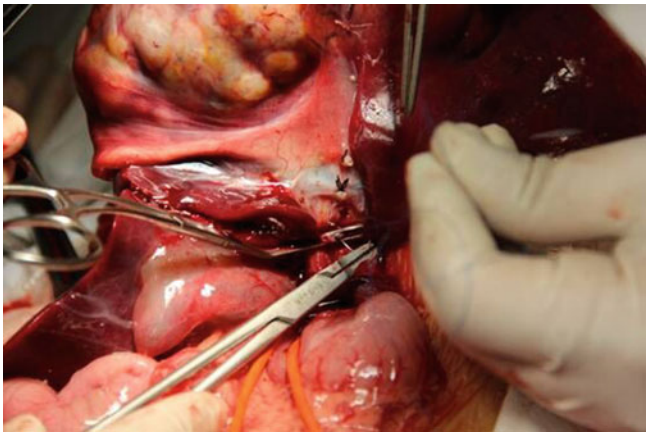

Fig. 23.4 The first hepatic hilum is dissected

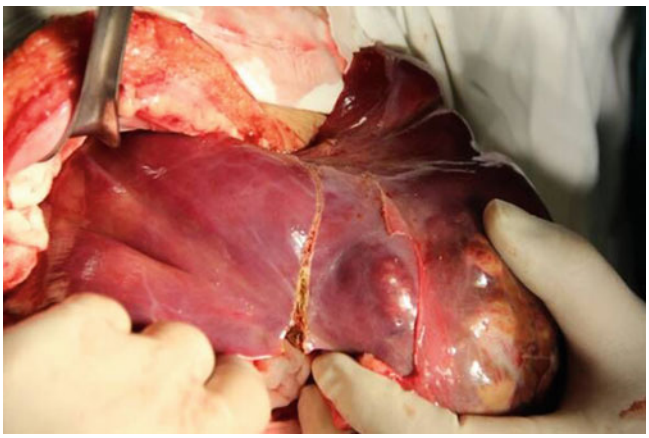

Fig. 23.5 The division line is superficially outlined with a cautery

or ligated. The surgical area is rinsed and covered using normal saline. The cutting surface is covered by the remnant falciform ligament, hepatogastric ligament or even the great omentum using interrupted suture. Drainage is placed under the left diaphragm.

23.7.2 Left-Side Semi-hepatectomy

Left-side semi-hepatectomy is defined by the central fissure and consists of removal of the left lateral lobe and the left internal lobe.

1. Incision: Similar to that of left lateral lobectomy. Satisfactory vision is generally achieved using a subcostal incision.
2. Hilar handling: The hepatic hilum should be generally handled first to reduce the chance of bleeding and tumor cell spread upon dividing the liver. The hepatic arteries can be exposed by cutting open the left peritoneum of the hepatoduodenal ligament. The left hepatic artery can be ligated and cut when it is confirmed not to influence the right hepatic artery. The left bile duct and transverse part of the left branch of the portal vein can be ligated and cut, respectively, after the hepatic transverse fissure is exposed by pulling the left internal lobe upward (Fig. 23.4).
3. Mobilization of the left lobe: Same as for left hepatolobectomy.
4. Ligature of the left hepatic vein: Same as for left hepatolobectomy.
5. Left side semi-hepatectomy: The liver capsule is cut open 1 cm left of the central fissure. The hepatic parenchyma is bluntly divided using a scalpel handle or forceps; vessels or bile ducts are ligated when encountered. Attention should be given to middle hepatic vein, which runs in the central fissure and occasionally converges with the left hepatic vein before joining the IVC. The branches of the middle hepatic vein, which drain the left internal lobe, should be ligated and cut on separation of the hepatic parenchyma. The middle hepatic vein needs to be preserved; soft handling is therefore required on blunt division. Ligature of the middle hepatic vein should be avoided when of the end of the left hepatic vein is ligated (Fig. 23.5).
6. Management of hepatic cutting surface: Same as for left hepatolobectomy.

23.7.3 Right Semi-hepatectomy

1. Incision: Abdominothoracic incision is usually adopted. An incision across the right upper rectus abdominis is used for exploration. When a right semi-hepatectomy is performed, the incision is extended from the right seventh

intercostal space to the middle axillary line on the right and to the xiphoid process upward.

2. Mobilization of the right lobe: The right lobe is pulled to the left after the falciform ligament is separated from the liver. The right lobe is mobilized by cutting the hepatocolic, hepatorenal, right triangular, and right coronary ligaments. The IVC can be seen by pushing the right adrenal gland downward.
3. Hilar dissection: The first hepatic hilum is exposed by lifting the liver. The cholecystic duct is ligated and cut 0.5 cm from the common bile duct after the hepatoduodenal ligament is cut open. A cholecystectomy is performed after the cholecystic artery is ligated. The hepatic artery and portal vein can be exposed after cutting open the Glisson capsule covering the right hilar notch, which is located above the cholecystic neck. The right branch of the portal vein is then ligated. The ligature and separation of the right bile duct follows. If a short right portal vein is present, amputation after ligature should be postponed to prevent hemorrhage.
4. Right hepatic vein handling: The right hepatic vein is large. It is difficult to expose the right hepatic vein because it predominantly lies deep inside of the hepatic parenchyma. The liver capsule is cut open at the distal end of the root of the right hepatic vein after lifting the right hemiliver to the left. An intrahepatic length of the right hepatic vein, exposed after separating the hepatic parenchyma, is ligated inside of the liver. Short hepatic veins are then ligated.
5. Hepatic partition: Resection starts 1 cm to the right of the central fissure (the connecting line between the cholecystic fossa and the left margin of the IVC). The resected region is determined by discolored parenchyma after the right conduits are ligated. The hepatic parenchyma is separated bluntly after the liver capsule is cut open where the right branches of the middle hepatic vein is ligated and cut. However, the trunk should be preserved. The right hepatic vein is finally cut and sutured (Fig. 23.6).
6. Management of hepatic cutting surface: Same as for left hepatolobectomy.

23.7.4 Right Trisegmentectomy

A right trisegmentectomy comprises removal of the hepatic parenchyma on the right side of the falciform ligament, including the right hemiliver and the left internal lobe. Normal liver function by the remnant liver should be ensured due to the large volume that is removed.

1. Incision: Abdominothoracic incision, same as for right semi-hepatectomy.
2. The mobilization method for the right lobe is similar to that during the right semi-hepatectomy after the abdomen is entered. The right portal vein, right hepatic artery, and right bile duct are exposed accordingly. The cholecystic duct, cholecystic vessels, right hepatic artery, and right portal vein are cut accordingly.
3. The short hepatic veins and branches of inferior right hepatic vein are ligated and cut in a similar way as for a right semi-hepatectomy.
4. Hepatic partition: The liver capsule is cut open at 1–1.5 cm right to the falciform ligament, and the hepatic parenchyma is separated to the IVC. The middle and right hepatic veins are ligated after the liver is gently lifted upward. Sudden torsion of the IVC induced by traction can lead to shock and cardiac arrest; gentle handling is therefore important.
5. Management of the hepatic cutting surface: Same as for left hepatolobectomy.

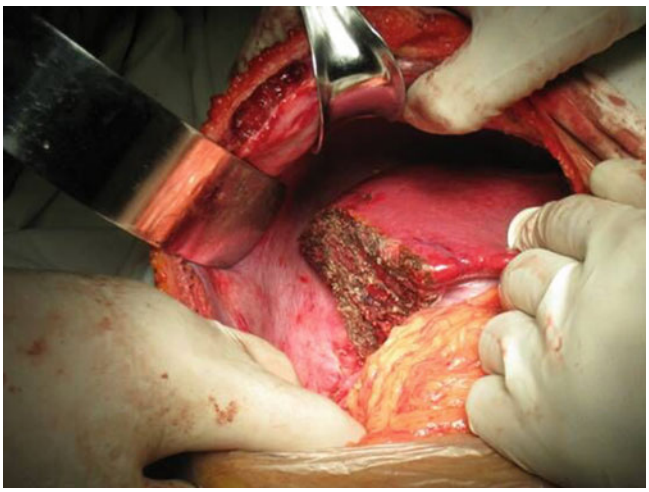

Fig. 23.6 The live tissue is divided using a Cavitron Ultrasonic Surgical Aspirator (CUSA) ultrasonic instrument

23.7.5 Middle Hepatic Lobectomy

The middle hepatic lobe, including the left internal and right anterior lobes, lies between the first and second hepatic hila. The blood supply comes from left internal branch of the portal vein and the right anterior hepatic artery. The middle hepatic vein drains the middle hepatic lobe. The bile of the middle hepatic lobe is drained into the hepatic bile ducts of the left internal and right anterior lobes, which then join the left and right hepatic ducts.

1. An incision across the right rectus abdominis or oblique incision under the costal margin is used for exploration. When a middle hepatic lobectomy is decided, the incision is extended to the xiphoid process and the middle axillary line through the seventh intercostal space, forming an abdominothoracic incision.

2. Hepatic mobilization: The middle hepatic vein cannot be handled until the middle hepatic lobe is adequately exposed by cutting off the ligament teres hepatis, the falciform ligament, the right coronary ligament, and the right triangular ligament. The hepatic partition begins along the central fissure. The middle hepatic vein can be found 2–3 cm from the liver surface and ligated inside the hepatic parenchyma.
3. Hilar dissection: The right hepatic notch can be exposed after the cholecystic duct and cholecystic vessels are ligated and cut off at the first hilum. The right hepatic artery is ligated after the Glisson capsule, which covers the right hepatic notch, and is cut open; ligature and amputation of the right portal vein and right hepatic bile duct follow. Exposure and ligature of the left hepatic artery is performed on the left side of the common bile duct. The connective tissue from the hilar transverse fissure and the left longitudinal fissure is removed. The left portal vein and hepatic bile duct are ligated when the hepatic parenchyma is lifted out of the way.
4. Middle hepatic lobe removal: A dark-purple region demarcated between left and right posterior lobe is present when the blood supply to the middle hepatic lobe is controlled. The liver capsule is cut open according to the demarcation, and a blunt hepatic partition is performed using a scalpel handle. The IVC should be protected when the partition reaches the back of the liver.
5. Management of the hepatic cutting surface: The cutting surface is carefully checked for bleeding and is covered by the greater omentum. The remnant left and right lobes are approximated by an interrupted suture.

23.7.6 Partial Hepatectomy or Wedge Hepatectomy

1. Partial hepatectomy: This procedure is commonly performed with an irregular hepatectomy. The affluent hepatic blood supply is stopped at the hepatoduodenal ligament. A blunt hepatic partition is performed when the liver capsule is opened according to the determined cutting line. The hepatic cutting surface is closed by suture or covered with the greater omentum.
2. Wedge hepatectomy: Two rows of wedge-shaped mattress suture are placed 2–4 cm away from the tumor. The liver capsule is cut open at 0.5 cm from the superficial margin between two rows of sutures. The hepatic parenchyma is divided bluntly at the same time that bleeding is handled. The wound is approximated by suture after the tumor is removed.

23.8 Postoperative Management

1. Hepatectomy is a traumatic procedure; as a result, it requires close observation and intensive care after operation. A sufficient circulation volume, stable blood pressure, and shock prevention both intra- and postoperatively are necessary, and regular liver function should be examined.
2. Water and electrolyte balance should be maintained. Daily intravenous nutrition supply (adequate glucose, vitamin C, amino acids, and fat emulsion) is necessary. An injection of vitamin K, vitamin B_1, CoA, and insulin may be necessary.
3. Plasma colloid osmotic pressure that could be interfered due to abrupt reduction of plasma albumin after a wide hepatectomy can be corrected by infusion with human blood albumin, plasma, or fresh whole blood.
4. Broad-spectrum antibiotics are used to reduce intestinal bacteria and prevent infection.
5. Interval oxygen inhalation after operation can enhance oxygen supply to the liver.
6. Drainage should be kept unobstructed, and gastric decompression should be discontinued.
7. Medication that can cause hepatic injury or is processed by the liver should be avoided.
8. Immediate intravenous infusion of arginine or monosodium glutamate is given to prevent hepatic coma when any sign of hepatic coma, such as elevated blood ammonia or poor psychiatric status, is present.

23.9 Metabolic Alteration after Hepatectomy

The leading factors that predispose a patient to postoperative metabolic alterations are as follows: ① anesthesia, ② trauma from the operation, ③ large amount of blood transfusion, ④ hepatectomy, and ⑤ underlying diseases.

1. Fluctuation of plasma protein: The level of plasma protein drops dramatically after the operation, and albumin predominates. The level of plasma protein reaches its lowest point at 1 week and rebounds at 2 weeks after the operation, remaining lower than normal. Protein levels usually become close to normal 2–4 weeks after the operation. Therefore, a large amount of albumin is given to patients undergoing wide hepatectomy within 2 weeks of the operation.
2. Change of liver function: The level of serum bilirubin rises dramatically and proportionately to the volume of the removed liver after a wide hepatectomy. Jaundice, if

present, improves after 7–10 days. The level of serum bilirubin rebounds when infection, decompensated liver function, or deterioration occurs.

3. Change in the enzyme system: The serum aminotransferase (SGPT) level increases significantly and declines close to or slightly beyond normal 5–7 days after operation. The elevated degree and recovery time of SGPT are not correlated to the volume of resection or serum bilirubin levels. However, postoperative SGPT remains normal or slightly elevated in patients with drainage in the common bile duct. A postoperative elevation of SGPT may be associated with pressure inside the bile duct.
4. Fluctuation of blood glucose: A wide hepatectomy results in reduced hepatic glycogen storage capacity; hence, discontinuation of glucose leads to hypoglycemia.
5. Electrolyte change: Reductions in serum potassium, sodium, and chloride 1 week after the operation are related to surgical trauma.
6. Change of coagulation function: Postoperative alterations in coagulation function are associated with the infusion of a large volume of banked blood product, hypoxia, and hepatectomy during the operation. The levels of prothrombin and coagulation factors, such as V and VII, drop after operation. The levels of coagulation factors V and VII rebound 2 weeks and 3–6 weeks after operation, respectively. The blood platelet count also decreases after the operation. If fibrinolytic enzymes become more active and plasma fibrinogen declines within 3 days after the operation, postoperative bleeding can result.
7. Hepatic compensation: Compensated proliferation of the remnant liver occurs primarily within 2 weeks after the hepatectomy. The remnant liver can gradually grow close to its original size.

23.10 Major Complications

1. Intra-abdominal infection: Blood oozing continues after the hepatectomy. If there is inadequate drainage, secondary pyogenic infection or even septic shock might occur. Intra-abdominal collections require drainage when they are located and demarcated.
2. Liver failure and hepatic coma: Commonly occur within 2 weeks of the operation and require liver-conserving treatment.
3. Postoperative bleeding: Commonly caused by inadequate hemostasis or hepatic necrosis or altered coagulation function. Bleeding can be treated using anticoagulant drugs; however, immediate re-laparotomy after continued transfusion and shock correction is required when hemorrhagic shock occurs or if a great deal of fresh blood is drained.
4. Bile fistula: Bile leak from open bile duct ends of the cutting surface due to suture slippery and, if well drained, can lead to a secondary bile fistula instead of bile peritonitis. Elective biliary fistula repair can be considered when the fistula channel persists.
5. Other complications: Atelectasis, pneumonitis, respiratory distress syndrome, peritonitis, renal insufficiency, vein thrombosis, etc.

Laparoscopic Liver Resection

24

Rong Liu

24.1 Over Review

Until now, over 20 years has elapsed since the first conduction of laparoscopic liver resection (LLR), which was reported in 1991 for the treatment of benign liver tumors incidentally found in a gynecologic laparoscopic surgery [1]. Although numerous doctors attempted to perform LLR after the abovementioned case, the development of minimally invasive hepatic surgery was slow in the first decade, when most of the cases were laparoscopic cystic fenestration. What is more, the resections of solid tumor were mainly limited in the left lateral section or the margins of the liver [2], and very few specialized centers attempted and managed to perform laparoscopic major liver resection, which was defined as resections of three or more liver segments.

The underlying reasons were complicated, which may include the risk of massive hemorrhage in all forms of hepatic surgery, the difficulty in safe and effective laparoscopic dissection of the parenchyma, the concern for the ability to obtain adequate margins in resection of malignant tumors, the theoretical risk of gas embolism, etc. As a result, the feasibility and efficiency of LLR had been questioned. For a long time, LLR had been considered as a procedure of significant risk and technically demanding, which requires experienced liver surgeons with a high level of laparoscopic skills and carefully selected patients [3].

Benefit for the technological advances in the past decades, such as the developments and refinements of coagulating parenchymal dissection tools and laparoscopic ultrasound, LLR had been increasingly used in clinical routine. From 1992 to 2008, a total of 2804 cases of LLR were reported worldwide. Although only 17 % of them were major hepatectomy and less than ten centers had published LLR series with greater than 50 patients [4], it is undeniable that LLR had undergone great development. In 2008, a consensus of experts in both open and laparoscopic liver surgery established the Louisville Statement, which declared that laparoscopic liver surgery is a safe and effective surgical approach to manage liver diseases in the hands of trained surgeons with experience in hepatobiliary and laparoscopic surgery [5].

By now, more than 3000 cases have been reported in literature worldwide [6], and 50 % of them were applied for that of malignant lesions. An increasing number of centers are performing major resections, including hemihepatectomy and even extended hemihepatectomy. According to Koffron et al. in Feinberg School of Medicine, Northwestern University, the percentage of LLR performed in their group had increased from 10 % in 2002 to 80 % of all liver resections in 2007 [7]. The application of robotic laparoscopic surgery [8] system also promoted the development of LLR, by turning some former relative contraindications into indications, for example, the cases which need hepatic portal dissection and digestive reconstruction [9–11]. Technical innovations were also reported, for example, LLR using a retroperitoneal approach [12] or a single incision approach was reported [13–15].

Of great importance, after years of experience, the theory of minimally invasive surgery for liver resection had been established [16], which greatly facilitated the clinical application of LLR. Although it was impossible for LLR to replace open hepatectomy, it has been generally accepted that LLR has advantages such as smaller local trauma, milder systemic reactions, less operative blood loss, shorter hospital stay, lower morbidity, and better cosmetic results [10, 17–24]. Our team started to perform LLR in 2002 and have finished more than 500 cases by now, including laparoscopic left lateral sectionectomy, laparoscopic hemihepatectomies, laparoscopic extended hemihepatectomies, and irregular LLR. We performed the first laparoscopic trisegmentectomy worldwide [25], investigated the clinical application of LLR

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using a single incision approach [26], developed the novel retroperitoneal approach to perform LLR [12], and explored the application of robotic-assisted LLR [27]. In this chapter, we would like to discuss the principles and technical details of LLR, to share our experiences, and hopefully, to promote the application of minimally invasive liver surgery.

24.2 Indications

24.2.1 General Criteria

The indications for LLR should follow the same guidelines for open liver resection (OLR) and be limited to patients willing to receive minimally invasive surgery. Stringent criteria based on surgeon experience as well as the lesion size and location must be complied with, especially for malignant tumors. Surgeons should have a full understanding of the hepatic anatomy, extensive experience in open liver surgery, and technical skills to process major vascular and biliary structures laparoscopically before embarking on LLR [28].

24.2.2 Size and Location

Although there is no absolute size criterion, patients with solitary lesions, less than 5 cm, and within peripheral segments may be more suitable for LLR [5]. We suggest that the size of benign tumors should be less than 15 cm, and that of malignant tumors should be less than 10 cm, for the reason of the occupation of laparoscopic space and the risk of capillary hemorrhage.

The localization of lesions is of crucial importance in LLR. Small, focal, and localized tumors on the anterolateral segments (segments II, III, IVb, V, VI, according to Couinaud nomenclature) are the most suitable candidate for LLR, because the periphery of the liver is devoid of large venous structures and the bleeding can be easily controlled with clamps or cautery [29]. Laparoscopic lateral sectionectomy has been considered as one of the golden-standard liver resections [17, 29–33], and laparoscopic left hemihepatectomy has also been recommended [24].

However, we have to say that the indication of LLR had been expanding because of the technical progress, and laparoscopic liver resection of segments VII and VIII [34], laparoscopic central hepatectomy [35, 36], laparoscopic extended hemihepatectomy, and caudate lobectomy [20, 21, 37] had all been performed, which were once considered as contraindications of LLR. The laparoscopic synchronous radical resection of liver metastatic colorectal cancer [22], laparoscopic repeat resection of recurrent hepatocellular carcinoma [38], and laparoscopic liver-donor hepatectomy for transplantation [39–41] were also reported. Some surgeon even thought that the limitation of LLR application according to tumor location for treatment of HCC will be overcome with further accumulation of experience and technical advances [42].

24.2.3 Liver Function

The Child-Pugh classification should be at least Grade B, and there should not be any other severe structural disease. The volume of resting liver has to be able to fulfill the physical demand. In cirrhotic patients with coexisting compromised hepatic function, laparoscopic liver resection showed good results. The authors of these studies concluded that preserving the abdominal wall vessels in the laparoscopic approach reduced postoperative hepatic decompensation in patients with portal hypertension [43]. However, patients with indocyanine green 15 min clearance retention rate (ICG-R15) more than 20 %, prothrombin activity lower than 75 %, serum albumin level below 35 g/l, and total bilirubin more than 1.5 mg/dl are not appropriate candidates for major hepatic resection. Cirrhosis is considered a limiting factor for a massive liver resection.

The indications and contraindications for any operation should change for different surgeons, different techniques, and different times. In the early stage, it was suggested that a surgeon start with laparoscopic limited liver resection and laparoscopic left lateral sectionectomy and perform complicated LLR when he has become familiar with the laparoscopic dissection and coagulation after 20–30 cases [44, 45].

Images of several patients who underwent LLR

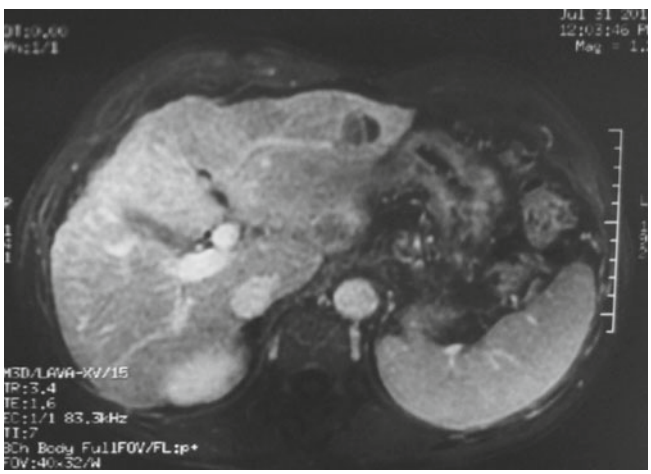

Fig. 24.1 Hepatic carcinoma in Couinaud II and III, with cirrhosis

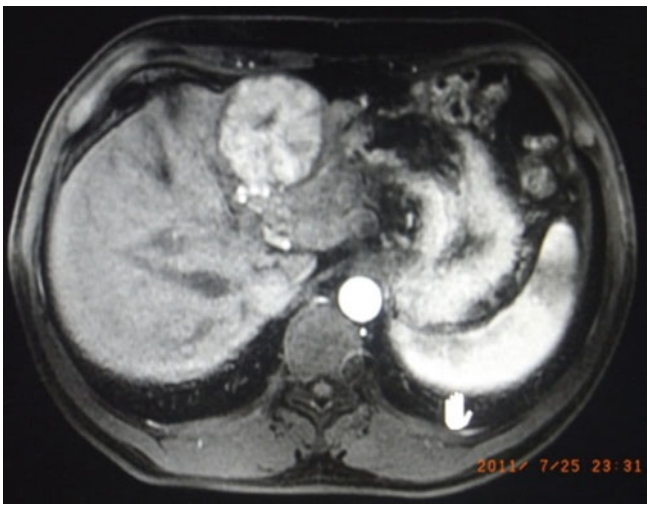

Fig. 24.2 Hepatic carcinoma in Couinaud III

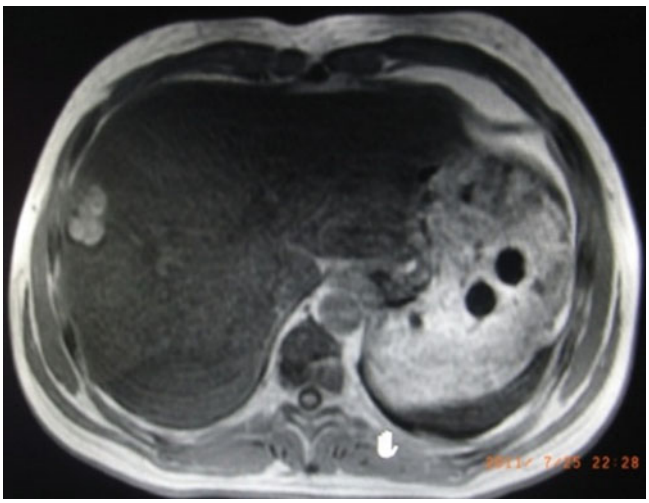

Fig. 24.5 Inflammatory pseudotumor in Couinaud V

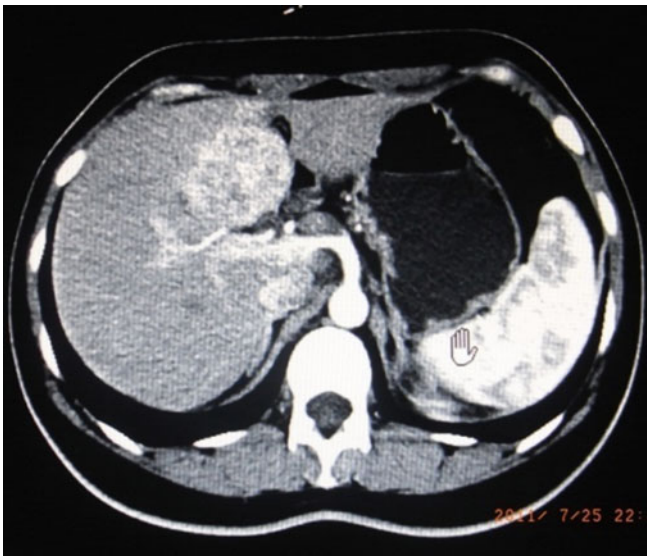

Fig. 24.3 Hepatic carcinoma in Couinaud IVb

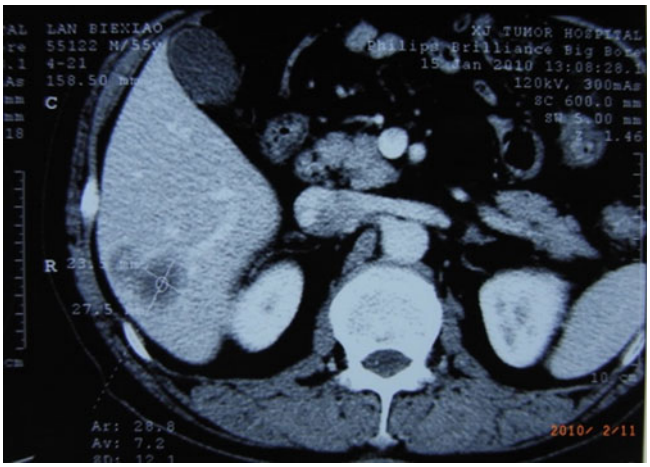

Fig. 24.6 Hepatic carcinoma in Couinaud VI

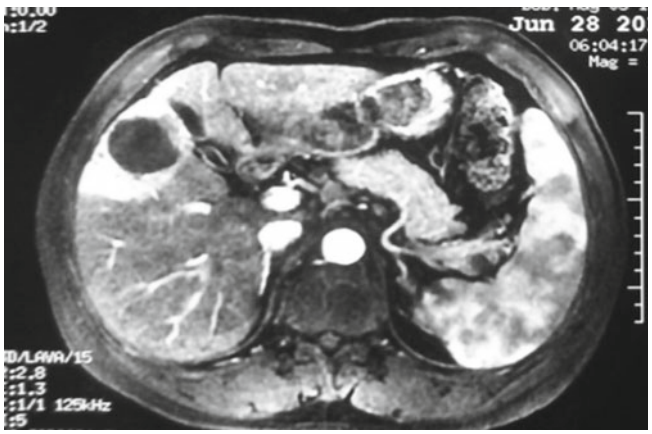

Fig. 24.4 Hepatic carcinoma in Couinaud V, with cirrhosis

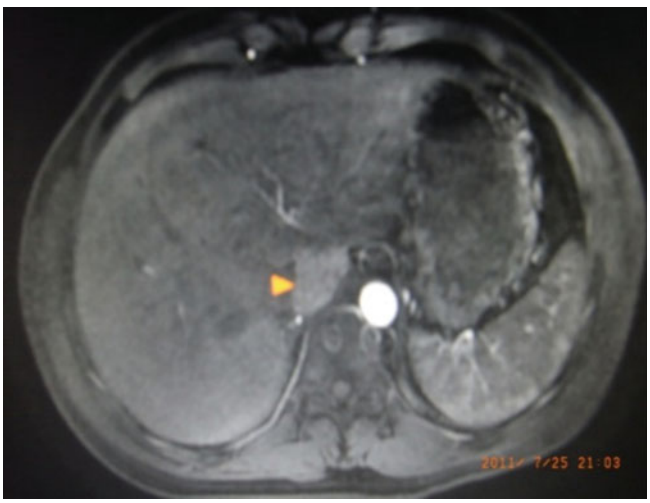

Fig. 24.7 Hepatic carcinoma in Couinaud I

Table 24.1 Indication and contraindication to laparoscopic liver resection

Lesions	Indication	Contraindication	
		Relative	Absolute
Size	<5 cm	>5 cm	
Location	Segments II, III, IVb, V, VI	Segments I, IVa, VII, VIII	Invading vasculature
Number	Solitary or multiple in same lobe		More than would be necessary to maintain adequate residual liver function
Vascular concerns	Distant from any vasculature	Near inferior vena cava, hepatic veins, hilum	Insufficient oncologic margin
Pathology	Benign or malignant hepatic neoplasms parasitic lesions	Require a larger parenchymal resection than necessary with OLR, gallbladder carcinoma and hilar cholangiocarcinoma [46, 47]	
Child class	A	B	C

24.3 Contraindications

The contraindications of laparoscopic liver resection include (I) contraindications of open hepatectomy; (II) contraindication of pneumoperitoneum; (III) patients with tumor extension to the hilum, central hepatic veins, or inferior vena cava; (IV) extensive intra-abdominal adhesions; and (V) the need for complex vascular or hepatobiliary reconstruction or extensive lymphadenectomy which should generally be approached as a hybrid or an open procedure (Table 24.1).

24.4 Signs for Conversion

Extensive intra-abdominal adhesions causing difficult dissection and severe bleeding or rupture of digestive tract.

Tumor with excessive size or inappropriate location and difficult exposure of primary and secondary porta hepatis.

Massive hemorrhage, especially for cirrhotic patients. For patients with benign tumors such as hemangioma, most of whom have good liver function, the operation can be continued with blood transplant; however, an amount of 800 ml should be considered as the warning value, and conversion should be forced when blood loss extends to 1500 ml [48].

Injury of extrahepatic veins, failed in fast management, to prevent gas embolism [49].

Sudden hemorrhage and rupture of large vessels or tumor.

Combined with intrahepatic metastasis, cancer embolus in portal vein, hepatic lymph node metastasis, or unclear margin.

24.5 Preoperative Preparation

24.5.1 Patient Preparation

A thorough medical history should be asked and physical examination be performed to evaluate the disease or previous abdominal incisions that might complicate the laparoscopic approach. Severe cardiac, pulmonary, or renal disease should be further evaluated. High-quality magnetic resonance or computed tomography imaging with vascular reconstruction should be reviewed to evaluate intrahepatic arterial and portal anomalies and to determine if the lesion is suitable for a laparoscopic resection. Magnetic resonance cholangiopancreatography is suggested before laparoscopic hemihepatectomy to learn enough information about the biliary system, especially congenital variation.

Informed consent should include a thorough discussion of the risks and benefits of laparoscopic surgery relative to those of open surgery, as well as the possibility of conversion to an open resection.

Patients are recommended to be admitted in no more than 7 days before the operation to conduct routine lab examinations including liver function tests, basic metabolic profile, complete blood count, coagulation series, and tumor markers.

24.5.2 Equipments and Instruments

Improved instruments have greatly improved the safety of LLR. Thus, it is critically important to be familiar with the relevant laparoscopic instruments and equipment. State-of-the-art equipment is required for LLR, and operating room nurses should be familiar with the proper setup of the equipment. The equipment required for LLR includes high-resolution electrical or optical laparoscopic system, 30° laparoscopes, video and picture collection/storage equipment, automatic high-flow insufflation unit, irrigation and suction devices, and instruments for conducting the operation.

A 10 mm tangential clamp should be prepared in laparoscopic regular liver resection, for the dissection of hepatic artery and portal vein in the porta hepatis. The video should be stored routinely.

Generally, the use of two monitors and 10 mm 30° laparoscopes is recommended, which provides better visualization. High-definition monitors are positioned laterally to each shoulder and above the patient's head. To date, CO_2 pneumoperitoneum is considered safe. In many high-volume centers, LLR was performed at a pneumoperitoneal pressure less

than 12 mmHg, and reports indicated that the rate of clinically severe gas embolism was low [49].

For the dissection of liver parenchyma, we suggest the combination use of three instruments: ultrasonic dissectors, BiClamp, and argon beam coagulator. Endoscopic linear cutter stapler should also be prepared.

The ultrasonic dissectors are necessary, which work through a vibrating blade or scissor and can be used for tissue dissection and coagulation and mostly were used for the dissection of liver parenchyma and detailed dissection in porta hepatis. It can effectively seal small vessels and bile ducts with minimal fogging of the camera lens and seldom adhere to the liver parenchyma as conventional electrocautery does. Compared to the crushing instruments for parenchymal dissection, the use of the ultrasonic dissector is beneficial because of less hemorrhage during dissection of liver parenchyma. Ultrasonic dissectors allow complete clearance of the liver parenchyma several millimeters around the pedicles, which ensures safe ligature. For the approach to the hepatic veins, ultrasonic dissection allows precise dissection without traction, minimizing the risk of tearing the fragile wall of the hepatic veins.

BiClamp is generally used in the coagulation of active bleeding in the liver incisional surface [50], and argon beam coagulator is generally used in the coagulation of capillary hemorrhage. The argon beam coagulator (ABC) is also useful for hepatic resections, primarily for superficial hemostasis. However, the appropriate use of the ABC system is very important in order to avoid the life-threatening complication of argon gas embolism.

LigaSure of 5 mm could also have a good performance in dissecting liver parenchyma.

Surgical clamps or adsorbable clamps can be used in the ligation of large vessels.

Endoscopic disposable clip appliers and vascular staplers can contribute to the reduction of major intraoperative bleeding during laparoscopic hepatectomy. Because of their safety, rapidity, and ease of application, these stapling devices are efficient in controlling and dividing the major hepatic veins. The size of nail box should be selected according to the thickness of tissue; generally, a nail box with a height of 3.5–3.8 mm and a width of 60 mm is used, and the brand name should be in coincidence with that of trocars. Titanium endoclips can be used to close the main vascular branches and bile ducts. Small vascular or biliary ducts are closed by bipolar coagulation or endoclips. Medium-sized hepatic veins and bile ducts in Glisson's sheath should be clamped with a clip.

Laparoscopic flexible ultrasonography is not only useful but also indispensable for precisely locating the boundaries of the tumor and the exact anatomy of the vessels, mainly the hepatic veins. Its guidance ensures the safety of both regular and irregular resections. The precise localization of hepatic vessels with color Doppler expands the indications of laparoscopic surgical resection [51, 52].

Gasless laparoscopy is an alternative to the use of CO_2 pneumoperitoneum and the abdominal wall lift device. It provides a tent-shaped operative field rather than the more spacious dome-shaped field provided by a pneumoperitoneum [53]. Intra-abdominal organs are closer to the laterally situated port sites, which increases the risk of injury and limits work area. However, gasless laparoscopy avoids the rapid changes in intra-abdominal pressure that are associated with a greater risk of gas embolism. Maintaining intra-abdominal pressure equal to that of the ambient environment may minimize this risk, especially when the hepatic vein is lacerated intraoperatively. Unfortunately, the exposure with the gasless approach is somewhat unsatisfactory. This laparoscopic procedure is recommended for liver cirrhosis patients with small HCC who are not candidates for major hepatectomy [54].

The bag is suggested, especially for malignant cases, to prevent port implant metastasis.

24.6 General Principles of Surgical Technique

24.6.1 Patient Position and Trocar Placement

After patient and procedure confirmation, general anesthesia is induced and a central venous catheter, an arterial line, and a large bore peripheral intravenous catheter, nasogastric tube, and Foley catheter are placed. Routine anesthesia monitoring includes heart rate, arterial blood pressure, oxyhemoglobin saturation, and blood gas analysis.

The patient's position and trocar placement are decided on the basis of the location of the tumor. Laparoscopic hepatectomy is generally performed with a four- or five-trocar technique.

Generally, the patient is positioned on the operating table in a supine position with the head higher than the feet, and the surgeon stands on the right side of the patient. A 10 mm trocar and 30° laparoscope, which provides a wide-angle view of the operative field, are placed below the umbilicus. After pneumoperitoneum is created by infusion of carbon dioxide, more trocars are inserted at the epigastrium and the bilateral subcostal lines for dissection.

When hepatic resection is performed on the anterior-inferior segment (segment V) or the posterior-inferior segment (segment VI), the patient is placed on a left-sided semireclining position. After pneumoperitoneum is created, three more trocars are inserted at the right subcostal line, the anterior clavicular line, and the epigastrium.

The placement of trocar in laparoscopic surgery is extremely important because it is directly related to the difficulty of the surgery. Four schematic diagrams of routinely used protocols of trocar placement are followed.

Schematic diagram of routinely used protocols of trocar placement

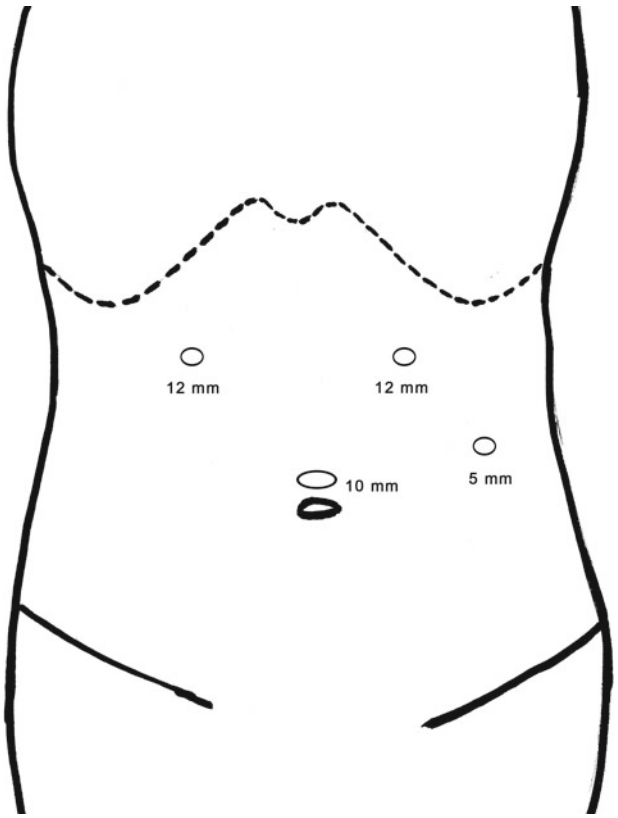

Fig. 24.8 Laparoscopic left lateral sectionectomy

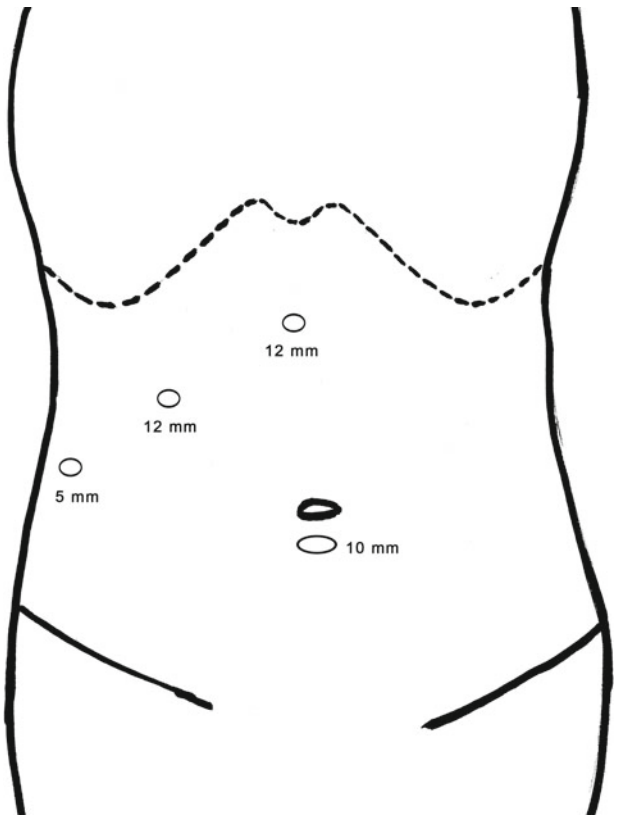

Fig. 24.9 Laparoscopic right posterior partial liver resection

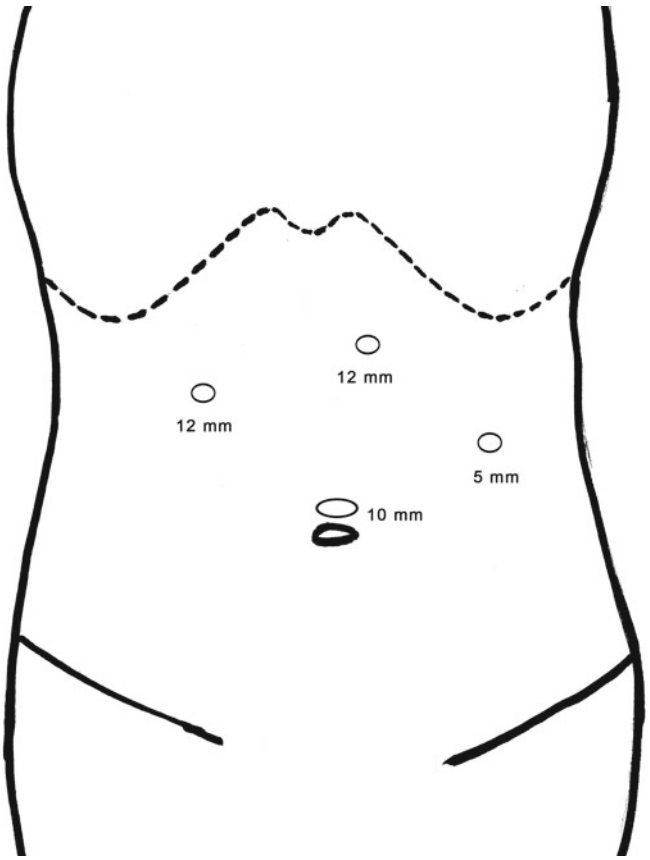

Fig. 24.10 Laparoscopic left hemihepatectomy

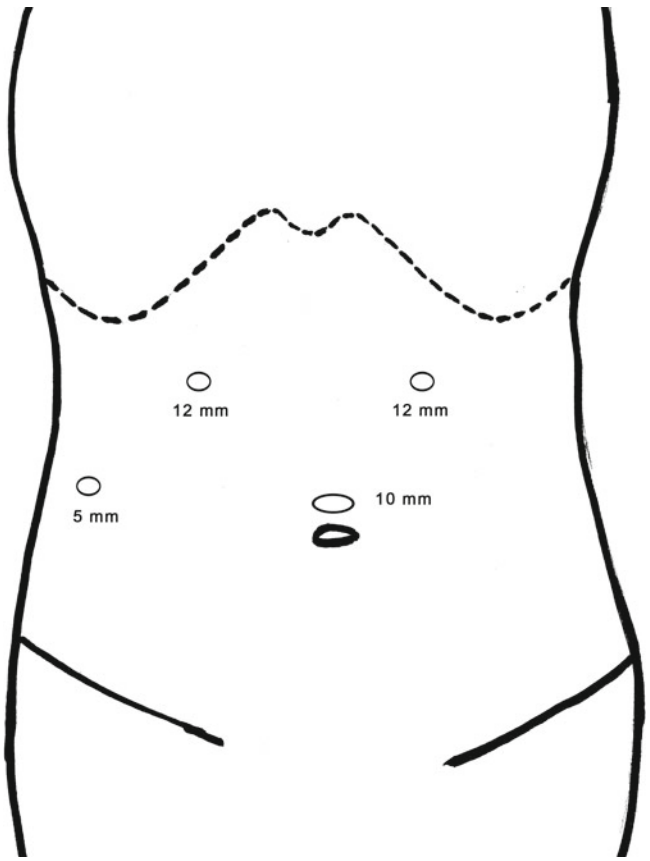

Fig. 24.11 Laparoscopic right hemihepatectomy

24.6.2 Mobilization of Liver and Control of Bleeding

Liver mobilization requires freeing the liver's ligamentous attachments from the diaphragm. The ligamentum teres hepatis and the falciform ligaments are taken down from the abdominal wall longitudinally to the confluence of the hepatic veins and vena cava. It is important that these ligaments should be transected close to the abdominal wall as to prevent dangling remnants from obstructing the view or soiling the scope.

The left triangular and coronary ligaments are divided close to the liver laterally to medially, similar with the method of dividing the attachment of the lesser omentum. If a replaced or accessory left hepatic artery is present, it should be transected between clips. The confluence of middle and left hepatic venous and the vena cava is exposed medial to lateral with cold sharp dissection.

Depending on whether a conventional or anterior approach is chosen, the right triangular and coronary ligaments can be divided before or after the parenchymal transection, respectively, taking advantage of the lateral position of the patient.

The occlusion of hepatic vascular inflow and outflow is not required for lesions ≤3 cm in diameter or when performing resection of the left lateral lobe. However, the hepatic vascular inflow and outflow must be occluded when removing lesions >5 cm in diameter or when performing anatomic liver resection.

If hepatic pedicle occlusion is anticipated, the Pringle maneuver, probably the simplest method of inflow limitation, currently can be achieved laparoscopically. Although total vascular inflow occlusion can be easily performed, ischemic reperfusion injuries can lead to increased postoperative morbidity. On the other hand, hemihepatic inflow occlusion, leading to hemihepatic ischemia, decreases the amount of liver parenchyma under reperfusion damage and offers the advantage of reduced blood loss. Half-Pringle maneuver is feasible and safe and may be achieved by the advanced armamentarium in laparoscopic right and left hepatectomy [55].

On the basis of the laparoscopic ultrasonography or demarcation lines induced by interruption of hepatic artery and portal vein flow, the transection plane is outlined on the liver capsule with monopolar electrocoagulation.

24.6.3 Parenchymal Resection

The main technical challenge of laparoscopic liver resection remains to be hemorrhage during major anatomic parenchymal dissection, especially in cirrhotic patients. The choice of technique for resection is therefore important. According to our experience, multiple instruments are needed, including ultrasonic coagulation scalpel, bipolar electrocoagulation, Hem-o-lok clips, and endoscopic linear cutter staplers (Echelon 60 mm). The hepatic capsule and the superficial 2–3 cm of parenchyma can be dissected by Harmonic ultrasonic scalpel. Vessels and biliary ducts less than 3 mm in diameter encountered during the dissection of the superficial and deep parenchyma can be ligated and transected using Harmonic ultrasonic scalpel or bipolar electrocoagulation. Larger arteries and bile ducts are ligated using Hem-o-lok. Endoscopic linear cutter stapler (Echelon 60 mm) is used for Glisson's pedicles, portal branches, and hepatic veins. The argon beam coagulator is primarily applied for the parenchyma resection margin hemostasis.

24.6.4 Specimen Extraction

In all cases, the specimen is placed in a plastic bag and extracted, and we suggest it be extracted through an enlarged port site. Except the benign lesions, fragmentation of specimen must be avoided to allow proper pathological evaluation.

24.7 Surgical Procedures

24.7.1 Laparoscopic Limited Resection

Recent data suggest that wedge resection is adequate for a benign tumor, a metastasis tumor, or a solitary and small malignant primary tumor in the liver [56–58]. Superficial lesions in segments 2–6 are the best indication to this procedure, which do not need dissection of the first and second porta hepatis.

The patient was placed in supine position; the surgeons stood on the left or right side of the patient, according to the lesion site. Four ports are necessary in this procedure. After the pneumoperitoneum, placement of trocar and the necessary free of the relative ligament were all finished, the margin of parenchymal dissection was marked 1–2 cm away from the tumor using electrocoagulation and subsequently the capsule was cut.

The operational field should be kept clean and clear. For the limited resection of tumor with a large size, the area of the liver wound was usually large, and it would be hard to coagulate because it was impossible to block the inflow and outflow of blood as was done in regular LLR. To solve this problem, the primary feeding vessel could be reconstructed using contrast-enhanced CT or MRI preoperatively and before the resection of tumor, ligated. The incisional surface was covered with hemorrhage materials optionally, and whether to place a drainage tube should depend on the area of incisional surface and the condition of coagulation.

If possible, laparoscopic ultrasonography was used to help localize the tumors, demarcation of vascular structures, satellite nodules (if any), and an adequate tumor-free margin. The surgeon must be able to visualize the lesion on cross-sectional imaging if no laparoscopic ultrasound probe is available and confirm that a safe margin can be obtained without damaging the pedicles or encountering large hepatic vein branch.

For malignant lesions, 10–20 mm margins are measured using ultrasonography and marked using electrocautery. For

benign lesions, a wide margin is not required. Parenchymal dissection is performed with the Harmonic scalpel and follows the marked margins. Hemostasis is achieved by bipolar electrocoagulation or laparoscopic argon beam coagulator. As larger vessels are encountered, clips should be applied. Maintaining a bloodless field is critical and can only be accomplished by constant irrigation of the dissection area. If significant veins, ducts, or segmental pedicles are encountered, a segmentectomy should be conducted to prevent necrosis or biliary fistula. The specimen was placed inside a large plastic bag and subsequently removed through the enlarged trocar port. For large cases, the specimen can be extracted by connecting two ports. Although suprapubic incision is usually used abroad, which is more hidden, the procedure is too tedious.

Laparoscopic limited resection for hepatic cellular carcinoma in the borderline of segments VIb and V

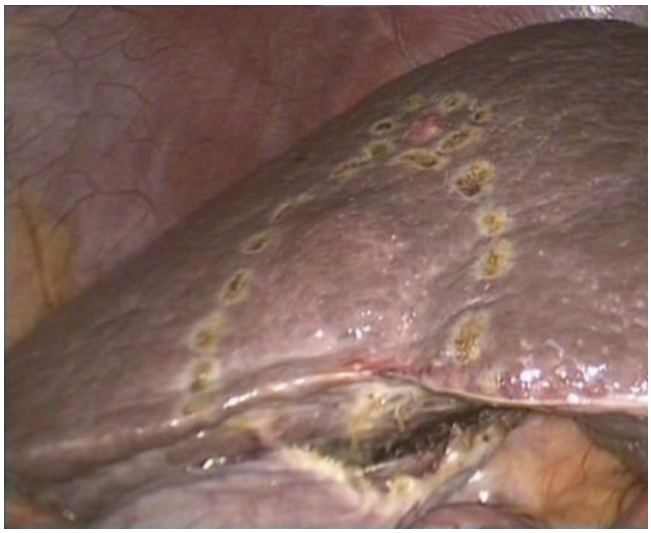

Fig. 24.12 The margins were marked using electrocautery

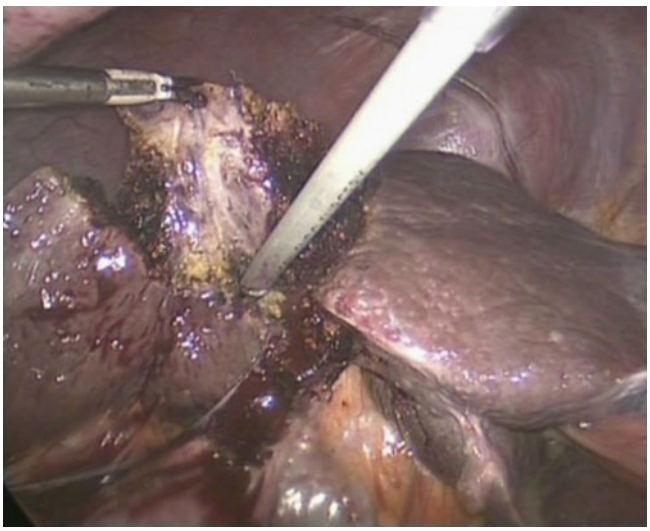

Fig. 24.13 The Harmonic scalpel and BiClamp were combined for transection of the liver

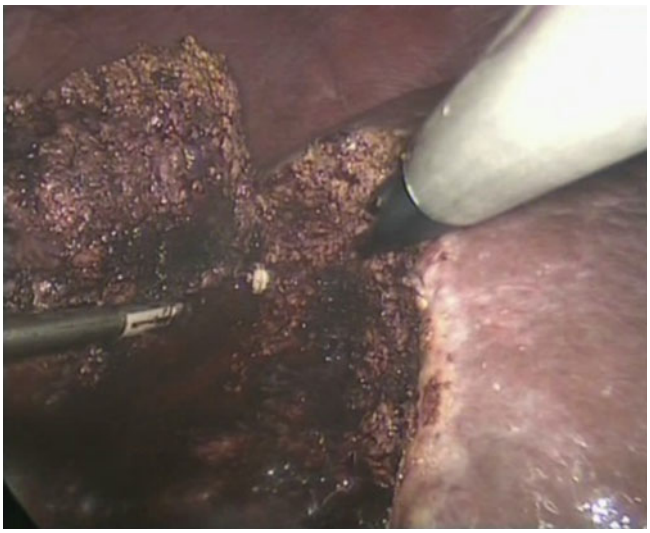

Fig. 24.14 The feeding vessel was clipped using absorbable clips

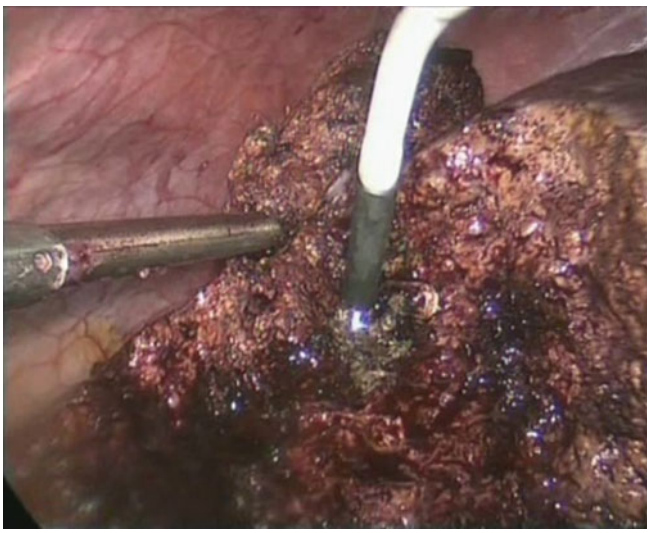

Fig. 24.15 Coagulation was achieved using argon beam coagulator

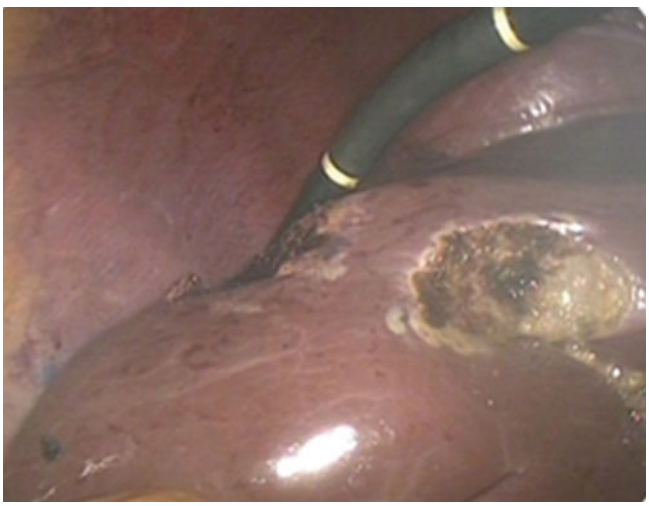

Fig. 24.16 Examination using laparoscopic ultrasound

Laparoscopic limited resection for hepatic cellular carcinoma in segment VI

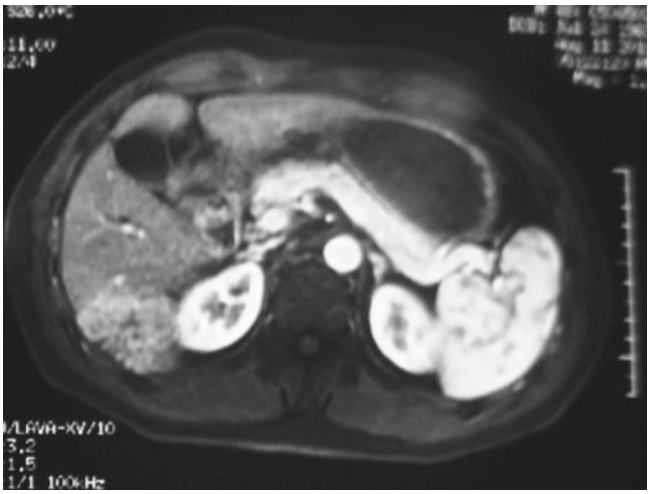

Fig. 24.17 Hepatic cellular carcinoma in segment VI

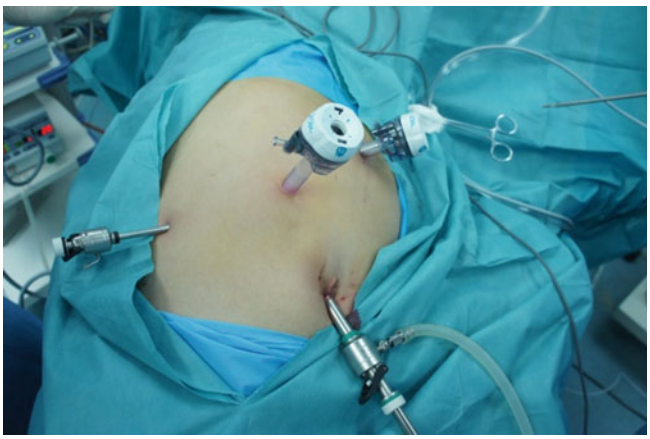

Fig. 24.18 The placement of trocar

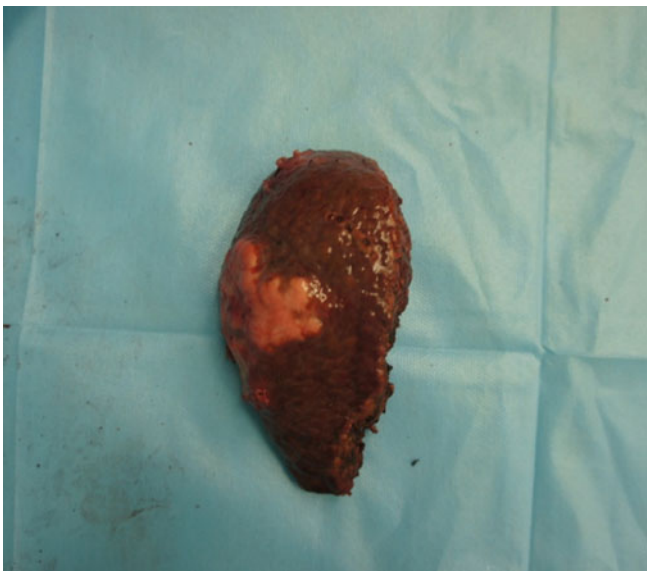

Fig. 24.19 Specimen

24.7.2 Laparoscopic Segmentectomy

Anatomic segmentectomy plays an important role in maximizing the postoperative liver function reserve. Besides, the oncological advantage of anatomic segmentectomy in eradicating potential intrahepatic metastases has been clearly shown in the surgical management of hepatocellular carcinoma. Therefore, laparoscopic segmentectomy that minimizes the loss of normal hepatic parenchyma while ensuring adequate oncological margins has been developed and performed for segments I to VIII [59].

Rather than reliance on surface anatomy, ultrasonography is used to determine Couinaud segmental anatomy and then mark on the liver's surface. Bilateral traction maintained by the assistance of atraumatic graspers allows the parenchymal transection plane to be seen clearly by the operating surgeon. During the parenchymal dissection, a combination of ultrasonic scalpel and bipolar electrocoagulation is used. Section pedicles are ligated with locking clips, and other vessels or ducts are ligated with metal clips as they are encountered. Additional hemostasis is obtained by using bipolar electrocoagulation and the argon beam coagulator. Drains are used only if there is concern about intraoperative injury of the biliary duct or the adequacy of hemostasis.

24.7.3 Laparoscopic Left Lateral Sectionectomy

Because of the favorable anatomy of the hepatic left lateral section, its resection was the first formal liver resection reported using the laparoscopic approach [60], which was also generally accepted as the introduction of LLR [17, 29–31, 33, 45, 61, 62].

We have summarized the protocol of laparoscopic left lateral sectionectomy as a modeling method [26, 38], and a number of case series proved the feasibility and safety. Currently, laparoscopic left lateral sectionectomy has been considered the most suitable anatomical resection for the laparoscopic approach and the standard surgery for lesions in segments II and III, and the technical details are as follows.

The patient was placed in a supine position with the surgeon and the assistant standing on the patient's right side and the scope handler on the left. The patients were usually held with head higher than the foot and the right side higher than the left. The monitor was placed in the head side of the patient, deviated to the left. Pneumoperitoneum is created by infusion of carbon dioxide under the umbilicus, and the other three trocars were placed as discussed above.

The ligamentum teres hepatis, the falciform ligament, the left coronary ligament, and the left triangular ligament were successively divided using the ultrasonic scalpel. The left lobe was lifted by the assistant to divide the lesser omentum to the base of the venous ligament (for some patients, the division of the lesser omentum is not necessary). Enough division is extremely important to the following surgery, and there is no need to expose the left hepatic vein or the inferior vena cava.

The liver parenchyma in the anterior, superior, and inferior of the vascular pedicle of the segment II/III was cut moderately, resulting a rough dissection of segmental pedicle. An endoscopic linear cutter stapler was placed through the right trocar and cut the segmental pedicle as well as nearby liver parenchyma. EC60 with golden nail box, Echelon, was suggested for the previous operation.

Transaction of the liver then continued, and the parenchyma in the anterior, superior, and inferior of left hepatic vein was slightly cut, resulting a rough dissection of the left hepatic vein, which should be able to be cut entirely by endoscopic linear cutter stapler. Then the left hepatic vein as well as nearby liver parenchyma was cut. To make sure that the left hepatic vein is entirely ligated, before the cut of the tissue, the assistant should put a grasper through the left trocar and grasp the left triangular ligament, pulling the left lateral section ventralward and downward and exposing the superior tip and the anterior tip at the same time. When the left hepatic vein was not ligated sufficiently, an absorbable clip could be used to clip the remnant tissue. Usually, the extrahepatic part of the left hepatic vein is not necessarily to be dissected.

The incisional surface and the hepatic stump were inspected for any bleeding and bile leak. Homeostasis was obtained using BiClamp for active bleeding points, and clips or Prolene sutures were used for any bile leak. A drain tube should be placed through the right trocar. The specimen is removed in an impermeable bag through an extended trocar.

Laparoscopic left lateral sectionectomy

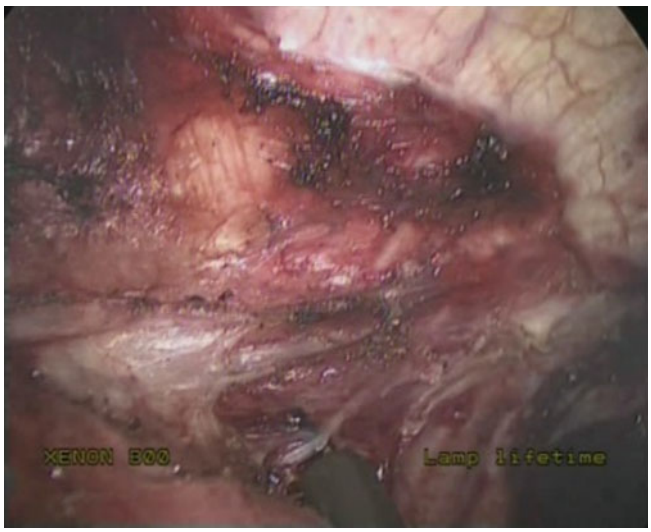

Fig. 24.20 The left triangular ligament was dissected

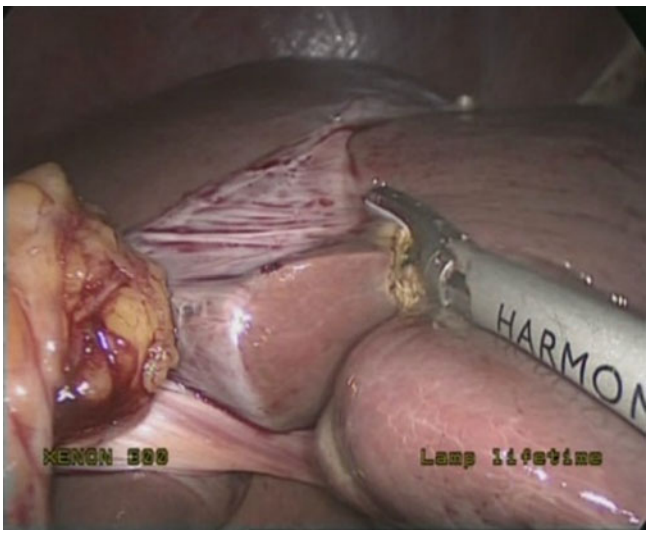

Fig. 24.21 The liver parenchyma was cut 1 cm from the falciform ligament

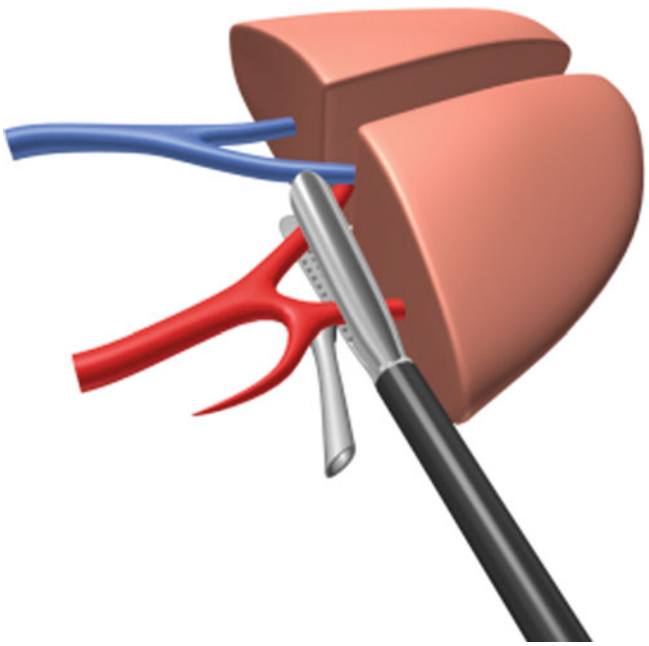

Fig. 24.22 The vascular pedicle was cut after rough dissection using an endoscopic linear cutter stapler. Schematic diagram

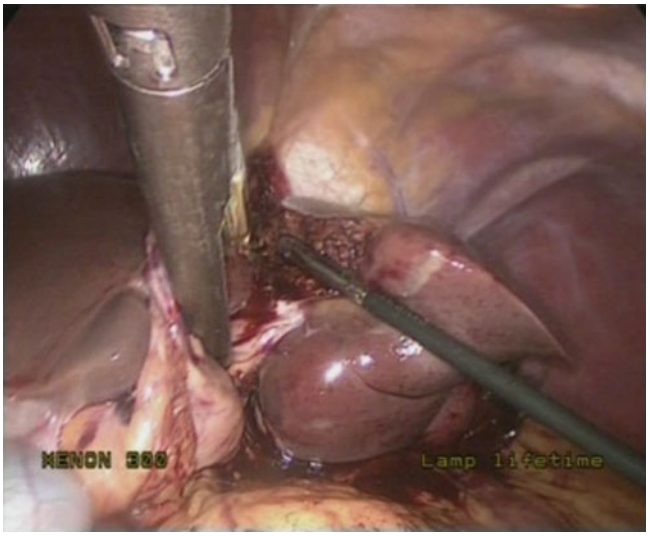

Fig. 24.23 The vascular pedicle was cut after rough dissection using an endoscopic linear cutter stapler. Snap picture of the video

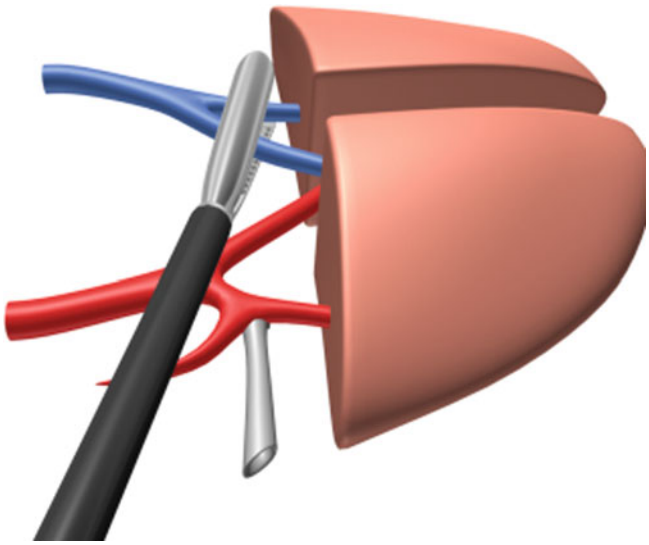

Fig. 24.25 The left hepatic vein was cut after rough dissection using an endoscopic linear cutter stapler. Schematic diagram

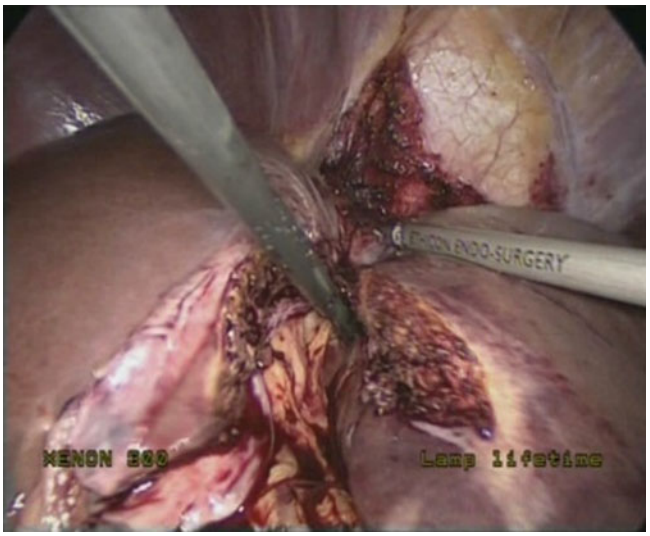

Fig. 24.24 The left hepatic vein was roughly dissected after the segmental pedicle was cut

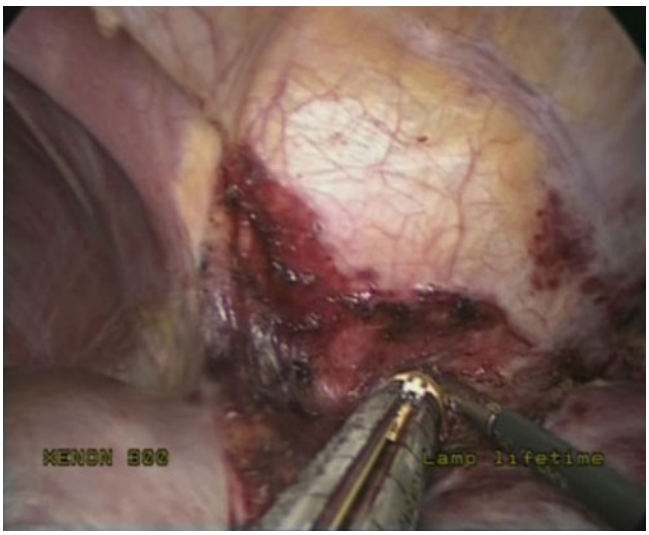

Fig. 24.26 The left hepatic vein was cut after rough dissection using an endoscopic linear cutter stapler. Snap picture of the video

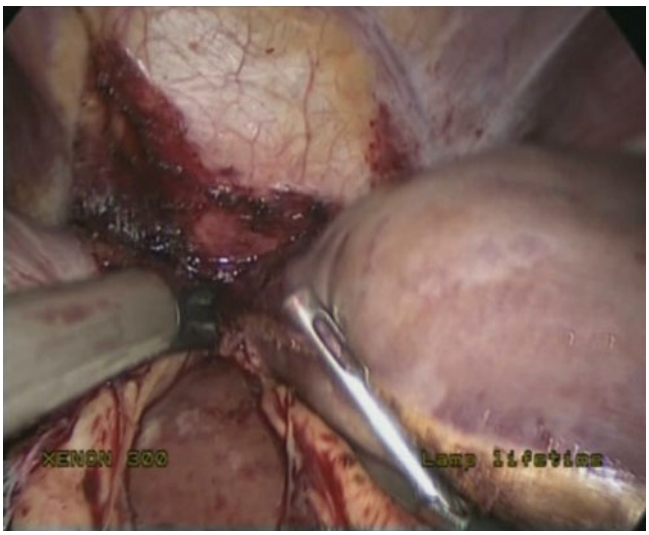

Fig. 24.27 The remnant parenchyma was clipped using absorbable clip

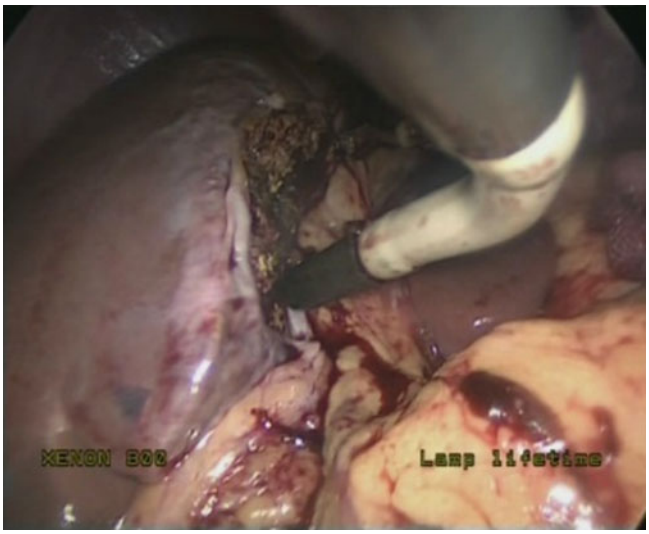

Fig. 24.28 Coagulation of the incisional surface using argon beam coagulator

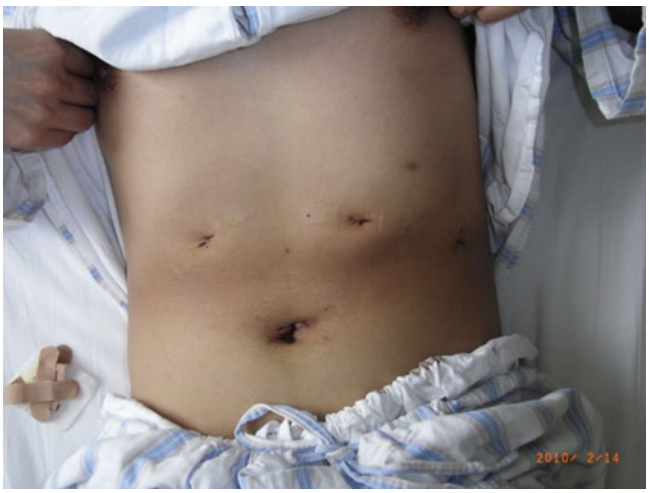

Fig. 24.29 The incision of patients underwent laparoscopic left lateral sectionectomy

24.7.4 Laparoscopic Left Hemihepatectomy

Laparoscopic hemihepatectomy is a more complex procedure because it involves deep parenchymal transaction and has to deal with major vascular structures both in the hilum and at the level of the main hepatic veins. Although the laparoscopic approach to these procedures was not fully standardized, the data from the current series has confirmed that laparoscopic left hemihepatectomy was a safe and feasible procedure and had significant benefits to be considered as a new standard of care.

The patient position and carbon dioxide pneumoperitoneum were similar with the laparoscopic left lateral sectionectomy. The liver and the surrounding organs were systemically explored, and laparoscopic ultrasound can be used for a clear understanding of the course of the vessels if necessary.

The dissection of the surrounding ligaments and the mobilization of the left lobe: the ligamentum teres hepatis, the falciform ligament, the left coronary ligament, the left triangular ligament, and part of the right coronary ligament were disconnected, and then the gastrohepatic ligament was also disconnected cautiously, with protection of the aberrant left liver artery in it. The assistant should lift the left lateral section using an aspirator when dissecting the left hepatic venous ligament, allowing the laparoscopy to enter below the liver, and then the porta hepatis was dissected to the second porta hepatis.

The dissection of the porta hepatis and the control of the hepatic inflow: the left hepatic artery and the left branch of portal vein were successively dissected, and the former was disconnected after ligation, while the latter was ligated or clamped without disconnection.

The transection of liver parenchyma: liver parenchyma was transected superficially to deep. The transection should be performed in situ, and absorbable clips are recommended for large vessels. The liver parenchyma was transected along the ischemic line to the porta hepatis, and active bleeding of the incisional surface can be coagulated using BiClamp.

The vessels in the porta hepatis were divided using endoscopic linear cutter stapler, and the gold nail box of EC60, Echelon, was still recommended. After that, the transection was carried on until the deep parenchyma was reached and the left hepatic vein was roughly dissected.

Lastly, the left hepatic vein was disconnected using endoscopic linear cutter stapler. The bleeding of incisional surface was coagulated using electrocautery or argon beam coagulator, and the exposed vessels can be clamped, electrocauterized, or ignited or sutured depending on the diameter.

The specimen was extracted, and 1–2 drainage tubes were placed through the right trocar. The ports were sutured intracutaneously.

Laparoscopic left hemihepatectomy

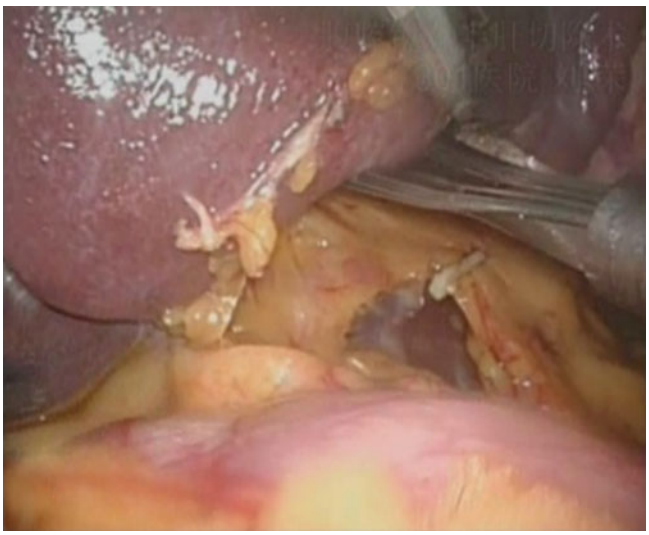

Fig. 24.30 The gastrohepatic ligament was disconnected

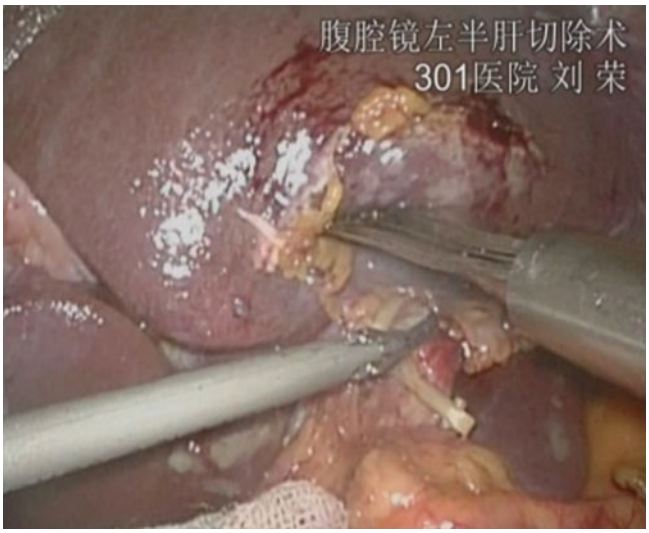

Fig. 24.32 The left hepatic artery was disconnected

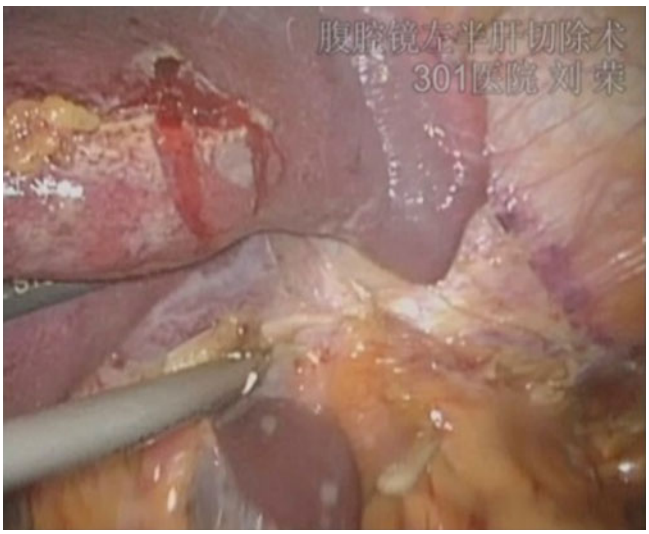

Fig. 24.31 The venous ligament was dissected

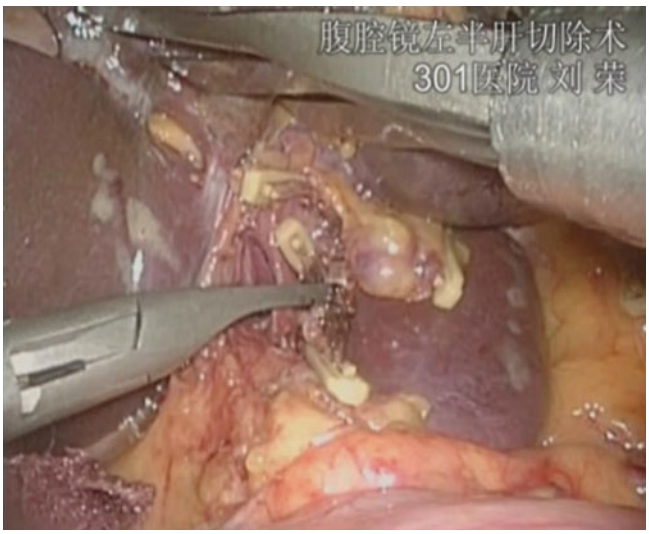

Fig. 24.33 The left branch of portal vein was clamped

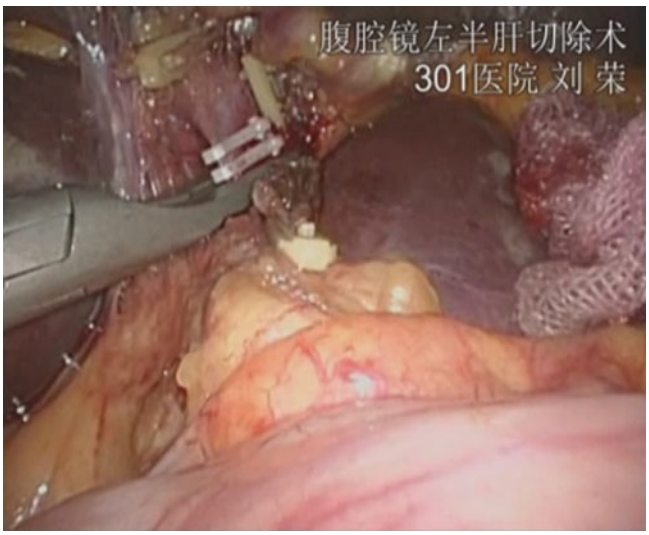

Fig. 24.34 The left branch of portal vein was clamped

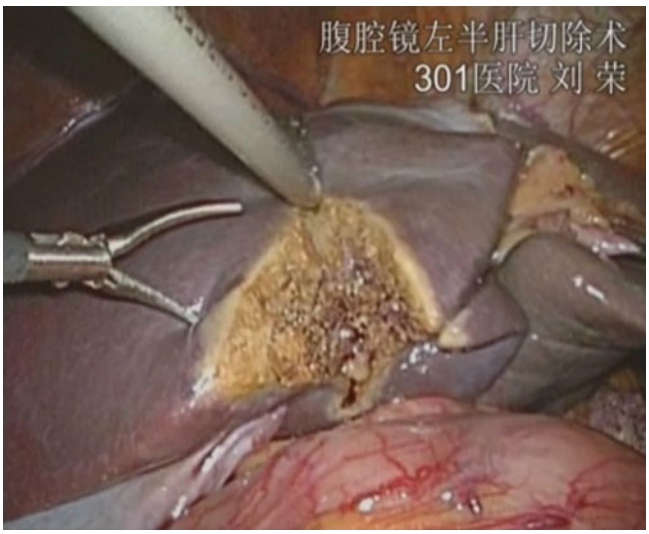

Fig. 24.36 The hepatic parenchyma was transected

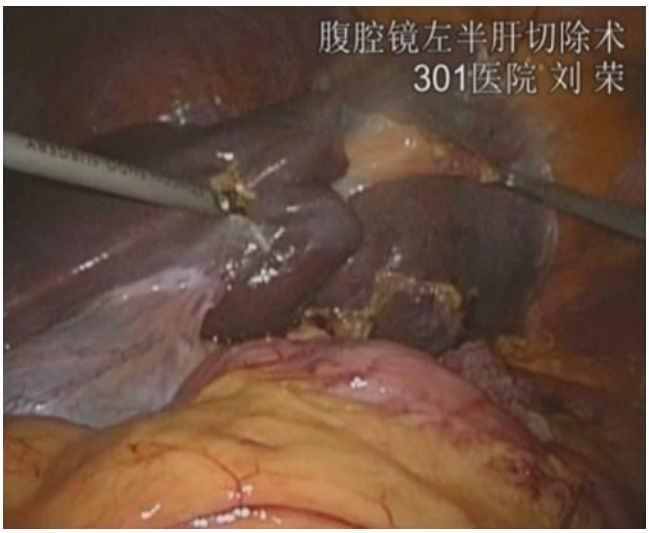

Fig. 24.35 The hepatic parenchyma was transected along the ischemic line

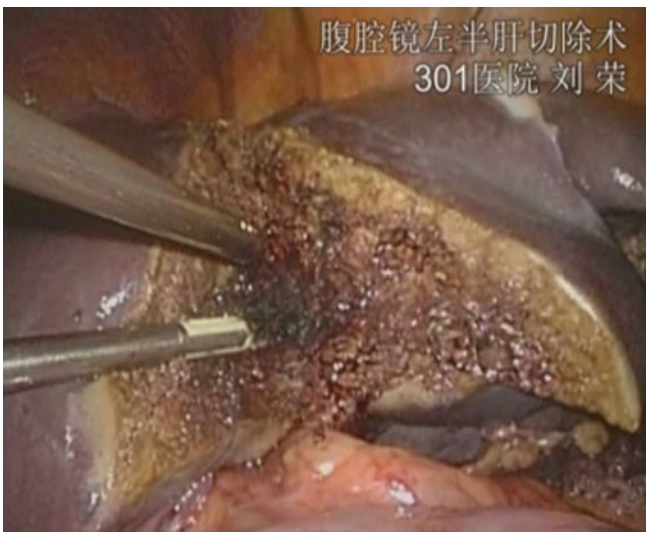

Fig. 24.37 The active bleeding of the incisional surface was coagulated using BiClamp

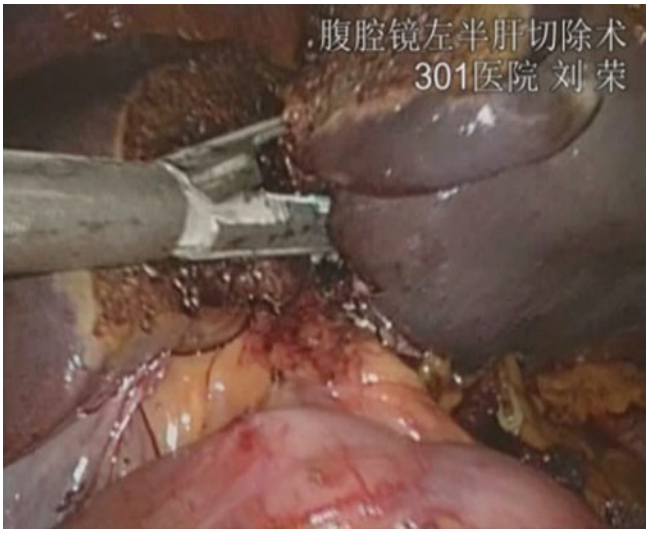

Fig. 24.38 The left porta hepatis was closed using endoscopic linear cutter stapler

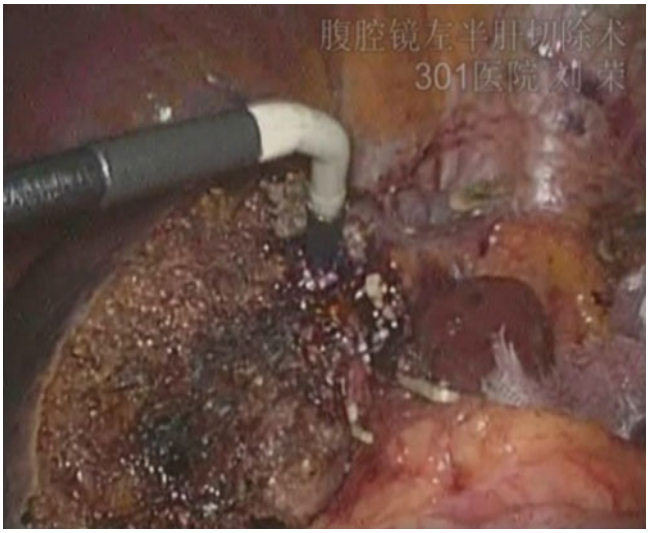

Fig. 24.40 The bleeding of incisional surface was coagulated

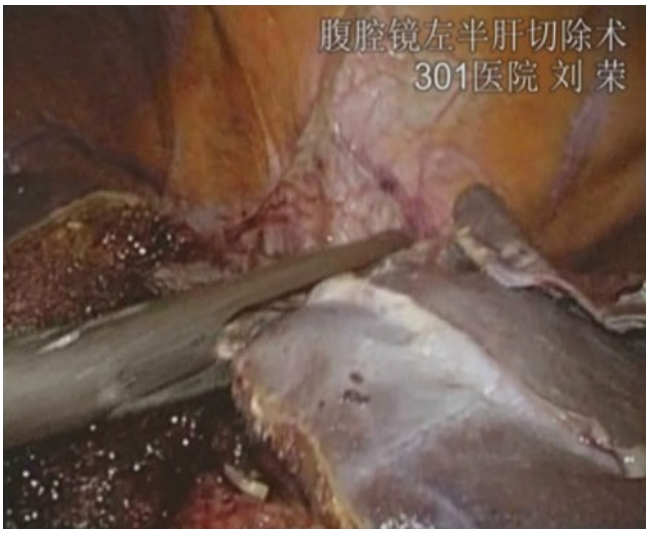

Fig. 24.39 The left hepatic vein was closed using endoscopic linear cutter stapler

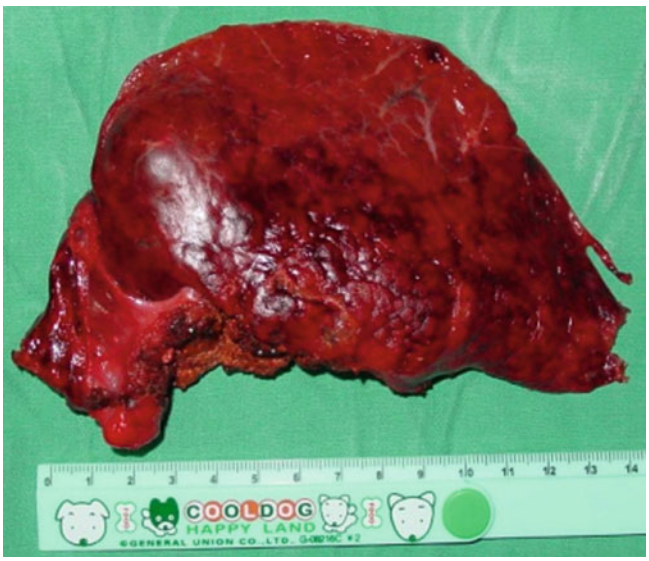

Fig. 24.41 The specimen

24.7.5 Laparoscopic Right Hemihepatectomy

The ligaments around the liver was disconnected after exploration to achieve sufficient mobilization of the right lobe of the liver. The short hepatic vein can be dissected and disconnected if necessary.

The gallbladder was resected and the vessels in porta hepatis were dissected. The right hepatic artery was disconnected after ligation, while the right branch of the portal vein was ligated or clamped without disconnection. Intrahepatic handling of the right hepatic duct was performed later.

The liver parenchyma was transected along the ischemic line, and the methods were as discussed above in the section of laparoscopic left hemihepatectomy. Also, two endoscopic linear cutter scalpels were used for the roughly dissected vessels in the first and second porta hepatis. The parenchyma was transected along the right side of the ischemic line in the diaphragmatic surface, while in the visceral surface, it can be transected in the right caudate lobe to avoid the handling of the right hepatic vein.

The incisional surface and the specimen were handled as was discussed in the section of laparoscopic left hemihepatectomy.

Laparoscopic right hemihepatectomy

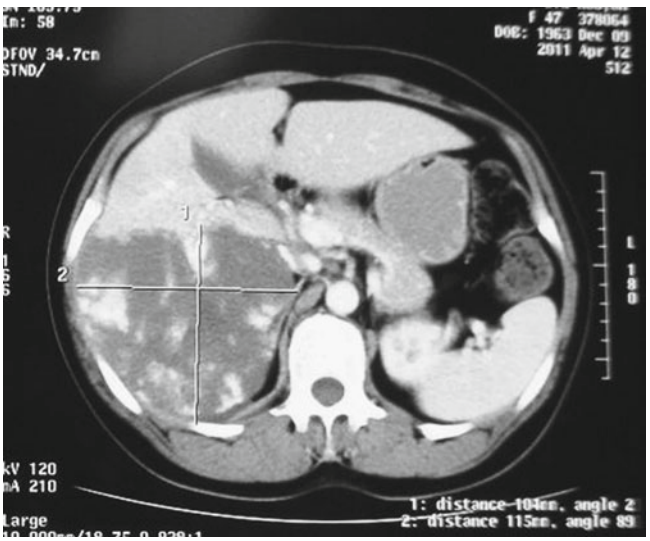

Fig. 24.42 A huge hemangioma in the right lobe

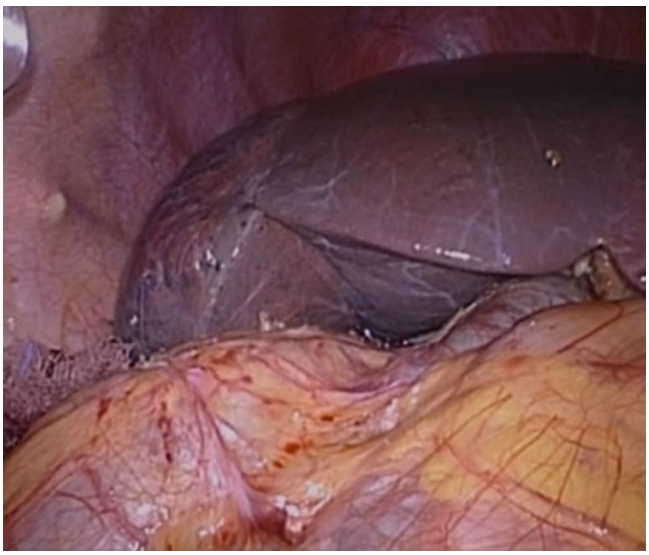

Fig. 24.43 The tumor was found to be located in the right posterior section intraoperatively

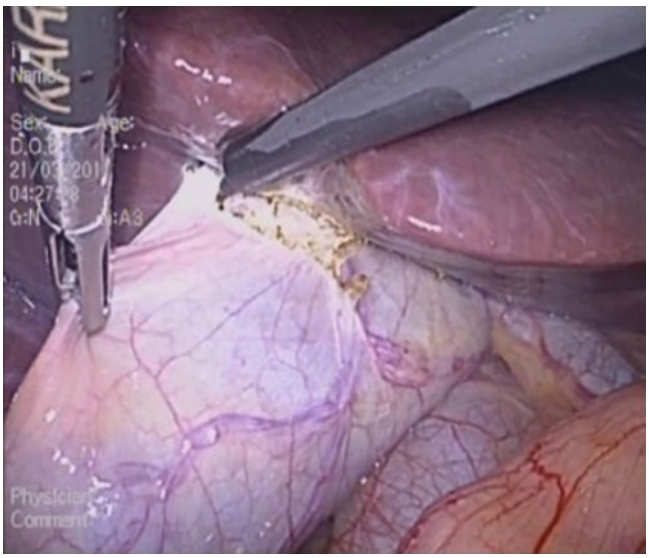

Fig. 24.44 The mobilization of the gallbladder

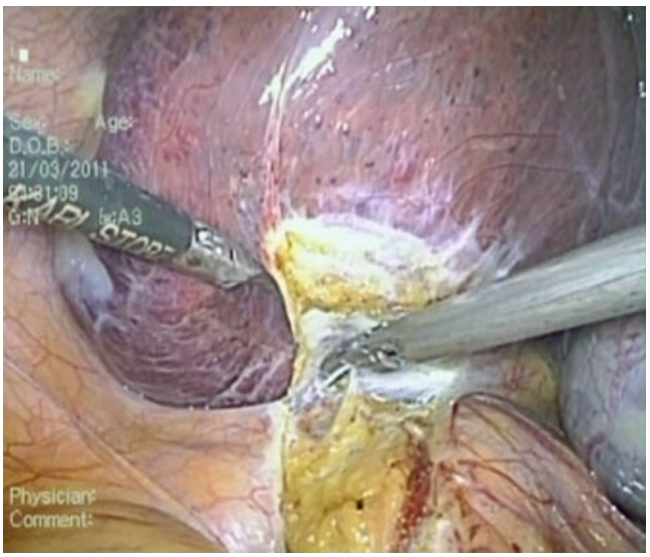

Fig. 24.45 The hepatorenal ligament was disconnected to mobilize the right lobe

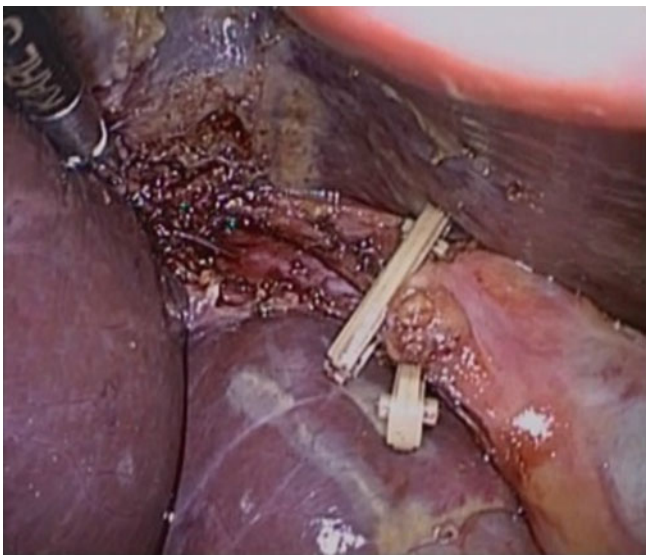

Fig. 24.47 The disconnection of right hepatic artery

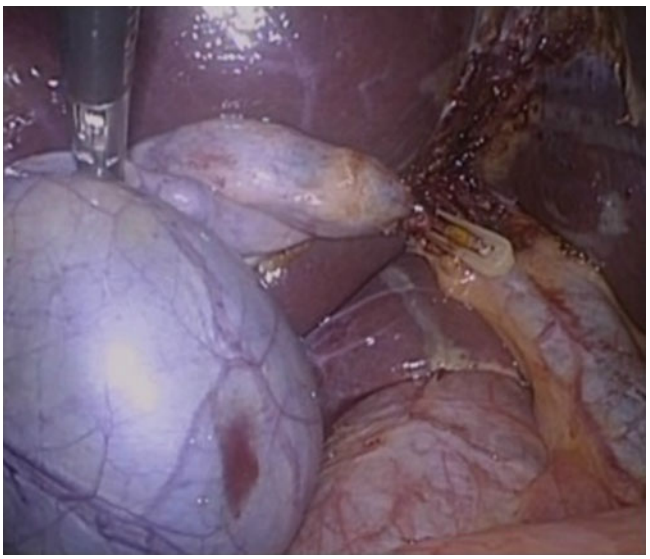

Fig. 24.46 The dissection of Calot's triangle

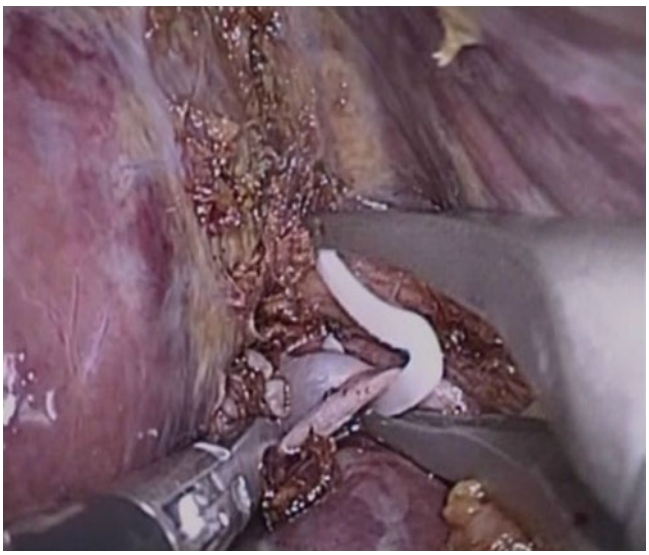

Fig. 24.48 The right branch of portal vein was clamped using Ham-o-lok

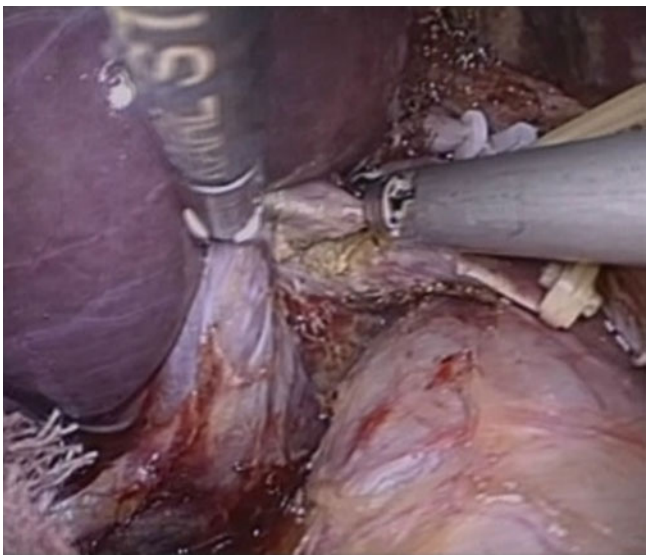

Fig. 24.49 The right caudate lobe was transected

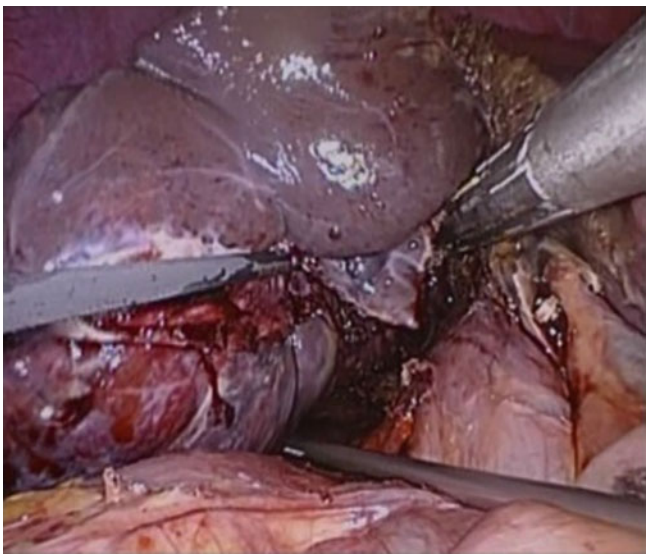

Fig. 24.51 The right porta hepatis was disconnected using an endoscopic linear cutter scalpel

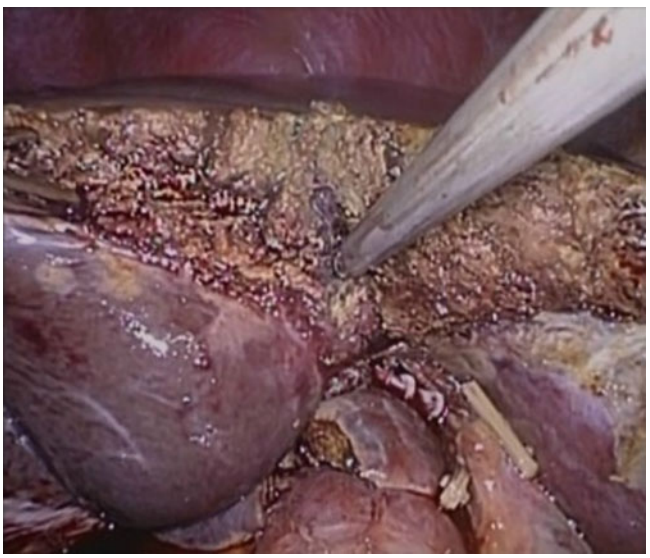

Fig. 24.50 The hepatic parenchyma was transected above the right porta hepatis

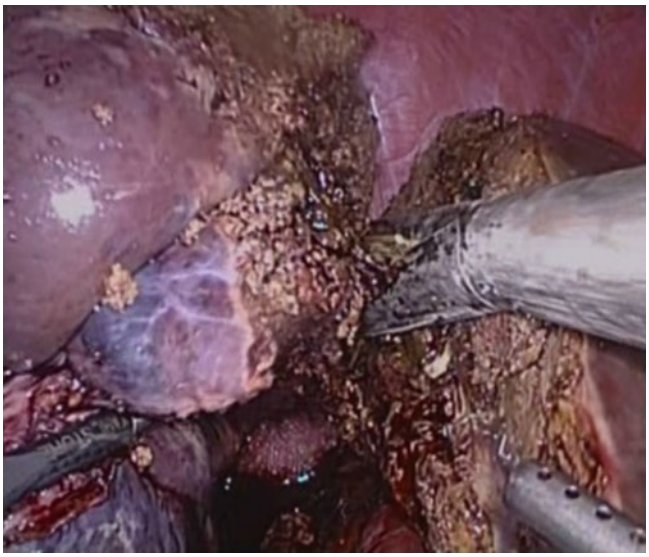

Fig. 24.52 The right hepatic vein was disconnected using an endoscopic linear cutter scalpel

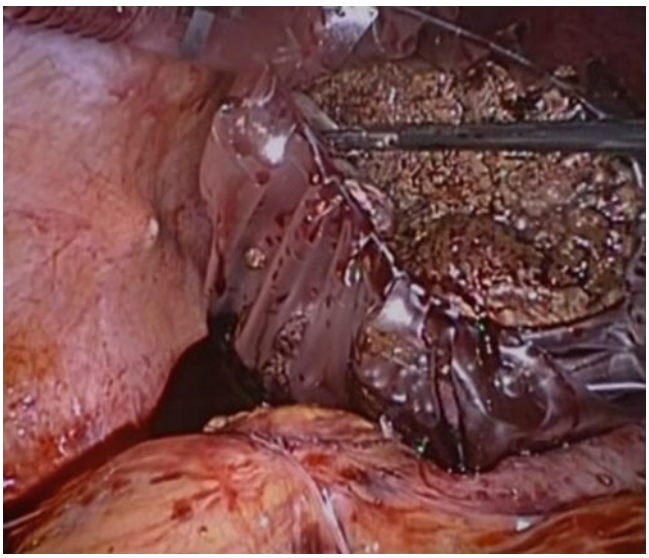

Fig. 24.53 The specimen was put in a disposable bag

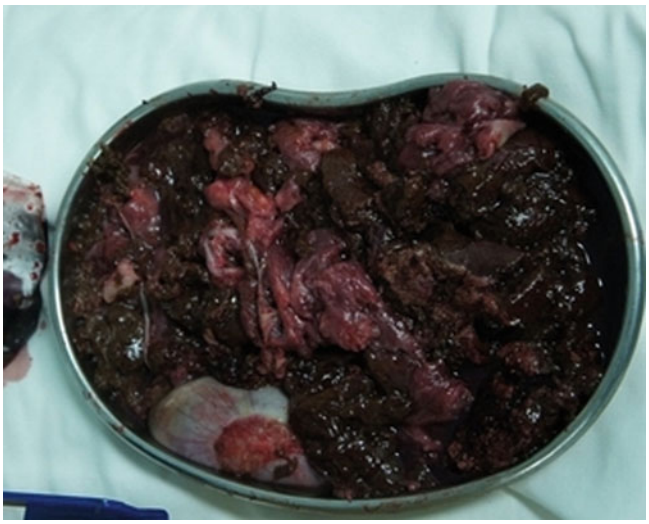

Fig. 24.54 The specimen was clamped and extracted

24.7.6 Retroperitoneal Laparoscopic Hepatectomy

This method was first reported by our team, which was a novel, simple, and direct approach. However, the indications are relatively limited, which were some superficial tumors near the adrenal gland (mainly located in segment VI), especially when the patient had a history of abdominal surgery which results in difficulty in exposing the tumor laparoscopically. This method expanded the indications of LLR.

The patients were first placed in the left lateral recumbent position, with a lunar pad inserted to lift the waist and relax the left hypochondriac region. A 2–3 cm incision was created below the tip of the twelfth rib, and a blunt dissection of subcutaneous tissue, abdominal muscles, and transversalis fascia was performed. A disposable balloon catheter of 600 ml was inserted for 3 min. After that, a 5 mm trocar was inserted below the left costal margin of the eleventh rib, a 10 mm trocar was inserted 2 cm above the iliac crest in the midaxillary line, and a 12 mm trocar was inserted in the abovementioned incision, and the incision was sutured to avoid gas leak. Three ports were needed. The establishment of retroperitoneal space and the placement of trocars can be performed similar as the methods used in laparoscopic retroperitoneal pancreatectomy [63].

After the retroperitoneal space was established, an ultrasonic scalpel was used to dissociate all of the retroperitoneal fat tissue from top to bottom, and the perirenal fascia and the lateroconal fascia were exposed, which were cut inside of the peritoneal fold. The tissue was continuously dissociated toward the superoanterior area along the perirenal fascia to expand the perirenal space up to the posterior edge of the right lobe of the liver.

The peritoneum around the right posterior segment of the liver was dissociated to expose segment VI of the liver, and exploration of the tumor can be performed.

The ultrasonic scalpel was used to cut the liver parenchyma, and the tumor was resected. The wound was coagulated using an argon beam coagulator, and the specimen was placed into a disposable bag and removed from the 12 mm trocar. One to two drainage tubes were placed through the side port.

Ham-o-lok can be used to clamp the leak site when the peritoneum was injured, and a 5 mm trocar can be used for exhaust if the Ham-o-lok did not work well.

Retroperitoneal laparoscopic hepatectomy

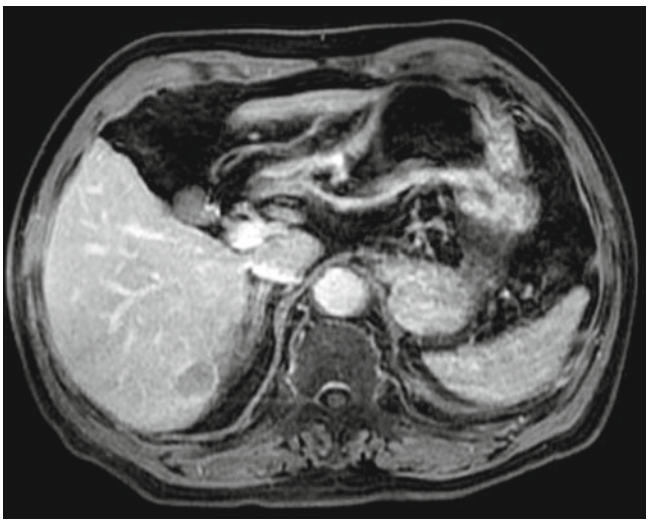

Fig. 24.55 The tumor was located in segment VI, near the adrenal gland

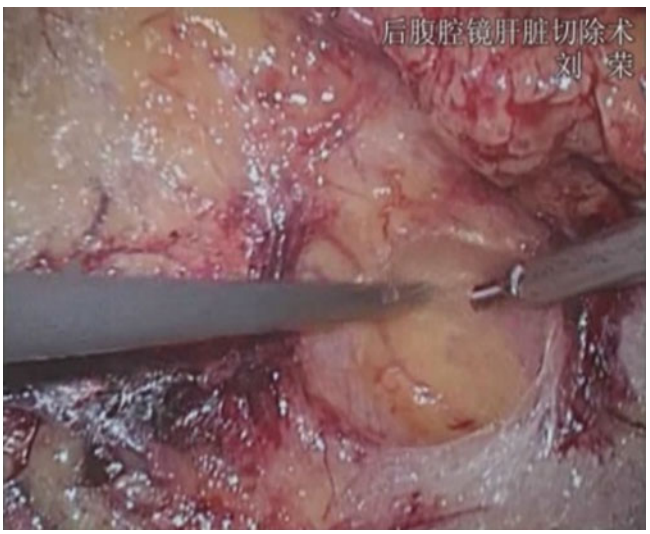

Fig. 24.56 The perirenal fascia and lateroconal fascia were cut inside of the peritoneal fold to enter perirenal space

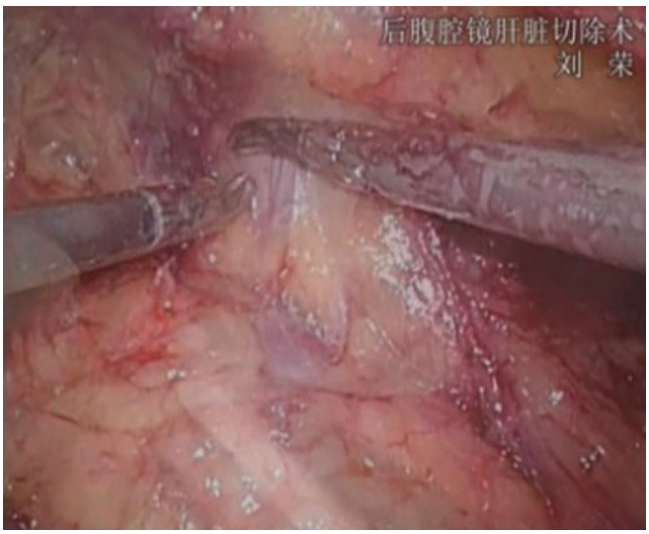

Fig. 24.57 The perirenal fat was dissociated toward superoanterior to expand the perirenal space

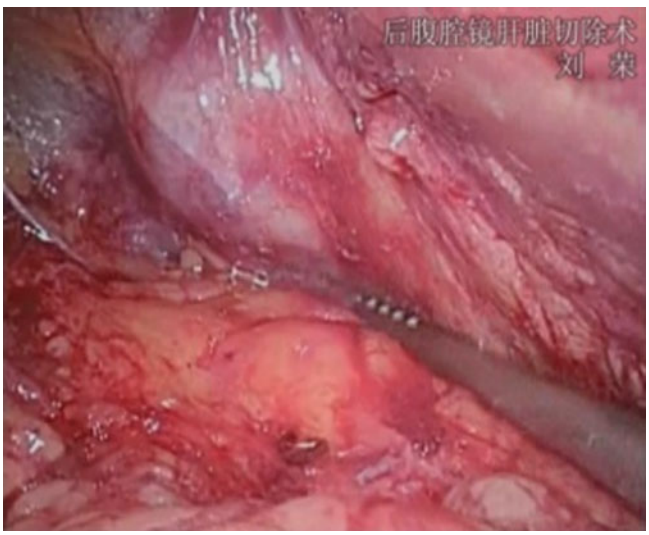

Fig. 24.58 The tumor in segment VI was exposed

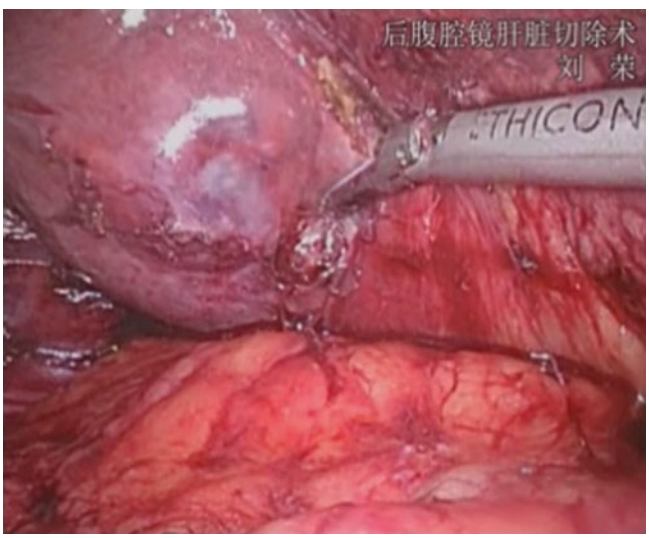

Fig. 24.59 The peritoneum around the right posterior segment of the liver was dissociated

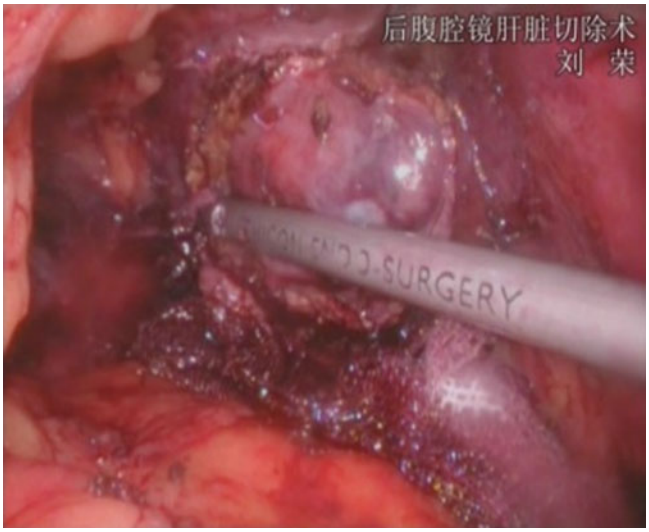

Fig. 24.60 The tumor was resected using ultrasonic scalpel

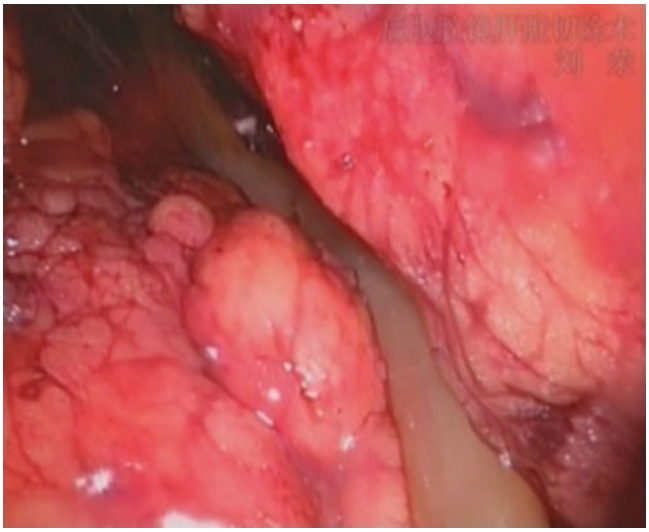

Fig. 24.62 A drainage tube was inserted

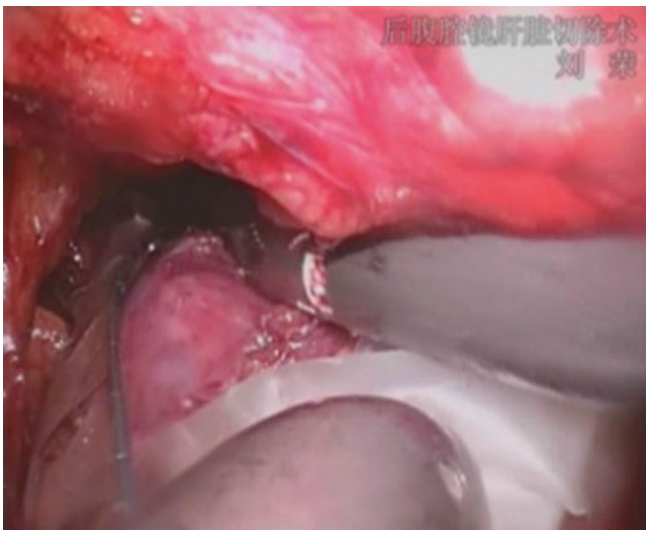

Fig. 24.61 The specimen was placed in a disposable bag

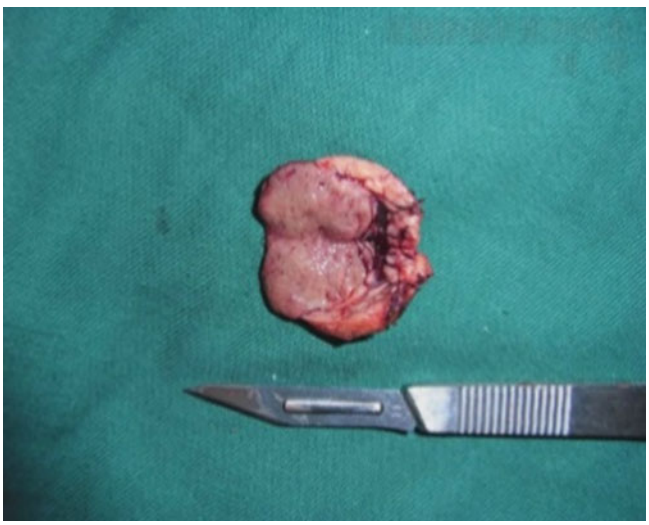

Fig. 24.63 The specimen

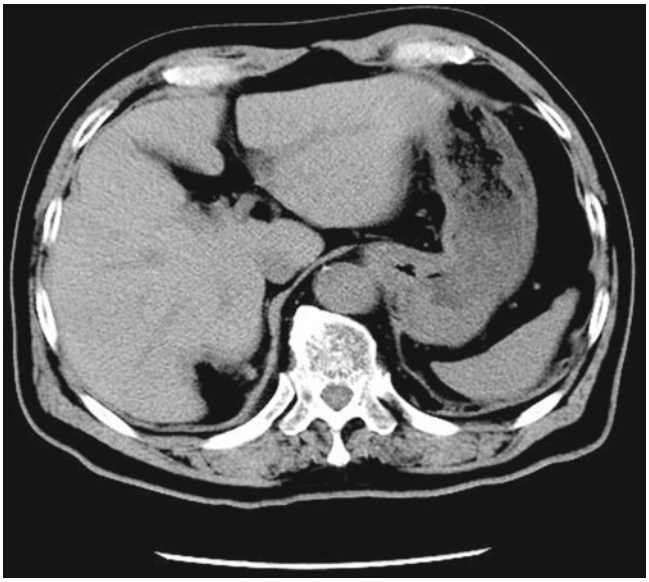

Fig. 24.64 The CT images 1 week after the operation

24.8 Complications

The mortality and morbidity rates of laparoscopic liver resection reported in literature are at least equivalent to if not better than those of large series of open-liver resections. Nguyen and colleagues [17] found a cumulative mortality rate of 0.3 % which was favorable compared to the 0–5.4 % reported in an open resection literature from high-volume centers. All deaths were postoperative and most often caused by liver and multiorgan dysfunction. Of 2804 patients, a total of 295 cases of complications were reported (10.5 %). Liver-specific complications included bile leaks (1.5 %), transient liver failure/ascites (1 %), and abscess (2 %). The remaining 6 % complications were those common to all operations, including wound infection, hernia, bowel injury, arrhythmia, and urinary or respiratory tract infections.

Despite the recent improvements in sealing parenchymal vessels, intraoperative hemorrhage remains the most common life-threatening complication which may lead to conversion to open surgery and postoperative complications. To assess existing resources and validated methods available to control bleeding during laparoscopic liver surgery, Hasrien and colleagues [64] conducted a comprehensive review of the literature. They recommend that (1) a pneumoperitoneum of 10–14 mmHg should be used as it allows a good control of the bleeding without significant modifications of hemodynamics; (2) a low central venous pressure (<5 mmHg) should be used; (3) laparoscopy facilitates inflow and outflow control; and (4) surgeons should be experienced in the use of all surgical devices for liver resection and should master laparoscopic suture before starting LLR. Precoagulation with radiofrequency can be useful, particularly in cases of atypical resection.

Laparoscopic liver resection carries an increased risk of gas embolism when compared with an open approach [49]. Gas embolism is a life-threatening complication in the presence of pneumoperitoneum, but it is very rare. Based on our experience, there is hardly any risk of gas embolism if the blood flow in large vein is not exposed to gas.

Barriers to the wide acceptance of laparoscopic surgery such as threat of gas embolism, violation of oncologic principles, port-site metastases, and significant bleeding have not been evidenced in the literature. Other less frequent complications, such as intestinal or organ damage, are usually the results of technical error.

24.9 Summary

As is discussed above, laparoscopic liver resection is technically feasible and safe. Small tumors located in the left lateral section are most suitable for the laparoscopic approach. Complicated liver resection can be feasible if patient selection is appropriate, the surgeon is with expertise, and the appropriate instruments are available. Complication and conversion rates are acceptable. Although the indications for laparoscopic surgery were once rigid in relation to lesion size and location, increasing experiences and newly developed technology are continually expanding the possibilities of this procedure.

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Application of PVE in Hepatic Surgery

25

Hong Wu, Yong Zeng, Jiaxin Li, and Jingcheng Hao

25.1 Definition

Portal vein embolization (PVE) is a method for selectively embolizing a branch of the portal vein, changing the hemodynamics of the portal vein, or increasing portal vein flow in a non-embolized liver lobe, resulting in non-embolized lobe regeneration and embolized lobe atrophy. Due to its beneficial effects with respect to liver volume and function, the complication rates of major hepatectomy have been reduced, and surgical options have been brought to patients with future liver remnant (FLR) that are insufficient for a direct operation. This pre-hepatectomy procedure has therefore been widely utilized in the context of major hepatectomy (Fig. 25.1) [1–3].

25.2 History

In 1920, Rous first observed ligated lobe atrophy and unligated lobe regeneration after ligation of one branch of the portal vein in rabbit. In 1975, Honjo reported on portal vein ligation in HCC patients. In 1986, Kinoshita first utilized PVE to control tumor progression in HCC patients who failed TACE and accidently discovered that the non-embolized lobe regenerated. In 1987, a preoperative selective PVE of the right PV was applied in an extended right hemihepatectomy of a liver tumor metastasis. In 1990, Mukuuchi first used PVE in a major hepatectomy for hilar cholangiocarcinoma. Preoperative PVEs were infrequently performed in Japan and France in the 1990s, with global adoption of the technique being a recent event. This method extends the indications of liver resection, increases the safety of surgery, and reduces complications, which explains why PVE has been widely adopted [1, 4–7].

25.3 Indications and Contraindications

Indications: PVE can be performed in major hepatectomies that are intended for curative resection, such as for large volume or certain locations of primary (or metastatic) liver cancer, hilar cholangiocarcinoma, and gallbladder carcinoma. Due to the high risk of a direct operation, PVE can also be considered in patients with FLR/TLV <25 % and a normal liver or in patients with FLR/TLV <40 % and an abnormal condition [8–10].

Contraindication: Absolute contraindication: Patients with portal vein obstruction, serious cirrhosis or esophageal varices, extrahepatic metastasis, or lymphadenectasis around the portal vein. Relative contraindication: cachexia; dysfunction of the heart, lung, or renal system; seriously reduced liver function; coagulation disorders; and intrahepatic metastasis.

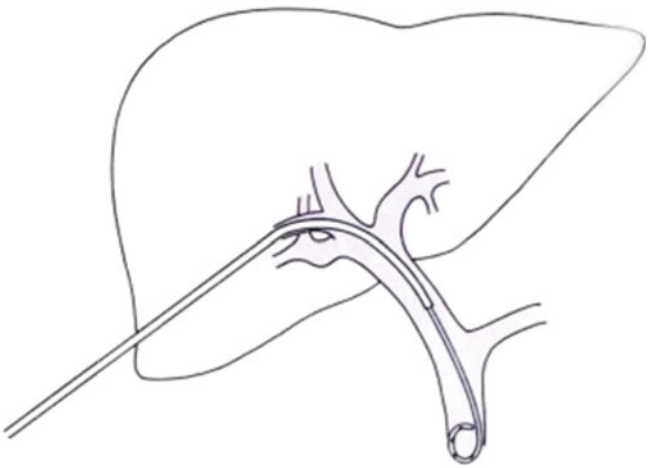

Fig. 25.1 Portal vein puncture

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25.4 Choice of Embolic Agents

The ideal embolic agents for PVE should be economical, nontoxic, permanent, complete, non-recanalizing, and radiopaque. There are many current options, such as gelatin sponges, dehydrated alcohol, polyvinyl alcohol (PVA), and steel bands. Recanalization is guaranteed with the use of a gelatin sponge with fibrin sealant. Periportal fibrosis, which can make the following surgery difficult, is frequently impermanent, and various degrees of stomachache can occur following the use of dehydrated alcohol. PVA for distant branches and springs for the proximal portal vein are stable and permanent and also contribute to the regeneration of the FLR after PVE and preventing PVA contraflow; however, these methods can result in peripylephlebitis.

25.5 Clinical Procedure

There are two main procedures for PVE: percutaneous transhepatic portal vein embolization (PTPE) by ultrasound and transileocolic portal embolization (TIPE) [11, 12].

25.5.1 PTPE

This procedure can be performed via a contralateral or ipsilateral approach. The contralateral approach (i.e., not the embolized side) is an easy and direct approach for puncturing the vein for large tumors. PTPE can be used to avoid injuring the remnant liver when performed via an ipsilateral approach, but it is technically demanding due to the anatomy of ipsilateral tumors and the right portal vein [13].

Steps:

Puncture the portal vein: *Local anesthesia should be applied first. Using ultrasound, a Chiba needle should be used to puncture the portal vein branch of the pre-resected liver lobe. The vein should then be catheterized into the cranial mesenteric vein.*

Note: It is better to puncture during normal breathing and to avoid puncturing the lung, which results in aeropleura when the right spatium intercostale approach is adopted. There should be no tumors or blood vessels along the route to the puncture site. Therefore, the second branch is the optimum level.

Portal vein radiography: *A favorable position should be selected, such as the right anterior oblique of 30°, to ensure the situation of the right portal vein branches* (Fig. 25.2). *The flow rate of the contrast agent should controlled at 6 ml/s for 4 s.*

Next, catheterize the branch to be embolized, and use a gelatin sponge, springs, dehydrated alcohol, or PVA to completely embolize the branch. Perform radiography following the procedure to ensure that the branch is completely embolized (Figs. 25.3 and 25.4).

Use a gelatin sponge and steel bands to embolize the puncture, thereby avoiding abdominal cavity bleeding.

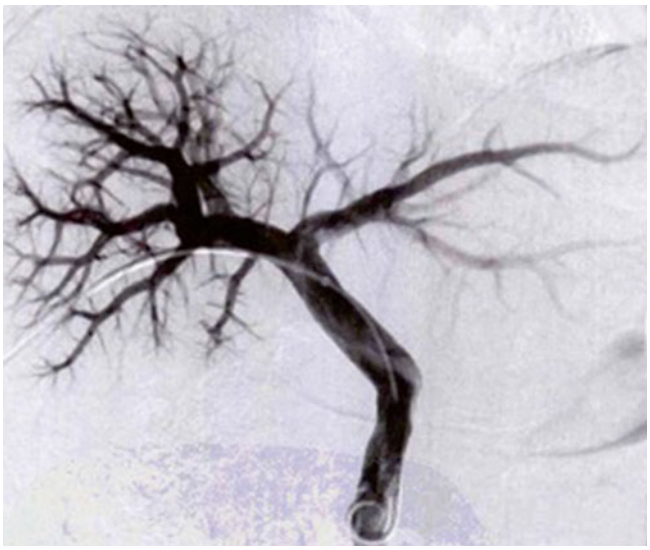

Fig. 25.2 Portal vein radiography

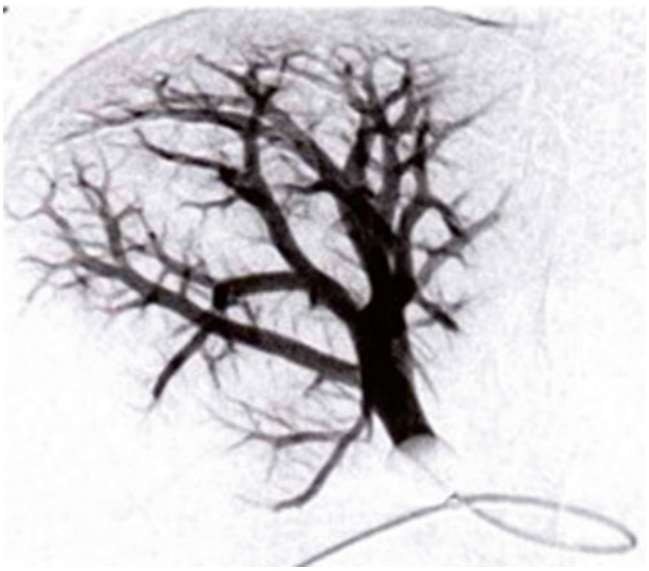

Fig. 25.3 Right anterior branch blocked by the balloon

25.5.2 TIPE

TIPE can be performed due to the requirements of the institution and can be performed as an open or laparoscopic TIPE. This method is usually utilized when a PTPE cannot

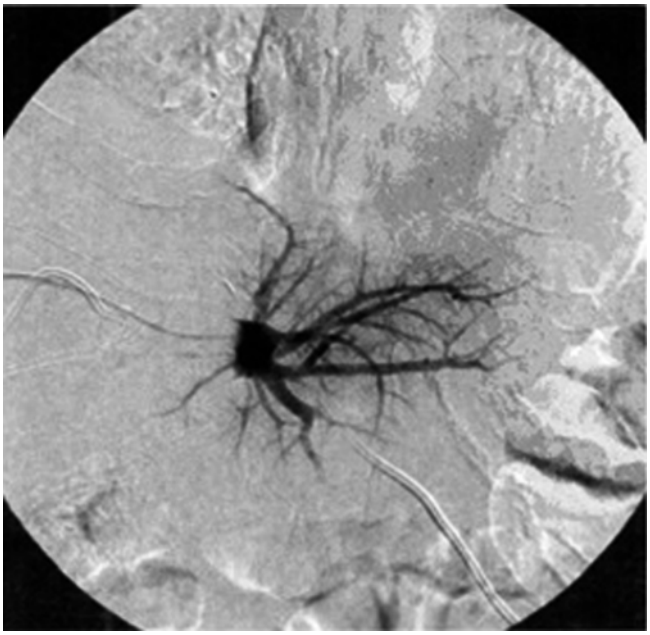

Fig. 25.4 Image of the left branch following blockage of the right branch by the balloon

be performed or when a hepatectomy is not possible because of the high risk of liver failure due to an insufficient FLR. For these reasons, TIPE is therefore little used.

25.6 Complications

PVE-related complications are infrequent (9.1–12.8 %) and include ectopic embolization, portal vein thrombosis, and portal hypertension. Complications can result in esophageal varices bleeding, hepatic subcapsular hemorrhage, bile duct hemorrhage, etc. These issues are primarily technical complications and relate to the puncture position and surgical method.

25.7 Seize the Opportunity to Perform a Hepatectomy

Whether a hepatectomy can be performed depends on liver function recovery following the PVE. The normal liver has a powerful ability to regenerate; the FLR volume can increase by 10 % and the embolized lobe can decrease by 10 % within 2–8 weeks after PVE. For the PVE method, which uses steels bands and PVA, the non-embolized lobe is significantly stimulated to regenerate 2 weeks after PVE. A major hepatectomy could be performed 2–3 weeks after PVE. Therefore, liver volume should be evaluated 2–3 weeks after PVE if liver function is normal and 3–4 weeks after PVE if the liver

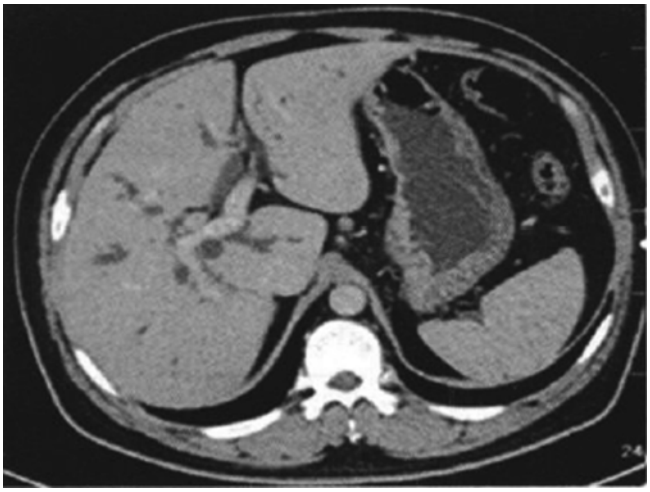

Fig. 25.5 Preoperative CT

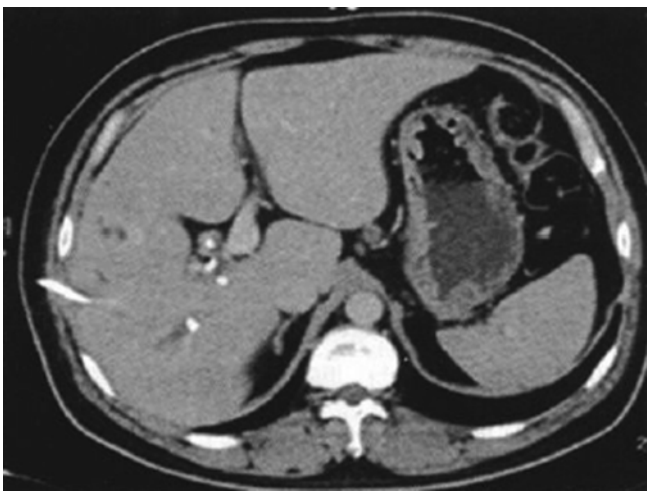

Fig. 25.6 Two weeks postoperative CT

function is abnormal. Once the liver volume is sufficient, the opportunity to perform surgery should be seized depending on other relevant factors (Figs. 25.5, 25.6, and 25.7) [14, 15].

25.8 Prospects

Although PVE was proposed more than 20 years ago, the mode of embolization and the choice of embolic agent remain controversial. However, PVE results in liver function compensation and increases the FLR volume. PVE also contributes outstandingly to expanding the indication of major hepatectomy and to increasing both the safety of the surgery and the survival rates. However, some studies have reported that FLR regeneration cannot be expected in the context of cirrhosis. The indication for PVE should be extended once there is further technical progress, improved operative

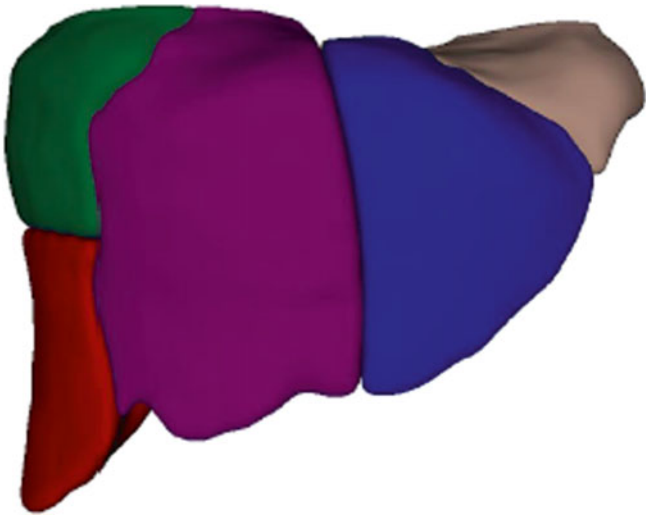

Fig. 25.7 Three-dimensional liver reconstructed to calculate the volume

technique, and more in-depth studies on liver regeneration. More studies are necessary to improve PVE from methodological and technical standpoints and to improve the quality and speed of FLR regeneration.

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Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy

26

Hong Wu and Gang Pan

26.1 Definition

Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) is a novel method in which the right portal vein is ligated with in situ splitting to induce rapid remnant liver regeneration and a complete second-stage hepatectomy is performed 2–3 weeks following the ligation after regeneration is evaluated [1–4].

26.2 History

In 2007, the German doctor Schlit accidentally discovered that the left lobe could rapidly regenerate 8 days after portal vein ligation and in situ splitting along the falciform ligament. Then, Schlit performed this method on a series of selected patients before communicating with other surgeons in Germany on two cases. Baumgart first reported the outcome of three cases of ALPPS in a poster presentation in 2011. Schnitzbauer summarized the clinical data of 25 cases of ALPPS in five centers in Germany, publishing them in the *Annals of Surgery* in 2012. At this point, this method was formally named ALPPS. Recently, ALPPS has become a focus in the field of liver surgery, and its use is widespread around the globe.

26.3 Characteristics of and Traditional Ways to Increase the Future Liver Remnant Volume

Portal vein embolization proposed by Makuuchi, 1990 (Fig. 26.1) [5]

Two-stage hepatectomy proposed by Adam, 2000: First, resect the tumors from the FLR (infrequently, this step is combined with PVE); then, perform the hemihepatectomy after the FLR regenerates (Fig. 26.2) [2].

Two-stage hepatectomy proposed by Clavien, 2007: Perform a wedge-shaped resection of all left-side tumors, and ligate the right portal vein during the first stage. Complete the extended right hemihepatectomy when the left lobe is adequately regenerated, after a few weeks (Fig. 26.3) [4].

Characteristics of the two-stage hepatectomy:

Advantages: This procedure stimulates FLR regeneration and leaves open operative opportunities for patients with giant liver cancer [6].

Limitations: (1) The tumor may progress in the long interval between the two stages, which exceeds an average of 4 weeks. (2) The adhesion that results from the first stage may make the second stage more difficult. (3)FLR regeneration may not be satisfactory (10–46 % in 2–8 weeks) [7].

26.4 Initial Proposition of ALPPS

Schnitzbauer summarized the clinical data of 25 cases of ALPPS in five centers in Germany, constituting the initially proposed technique (Fig. 26.4).

Advantages: (1) The adhesion can be easily handled due to the short interval (~1 week) between the two surgeries. (2) The FLR regenerates rapidly, within 7 days after the first surgery (74–87 %). (3) The tumors in the FLR or in other organs can simultaneously be resected in the first stage [7].

Limitations: (1) High morbidity (53–90 %) and mortality (0–28 %) and (2) no report on long-term outcome.

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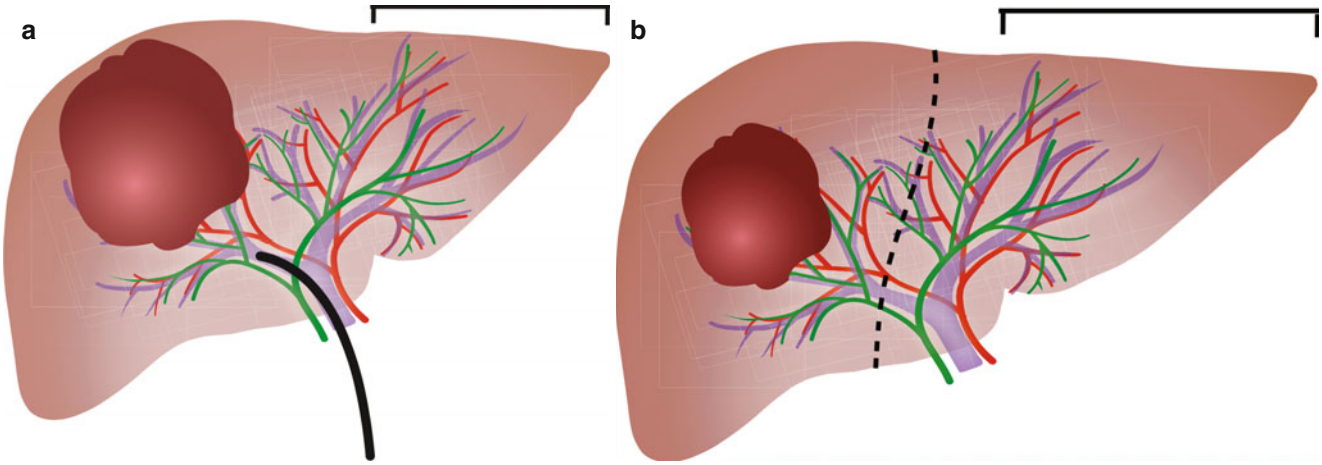

Fig. 26.1 (**a**, **b**) Portal vein embolization to induce FLR regeneration

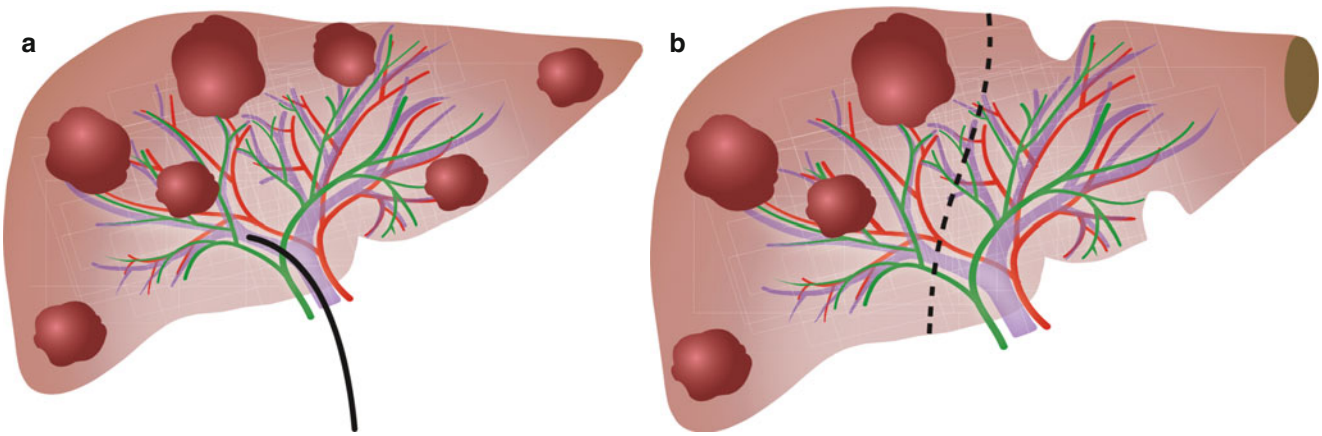

Fig. 26.2 (**a**, **b**) Tumor resection of the FLR combined with PVE to induce FLR regeneration

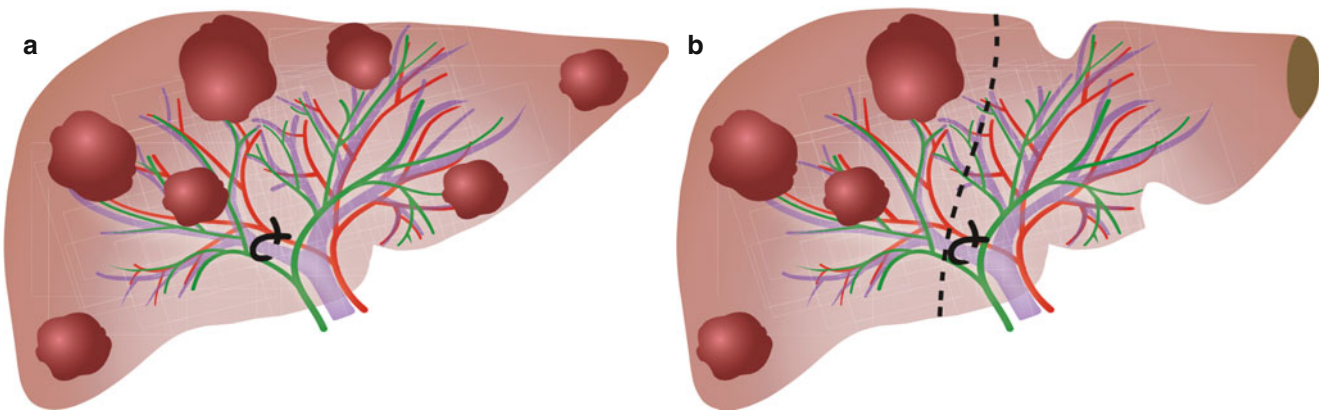

Fig. 26.3 (**a**, **b**) Tumor resection of the FLR and ligate the right portal vein to induce FLR regeneration

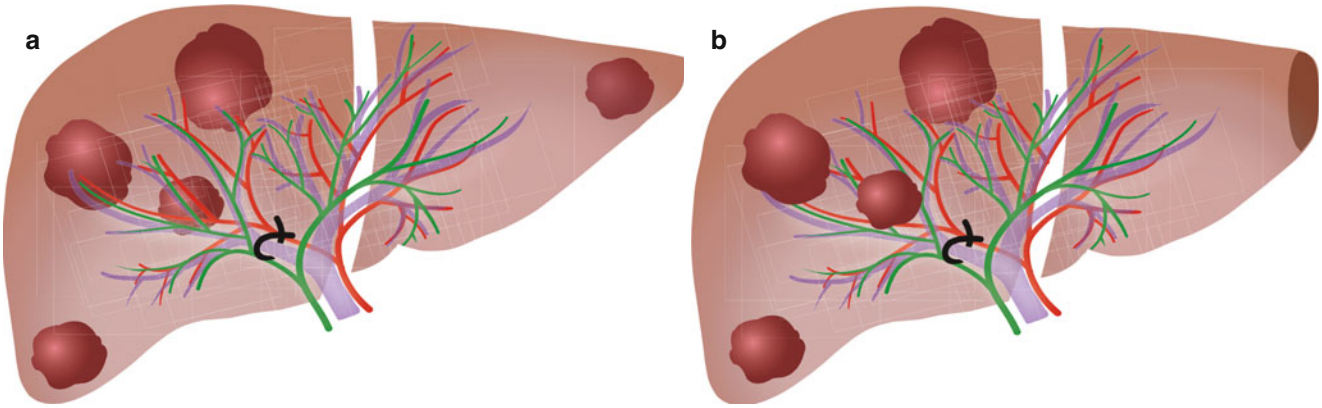

Fig. 26.4 (**a**, **b**) The right portal vein is ligated with in situ splitting to induce rapid remnant liver regeneration

26.5 Indication

(1) Normal liver, FLR <30 %; (2) liver with jaundice or cirrhosis, FLR <40 %; (3) liver metastases from colorectal cancer, giant HCC, or ICC; or (4) FLR cannot reach the expected volume after PVE

26.6 Contraindication

(1) Unresectable tumors in FLR, (2) unresectable primary tumors or extrahepatic metastases, or (3) unreachable R0 resection of liver metastases [8–10]

26.7 Technical Points

1. Steps: Ligation of the portal vein with in situ splitting, followed by major hepatectomy [11, 12]
2. Operation method: Open or laparoscopic

Technical Points of Open ALPPS

1. Choice of incision
   An inverted "L" incision is regularly adopted due to the better operative field and convenient hilar handling (Fig. 26.5).
2. Skeletonize the first portal and expose the hepatic artery, bile duct, and portal vein. Then, ligate the portal vein if needed. Wrap silk sutures around the hepatic artery and bile duct to ligate during the second stage (Fig. 26.6).
3. Parenchymal dissection with an anterior approach to the caval vein. Maintain rigorous hemostasis on bilateral sections and ligate the bile capillary (Fig. 26.7).
4. Evaluate the FLR 1 week after surgery (Fig. 26.8).

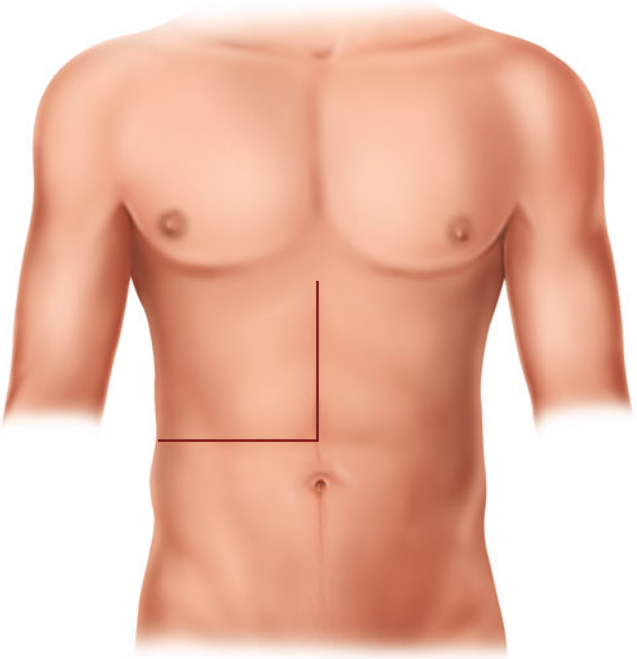

Fig. 26.5 The inverted "L" incision in the right upper abdomen

5. Ligate and cut the hepatic artery, vein, and bile duct; then, remove the abnormal liver (Fig. 26.9).

Technical Points of Laparoscopic ALPPS [13, 14]

1. Position of trocar (Fig. 26.10).
2. Based on the anatomy of the portal vein in the first port, use a Hem-of-lok to occlude the portal vein if needed. Circle a silk suture around the hepatic artery and bile duct to mark the ligation in the second stage (Fig. 26.11).
3. Parenchymal dissection in an anterior approach using ultrasound dissector or LigaSure, maintaining hemostasis using bipolar coagulation. Sutures can be made on the liver section using 4-0 Prolene, if needed. Hemostasis of

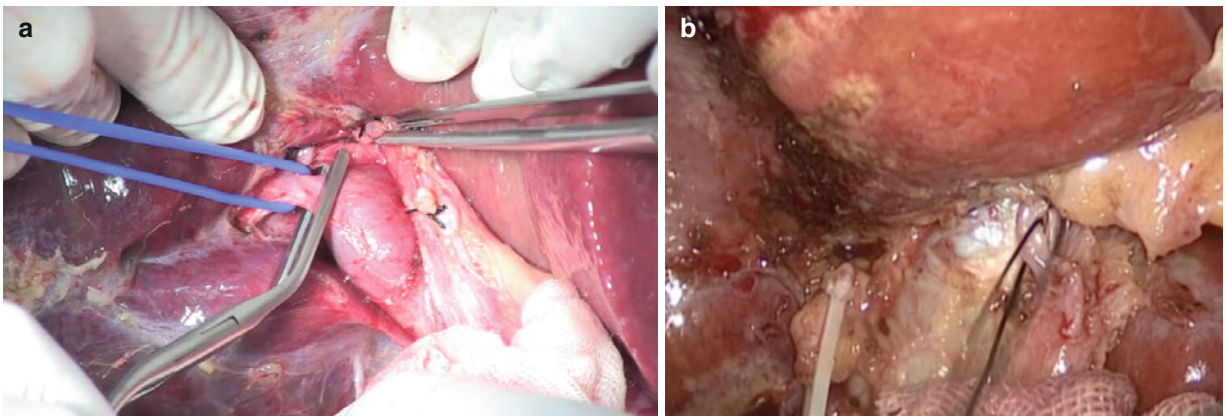

Fig. 26.6 (**a**) Skeletonize and ligate the portal vein; (**b**) wrap silk sutures around the hepatic artery

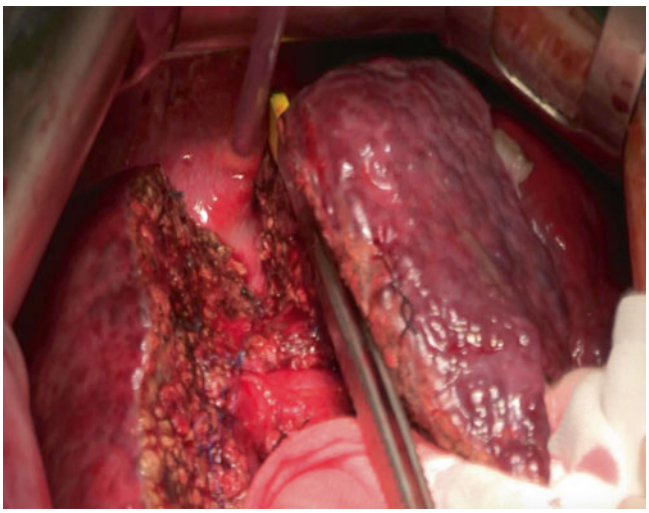

Fig. 26.7 Parenchymal dissection with an anterior approach

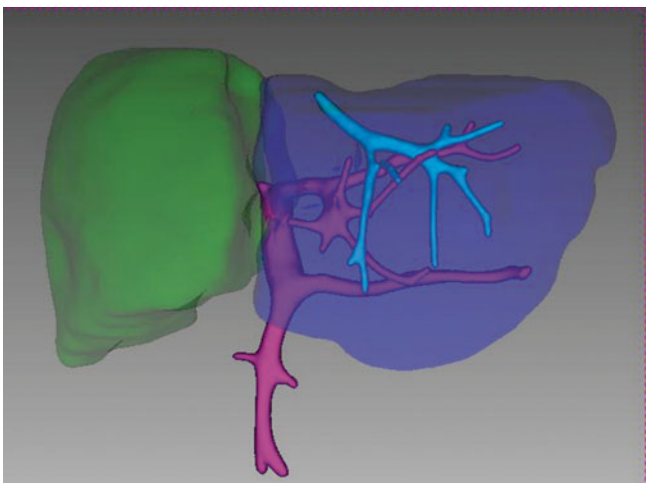

Fig. 26.8 Evaluate the volume of FLR after surgery

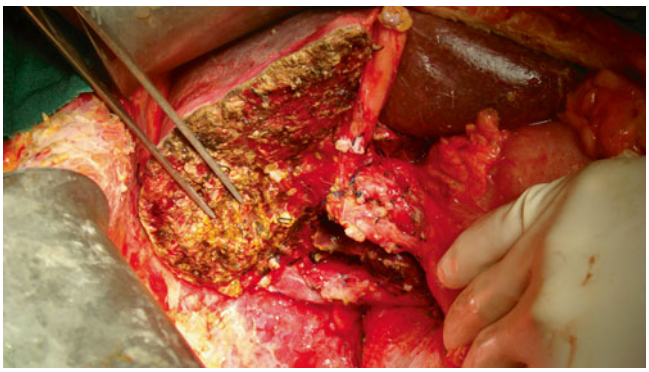

Fig. 26.9 The cutting surface of liver after second-stage hepatectomy

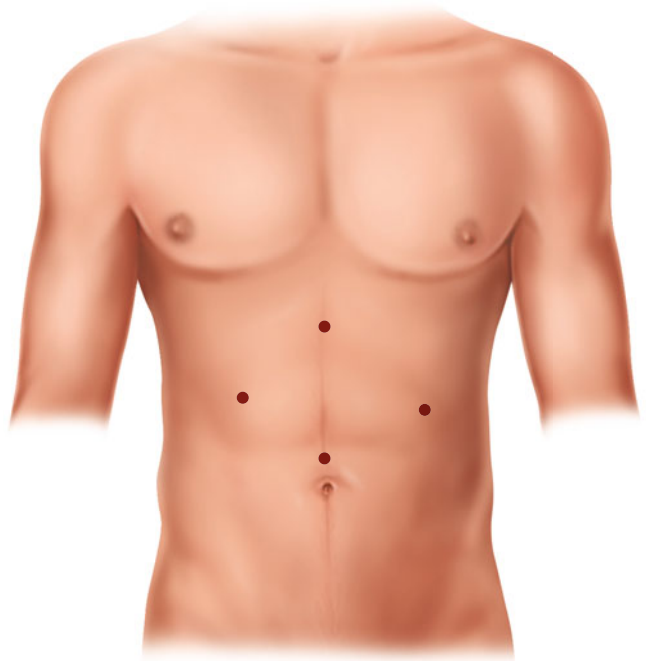

Fig. 26.10 Position of trocar

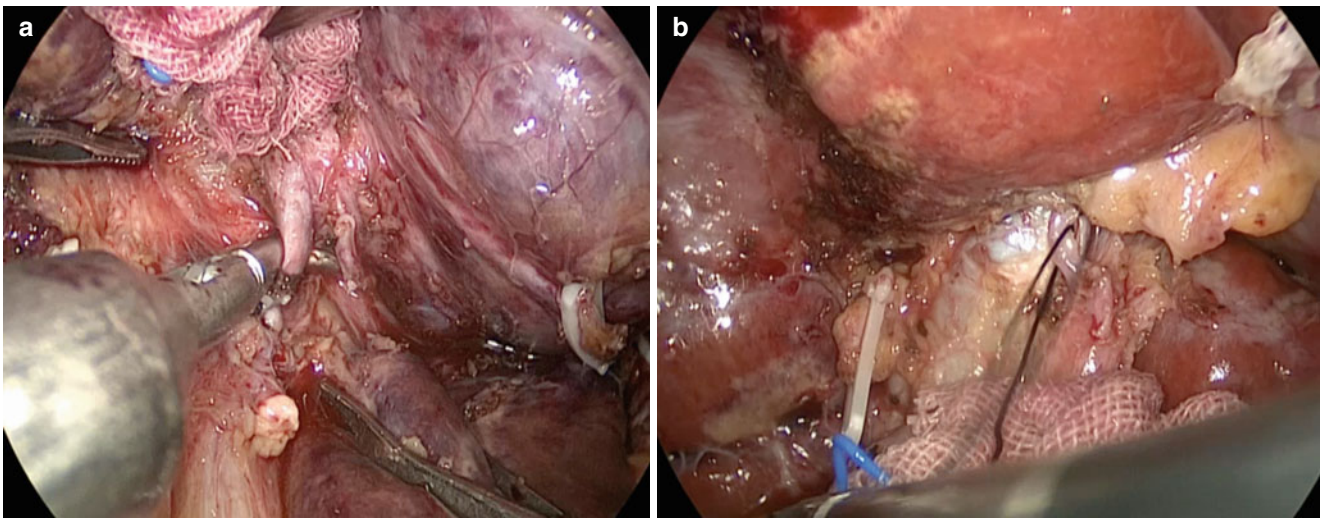

Fig. 26.11 (**a**) Skeletonize and ligate the portal vein by laparoscope; (**b**) wrap silk sutures around the hepatic artery by laparoscope

the liver section should be maintained, the abdominal cavity should be irrigated, and a lack of active bleeding should be confirmed. An adhesion barrier should be placed on the liver section, and the first port, right liver, and liver section should be drained (Fig. 26.12).

4. Evaluation of FLR and preparation for the second stage.

26.8 Handling of the Liver Section in First Stage

(1) Use a plastic bag to cover the right liver to prevent adhesion; in addition, drain the localized bile if leakage occurs. (2) Use Biogel to separate the liver section to prevent adhesion (to simplify the second stage). Drain the first port, right liver, and liver section.

26.9 Prevention and Cure of Complications

The complication rate of ALPPS is as high as 53–90 %, with complications including liver failure, bleeding, bile leakage, and abdominal infection [7, 11].

Prevention of liver failure: Ielpo indicated that the main reasons of liver failure post-ALPPS were hypertransfusion of the portal vein in the remnant liver, sinus hepaticus congestion, and hepatic cell dysfunction. He suggested that portal hypertransfusion should be alleviated by a splenectomy or lienorenal shunt.

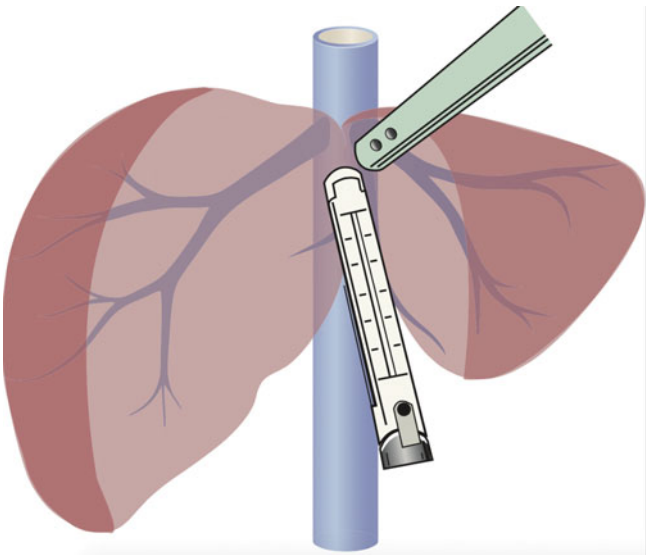

Fig. 26.12 Parenchymal dissection in an anterior approach under laparoscopic

Prevention of bleeding: Ligate the portal vein after the parenchymal dissection, avoiding increased portal vein pressure on the contralateral side, which can result in increased bleeding.

Prevention of bile leakage and infection

(1) Perform a routine preoperative MRCP to examine variations in the bile duct, (2) carefully inspect for bile leakage and ligate any leaks that are found, (3) perform operative cholangiography, (4) use Biogel to separate the liver section and drain the section, and (5) use antibiotics [11, 12, 15].

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Pediatric Living Donor Liver Transplantation

27

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27.1 History

The first deceased-donor liver transplant attempted by Thomas Starzl on March 1, 1963, involved a pediatric recipient with biliary atresia [1]. The next eight pediatric recipients operated by Starzl in 1967 had a 50 % 1-year survival rate. An immunosuppression regimen based on azathioprine, steroids, and antilymphocyte globulin was used in these patients. As pediatric cadaveric donors were exceedingly few in number, the concept of reduced liver transplantation was introduced in 1984 [2], wherein the remnant portion of the large liver graft was discarded. The first split liver transplantations, with one cadaveric donor used for two recipients, were done by Pichlmayr in Europe (1988) and Broelsch in the United States [3].

The improved understanding of liver anatomy and refinement of techniques of liver resection enabled the development of living-donor liver transplantation (LDLT) in 1989 [4]. The ethical considerations involved in a motivated parent donating a graft to a child were reasonably clear and without suspicion of coercion. The surgical risks involved in harvesting the left lobe or left lateral segment from a healthy donor were also surmountable. Development of LDLT has drastically reduced the number of pediatric patients with end-stage liver disease on the waiting list for DDLT [5]. In the United States, organ allocation system, the PELD (pediatric end-stage liver disease) score as well as the exceptions for certain indications tended to benefit the pediatric population over adult candidates using the MELD (Model for End-Stage Liver Disease) scoring system. Hence, LDLT for children has resulted in increasing the relative availability of grafts for adults with end-stage liver disease.

The first successful liver transplant from a brain-dead donor in Asia was performed in Taiwan in 1984. Pediatric liver transplants for biliary atresia and metabolic diseases were performed soon thereafter. The high endemic rates of viral hepatitis coupled with low organ donation rates due to sociocultural factors propelled the development of LDLT in East Asia. Pediatric LDLT was first performed in Taiwan in 1994. LDLT vastly improves the survival of children with end-stage liver disease, as it enables the availability of a matched size graft from a properly assessed healthy donor on an elective basis. Currently, pediatric LDLT is a significant component of most LDLT programs around the world.

27.2 Indications

Cholestatic diseases like biliary atresia are the most common indications for pediatric LDLT, unlike parenchymal diseases which are more common in adults (Table 27.1). Children with defects in the urea cycle and primary hyperoxaluria may require transplant despite the absence of cirrhosis, in order to manage the systemic effects of these metabolic diseases. More commonly, LDLT is done for end-stage liver disease or for congenital diseases refractory to medical management. The timing of transplantation should be optimal, in order to avoid the child falling off the growth curve.

27.2.1 Biliary Atresia

It is the most common cholestatic disorder of childhood and accounts for 50–75 % of pediatric LDLT in most centers [6]. It is characterized by a progressive inflammation of the extrahepatic bile ducts and if left untreated, inevitably leads to cirrhosis and death. A successful hepatic portoenterostomy (Kasai procedure) performed within the first 3 months of life has equivalent survival to liver transplantation performed within the first year [7]. Even then, the child may need a liver transplant at an older age due to increased frequency of cholangitis and failure to thrive. Patients with failed Kasai procedure and those presenting with complications of cirrhosis usually require liver transplantation before 2 years of age.

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Table 27.1 Indications for pediatric LDLT

Cholestatic diseases
Biliary atresia
Alagille syndrome
Familial intrahepatic cholestatic syndrome (Byler disease)
Primary sclerosing cholangitis
Idiopathic
Metabolic diseases
Wilson's disease
α1-Antitrypsin deficiency
Urea cycle defects
Primary hyperoxaluria
Glycogen storage diseases
Crigler-Najjar syndrome
Cystic fibrosis
Hemochromatosis
Familial hypercholesterolemia
Fulminant liver failure and cirrhosis
Neonatal hepatitis
Drug induced (e.g., acetaminophen)
Acute viral hepatitis
Autoimmune hepatitis
Other infectious hepatic failure (syphilis, toxoplasmosis, bacterial)
Idiopathic
Malignancy
Hepatoblastoma
Hepatocellular carcinoma
Hemangioendothelioma
Others
Budd-Chiari syndrome
Congenital hepatic fibrosis

27.2.2 Alagille Syndrome

The hepatic hallmark of this syndrome is the paucity of bile ducts. The cholestasis typically waxes and wanes, and ocular, cardiac, and skeletal manifestations besides hypercholesterolemia may be present. While biliary diversion and medical management may be beneficial in many, liver transplantation can provide a definitive cure in most patients with hepatic effects of this syndrome [8].

27.2.3 Wilson's Disease

This autosomal recessive disease is characterized by increased copper deposition, primarily in the liver and brain. Hepatic manifestations are more common than neurologic symptoms in children. It may present as acute hepatitis or may progress from chronic liver disease to end-stage liver disease. Liver transplant is a curative therapy, indicated for those with severe portal hypertension and those refractory to medical therapy [9].

27.2.4 α1-Antitrypsin Deficiency

This autosomal dominant deficiency in serum α1-antitrypsin is the most common genetic liver disease in children of Northern European descent and the most common metabolic cause of neonatal hepatitis. Children with end-stage liver disease benefit from liver transplantation.

27.2.5 Urea Cycle Defects

Deficiency of liver enzymes involved in metabolizing ammonia to urea results in hyperammonemia and neurologic sequelae. Liver transplantation before the onset of irreversible brain damage can be curative in these children.

27.2.6 Neonatal Hepatitis

It is predominantly caused by infections such as viral (enterovirus; herpes simplex virus; hepatitis A, B, C; cytomegalovirus, Epstein-Barr virus, rubella, etc.), bacterial (*Streptococcus pyogenes*, *Staphylococcus aureus*, tuberculosis, syphilis), toxoplasmosis, etc., although a significant proportion are of idiopathic origin. Other causes include inborn errors of metabolism, mitochondrial defects, adrenal insufficiency, Budd-Chiari syndrome, polycystic disease, etc.

27.2.7 Fulminant Hepatitis

Children of any age can be affected by acute liver failure. Other than the causes enumerated above for neonatal hepatitis, other causes like idiosyncratic or dose-related drug toxicity and autoimmune disease can also cause fulminant hepatitis necessitating liver transplantation.

27.2.8 Liver Tumors

Hepatoblastoma is the most common primary liver tumor in children. The majority of hepatoblastomas can be managed by liver resection and is preceded by chemotherapy if required. However, liver transplantation may be indicated for unresectable intrahepatic tumors. They comprise less than 3 % of pediatric LDLT. Other uncommon tumors like HCC with advanced cirrhosis, and benign tumors like adenoma or arteriovenous malformations replacing nearly all liver tissue, are also indications for liver transplantation.

27.3 Preoperative Evaluation and Management of Recipient

A potential recipient benefits from early referral to a transplant center for simultaneous evaluation and preoperative management by an experienced multidisciplinary team. The diagnosis, severity of disease, and need for liver transplant can be validated, and the evaluation protocol is initiated. The child is put on the waiting list for DDLT according to the regional guidelines. Management based on severity of liver disease, for the specific etiology, and for various complications can be started.

Close consultation among the transplant surgical team, pediatrician, hepatologist, anesthesiologist, radiologist, psychiatrist, nutritionist, social worker, and nursing team is essential. Depending upon coexisting morbidities, consultations from other specialties such as pulmonology, cardiology, nephrology, neurology, hematology, etc., may be required.

A thorough physical examination and investigations are carried out (Table 27.2).

Patients who are medically stable can be investigated on an outpatient basis, whereas those candidates with acute liver failure may need to be managed in an ICU setting. The PELD score was developed to assess the risk of mortality in children with chronic liver disease [10]. It is based on the principle that severity of liver disease is more when multiple hepatic functions such as protein synthesis, bile excretion, and metabolic and immunologic functions are compromised. The urgency for transplantation can thus be assessed using a formula based on the measurement of serum albumin, bilirubin, INR, and growth retardation.

$$\begin{aligned}\text{PELD Score} = 10 \times [&0.48 \times \log_e(\text{total bilirubin}) \\ &+ 1.857 \times \log_e(\text{INR}) - 0.687 \times \log_e(\text{Albumin})] \\ &+ 0.667 (\text{if height} < 2 \text{standard deviations for age}) \\ &+ 0.436 (\text{if age} < 1 \text{year})\end{aligned}$$

Fulminant liver failure (FHF) in children differs from that in adults in its etiology and time to progression. Some cases may resolve without transplantation, and the outcomes of transplantation for FHF are inferior to transplantation for chronic liver disease. Hence, the decision to proceed with LDLT is a difficult one. Prognostic scoring models like the King's College criteria [11], which is based on age, etiology, duration of jaundice, INR, and bilirubin, and the Clichy criteria (based on age and factor V levels) have been developed, but their positive predictive value for pediatric acute liver failure is low, which can possibly lead to higher transplantation rates [12].

At this stage of the evaluation, any possible contraindications for transplant are assessed. There are relatively few absolute contraindications to pediatric LDLT, such as uncontrolled sepsis or presence of extrahepatic malignancy.

Table 27.2 Investigations for potential pediatric recipient

Hematology
Complete blood count, blood typing and antibody screening, prothrombin time, INR (international normalized ratio)
HLA (human leukocyte antigen) typing and crossmatching with donor lymphocytes
Other laboratory investigations
Creatinine, blood urea nitrogen, eGFR (estimated glomerular filtration rate), albumin, bilirubin, liver enzymes (AST, ALT, alkaline phosphatase, γ-GT), electrolytes, ammonia
Arterial pH, serum lactate, phosphate, coagulation factors assay
HBsAg, HBsAb, HBeAg, HBeAb, HBcAb, HBV DNA
HCVAb, HCV genotype, and RNA
IgG, IgM, and antigens as required for CMV, HSV (herpes simplex virus), rubella, measles, EBV, varicella, hepatitis A, HIV, TB PCR
Autoimmune workup as required
Cholesterol, triglycerides, fat-soluble vitamins (A, D, E), iron, ferritin, thyroxine
α-Fetoprotein, CEA, CA 19-9, CA 125
Blood and venous catheter tip cultures
Ascitic fluid and urine examination
Radiology
Liver Doppler ultrasound
Chest X-ray and high-resolution CT
Liver CT angiography, MRCP
Others
ECG
EEG, brain CT
Endoscopy
Sputum and bronchial lavage studies
Workup for associated anomalies
Gene mutation analysis
Liver biopsy
Nutritional assessment

Massive brain injury or uncontrolled cerebral edema in metabolic diseases or fulminant liver failure, or progressive extrahepatic disease such as severe pulmonary hypertension with hypoxemia, also precludes liver transplantation. Technical factors such as associated anomalies or extensive portal thrombosis, presence of HIV infection, and developing multiorgan failure may be considered as relative contraindications for transplant.

It is vital that an excellent rapport is created between the child's family and the medical staff managing the patient. A long stay in the hospital involving complex treatment procedures and risk of numerous complications can strain relationships easily. The social worker can help identify logistic and financial issues besides social dynamics which can impact the management of the patient. At the same time, a psychosocial evaluation of the older child and making him aware about the illness and its management in an optimistic manner can be helpful.

The elective nature of LDLT permits optimization of the child's status before transplantation. A child with chronic liver disease may be mostly managed in an outpatient setting, while a child with acute liver failure may need aggressive treatment in an ICU.

Vaccination is more effective if given before transplantation and initiation of immunosuppression regimens [13]. An accelerated regimen of routine vaccines may be required considering the young age of many recipients. Achieving high levels of antibody to HBsAg by vaccination can help prevent de novo HBV infection after transplant [14].

Malnutrition is common with pediatric liver disease, and growth failure is one of the indications for transplantation. It is caused by multiple factors like increased catabolism, anorexia due to liver disease, and abdominal heaviness due to hepatosplenomegaly, malabsorption, cholestasis, and impaired parenchymal function. Preoperative malnutrition and sarcopenia can have significant negative impact on liver transplantation outcomes [15]. Anthropometric assessment and delayed milestones of development can guide nutritional therapy. Vitamin and medium-chain triglyceride supplements in normal diet, high-caloric-density preparations, nasogastric feeding, and parenteral nutrition may be required. Growth failure due to parenchymal disease cannot be corrected after a point by nutritional therapy, and hence, it is a strong independent indication for liver transplantation.

Coagulopathy in decompensated chronic liver disease or in acute liver failure is indicative of worsening condition. Management of coagulopathy before transplant can greatly improve surgical outcomes. It can also increase safety of invasive procedures such as liver biopsy or invasive intracranial pressure monitoring. Increased bleeding tendency in liver disease results from a decrease in both procoagulant and anticoagulant factors as well as due to factors like altered platelet activation, hemodynamic alterations of portal hypertension, endothelial dysfunction, sepsis, and renal failure. Correction of coagulopathy must hence focus on all these factors rather than simple replacement of depleted coagulation factors [16]. Hospital guidelines regarding transfusion of fresh frozen plasma, cryoprecipitate, platelets, recombinant factor VIIa, and plasmapheresis should be prepared, as the benefit of these measures is not broadly accepted.

Neonatal candidates for transplantation usually have acute liver failure, and pulmonary, renal, and cardiac dysfunction is common. Their small size makes management difficult, as interventional procedures such as hemofiltration are not easy to perform. They require hyperreduced size grafts, increasing the risk of surgical complications.

Survival outcomes of LDLT recipients weighing less than 10 kg are inferior to those with higher weights, and hence ideally LDLT should be done after the age of the child is at least 6 months old [17]. However, as liver failure results in growth retardation, LDLT may be required in children with low weights, if they are below the third percentile of the growth curve or if the severity of the liver disease so demands; hyperreduced size grafts are required in such cases.

27.4 Preoperative Evaluation of Donor

Donor evaluation is similar to that for LDLT in adults. Guidelines regarding degree of donor relationship and donor age are usually framed by the local health authority. For example, the Organ Transplant Act of Taiwan permits only adult relatives within fifth degree of consanguinity to be donors, whereas there is no provision for emotionally related donors. Donation should be voluntary, and the willingness of the donor should be thoroughly assessed in one-on-one psychosocial consultations. The donor should have an understanding of the potential risks associated with the surgery, especially as the donor may be an important caregiver for the recipient. Presence of social and family support systems for the donor and their comfort with the donor's decision should be assessed. Thus, a structured assessment and informed consent are of vital importance in donor surgery.

If there are multiple potential donors, then a basic screening is conducted to rule out contraindications for donation. Presence of active infection, malignancy, and systemic disease are obvious contraindications, whereas history of past infection or malignancy needs further assessment. Seropositivity for HBV, HCV, or HIV generally precludes organ donation, while LDLT with HBcAb-positive grafts may be done with pretransplant hepatitis B vaccination and if required, posttransplant antiviral agents [18].

ABO incompatibility is a major factor limiting the donor pool in LDLT. ABO-incompatible LDLT and DDLT have resulted in high rates of intrahepatic nonanastomotic biliary strictures, liver necrosis, and lower graft survival before the introduction of rituximab. On the other hand, outcomes of ABO-incompatible LDLT for recipients aged less than 1 year are similar to those of ABO-compatible LDLT, probably because the immune system is still developing [19]. In order to reduce the incidence and severity of reactions due to blood group incompatibility, various modalities like plasmapheresis to reduce blood group antibodies in serum, rituximab to reduce B cells via cytotoxic reaction, and local graft infusions of prostaglandins and steroids have been used. The outcomes for ABO-incompatible LDLT for older children are expected to improve as the immunosuppression protocols for ABO-incompatible LDLT in adults are being improved [20].

When inborn errors of metabolism are the indication for pediatric LDLT, there is a risk that the related donor may be affected by the same disease. Symptomatic donors are usually excluded during the evaluation process, but grafts from asymptomatic donors have been utilized without incident [21]. Many of these metabolic disorders are inherited in an

autosomal recessive manner, and hence, the recipient has homozygous affected genes, while the asymptomatic donor may have two normal genes or carry one affected gene. Alternative methods for investigating the donor for inheritable metabolic diseases include carrying out a metabolic loading test or taking a liver biopsy from the donor to accurately measure the target enzyme activity. Such methods may be particularly useful for ornithine transcarbamylase deficiency, an X-linked recessive inherited urea cycle defect, as even heterozygous female donors who carry the recessive gene may become symptomatic due to mosaicism [22].

Complete HLA matching is not a criteria for donor selection in liver transplants because of the tolerogenic nature of the liver and the paucity of donors, although it can lead to low rates of acute rejection and increased chances of developing operational tolerance after transplant (absence of graft rejection despite withdrawal of immunosuppression) [23]. Conventionally, the cytotoxic lymphocyte crossmatch between donor lymphocytes and recipient sera is performed to assess risk of graft rejection, although quantitative assays of donor-specific antibodies and DNA-based typing methods may be more accurate and efficient.

Normally, the main concern in liver transplantation is to avoid graft rejection (initiated when the recipient's immune system identifies graft antigens as foreign and initiates an immune response) rather than GVHD (graft versus host disease, where the lymphocytes in the graft recognize the recipient cells as foreign and initiate an immune response even though the recipient immune system is quiescent).

However, when a parent is the donor for a pediatric LDLT, the risk of GVHD has to be assessed. If the parent is homozygous for HLA allotypes and the child is heterozygous, then the recipient immune system tolerates the graft, but the graft lymphocytes may initiate a GVHD against the recipient's HLA allotypes. In such cases, an alternative donor may be needed. Preoperative identification of anti-HLA antibodies quantitatively and qualitatively may help in avoiding severe immune intolerance (e.g., by initiating immunosuppression regimens in the recipient similar to those for ABO incompatibility) and expand the donor pool [24].

27.5 Preoperative Operative Planning

Radiology and volumetry: The left lobe or left lateral segment is almost invariably used in pediatric LDLT. Numerous variations of size, shape, and anatomy can be encountered in both the donor and recipient in pediatric LDLT, and hence, good preoperative imaging is invaluable in preparing for the procedure. A left lobe graft leaves a safe remnant liver volume of more than 40 % of the standard liver volume in the donor. A graft-to-recipient weight ratio (GRWR) of 1–3 is ideal for pediatric recipients. Grafts may turn out to be small for size when a diminutive-sized donor is present for an adolescent or due to iatrogenic ischemia of a segment from a left or left lateral graft or due to portal hyperperfusion in advanced cirrhosis. More frequently in pediatric LDLT, there is the risk of having a large-for-size graft, if the donor is big or the child is too small. A GRWR greater than 5 predisposes to portal hypoperfusion, followed by graft ischemia and graft dysfunction. It is relatively straightforward to estimate the volume of a left lobe graft by CT volumetry. Estimation of the volume of a left lateral graft and a monosegment graft is more difficult and requires expert review. A fatty liver more than 30 % may not be preferred in most centers. It is also useful to estimate the volume of the spleen in the recipient, as the relative volumes of the liver and the spleen give an estimate of the portal hyperperfusion [25].

Apart from the graft volume, the dimensions of the graft and the abdominal cavity are also important. The anteroposterior diameter of the graft (the maximum distance between the anterior surface of the graft and the porta hepatis on CT imaging of the donor) should be accommodated inside the child's abdominal cavity (the distance from the vertebral body to the anterior abdominal wall on CT imaging of the recipient). A recipient with preoperative ascites or hepatomegaly may be able to receive a larger graft. While a difference of 2 cm between the graft size and the size of the abdominal cavity may be overcome due to the compliance of the pediatric chest wall and abdomen, any excessive disparity may require temporary abdominal wall closure using a prosthetic material, with its attendant risks [26].

Portal vein hypoplasia is common in patients with biliary atresia and so the portal vein size, portal flow velocity, and location of the splenomesenteric junction in relation to the pancreas and coronary vein should be assessed preoperatively. The coronary vein may be needed as a portal vein replacement or it may need to be ligated to increase portal perfusion. Early branching of P2 and P3 from the main portal vein, replacing the left portal vein is possible in the donor and should be looked for.

CT angiography of the donor liver gives important information about the arterial anatomy of the left side. An accessory hepatic artery or replaced left hepatic artery may arise from the left gastric artery and run through the lesser omentum. Unless it is extremely small, it is not sacrificed, but taken along with the graft. Adequate length of the hepatic artery may be obtained by dividing the left gastric artery proximally. The A4 may arise from the common, left or right hepatic artery and has to be carefully dissected for left lobe LDLT. The CT angiography gives information about the size of the hepatic arteries (which may be large in cases of biliary atresia with portal hypoplasia) and patency of the gastroduodenal and gastroepiploic artery (which is the nearest alternative inflow artery of suitable size and length if the recipient hepatic arteries cannot be used). The biliary anatomy is evaluated in the donor by

MRCP or three-dimensional reconstruction of high-resolution CT images. The left-sided graft more commonly has only a single bile duct.

A wide venous outflow reconstruction is crucial for obtaining good outcomes after LDLT. The middle hepatic vein (MHV) is usually taken along with the left lobe graft, and the middle and left hepatic veins usually form a single outflow tract. Occasionally, V2 and V3 may drain separately into the MHV instead of forming the LHV. When a hyperreduced size graft is required, preoperative imaging can guide the surgical technique, by delineating the vascular anatomy and estimating the volumes and dimensions of segments 2 and 3. Close coordination between the surgical teams operating on the donor and recipient ensures that no time is wasted and minimal graft ischemic times are achieved.

27.6 Donor Surgery

The left lobe hepatectomy for pediatric LDLT is similar to the adult donor hepatectomy. The common trunk of the MHV and LHV is exposed by suprahepatic dissection after dividing the falciform ligament. The left inferior phrenic vein is divided early in the dissection to prevent inadvertent bleeding. The gastrohepatic ligament is incised, taking care to preserve any accessory hepatic vessels running in the ligament. The Arantius duct is carefully transfixed where it enters the LHV and divided. This maneuver enables the common trunk of the MHV and LHV to be safely looped.

The gall bladder is mobilized away from its liver bed, and the cystic plate is separated from the hilar plate. Intraoperative cholangiography (IOC) is performed in left-sided grafts if there is history of previous biliary surgery in the donor or if the preoperative MRCP shows variations such as the right posterior sectoral duct arising from the left hepatic duct, trifurcation of the hepatic ducts, or branching of the left hepatic ducts within 1 cm of the confluence [27]. IOC is performed using an olive-tipped needle inserted into the infundibulum or the cystic duct. The gall bladder acts as a guide to the biliary and arterial anatomy of the hilum and is useful for retraction. Hilar dissection is started with the aim of exposing the left hepatic artery first. The A4 is identified if present. The left portal vein is looped after identifying and dividing its caudate branch(es). The arterial and portal inflow to the left lobe is temporarily occluded, and the left lobe demarcation is marked on the surface of the liver. The volume of the graft is estimated again by visual inspection.

If the caudate lobe is to be taken with the graft, then the caudate veins entering the IVC are carefully divided. It is wiser to suture rather than simply ligate the venous stumps on the anterior surface of the IVC. The caudate lobe is thus mobilized toward the right.

The parenchymal transection is started at the inferior border of the liver near the gall bladder fossa. The transection line follows the line of demarcation which is along the Cantlie's line. Inflow occlusion is not required. The aim is to preserve the MHV with the left lobe graft and ligate the V5 and V8 branches as they enter the MHV. Electrocautery is used to transect the liver capsule and superficial liver tissue. Further dissection is done using a combination of clamp fracture, ultrasonic dissector (CUSA®), bipolar electrocautery, and suture ligation. As the parenchymal transection approaches the hilar plate, the left hepatic duct, the Glissonian sheath, and the periductal tissue are encircled together. This complete hilar plate encircling ensures that the vascular supply of the graft left hepatic duct is preserved [28]. An IOC with the aid of a radiopaque marker over the left hepatic duct is useful to precisely delineate the biliary anatomy and the site of transection. The hilar plate is sharply divided (Fig. 27.1) and the peribiliary vessels are controlled with fine sutures.

A modified "hanging maneuver" facilitates faster and safer parenchymal transection. A Penrose drain or umbilical tape is passed between the RHV and MHV and along the anterior surface of the IVC. If the caudate lobe is not included in the graft, it is passed along the path of the Arantius duct. Inferiorly, it is brought up between the left hepatic vessels and the liver parenchyma. The tape is elevated before proceeding with the remaining parenchymal dissection.

Once the parenchymal transection is complete, heparin is administered intravenously, and the left hepatic artery (LHA) and accessory hepatic arteries are divided after applying vascular clamps. It is useful to mark the anterior surface of the left portal vein with a fine suture before division, to ensure that there is no twisting while performing the portal anastomosis in the recipient. The common trunk of the LHV and

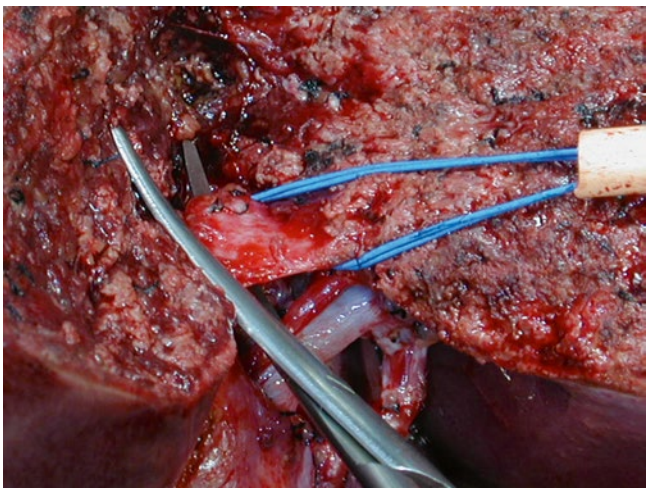

Fig. 27.1 Complete hilar plate encircling technique for left-side graft. The entire hilar plate and the hepatic duct, Glissonian sheath, and periductal tissue are dissected free, encircled, and sharply divided

MHV is clamped and divided. Inclusion of a thin cuff of the inferior vena cava (IVC) increases the size of the orifice and facilitates a wide outflow reconstruction in the recipient.

The graft is transferred to the back table and infused with chilled organ preservative solution (e.g., Custodiol®). A heparinized perfusate based on graft weight is used to reduce the risk of graft vessel thrombosis while also reducing the dosage of systemic heparinization of the donor [29]. On the backtable, the effluent should turn from hemorrhagic to clear. The outflow is observed, and venoplasty of the outflow orifices is performed if required.

The portal and hepatic vein stumps in the donor are closed with fine polypropylene or hexafluoropropylene-VDF (Pronova® – Ethicon US, LLC) sutures in a running fashion. Care must be taken to avoid a purse string effect while suturing which may result in vascular stenosis. The hepatic artery stump is sutured with fine polypropylene sutures. The stump of the left hepatic duct is sutured with polypropylene 4-0, and the patency of the common and right hepatic duct is confirmed by IOC. The hilar plate and the caudate process are examined for small bile duct openings, which are closed. Doppler ultrasound study is performed to confirm vascular patency in the remnant liver. Hemostasis is ensured and a closed drain is inserted into the hepatic fossa. The raw surface of the liver is examined for bile leaks and bleeding by keeping clean laparotomy pads. Abdominal wall closure is done.

When only the left lateral segment is to be harvested, then the technique of parenchymal transection is slightly different from that for a left lobe donor hepatectomy. The parenchymal transection is done in a plane slightly to the right of the falciform ligament. The intrahepatic segment 4 vasculobiliary pedicle is encountered early in the transection – it is kept as long as possible and marked with long suture before ligation and division, as it may be useful for canulating the portal vein intraoperatively if stenting is required [30]. An IOC is not routinely performed except for the conditions mentioned previously [27]. As the transection proceeds posteriorly, the union of the MHV and LHV is encountered. Occasionally, the V2 and V3 join the MHV separately, instead of forming the LHV. Such cases can be dealt in several ways – if the MHV is not the dominant outflow for the right lobe, then it may be harvested with the left lateral graft from the point where the V3 joins the MHV. This enables an easy outflow reconstruction in the recipient as V2 and V3 do not have to be dealt with individually, but it may cause congestion of the anterior sector in the donor.

If the MHV is of large caliber and carries significant drainage from the right lobe, then it is preserved. A patch of the MHV is taken along with the V2 and V3 which enables wide outflow reconstruction. The MHV in the donor is reconstructed in a tension-free manner to avoid stenosis (Fig. 27.2). Alternatively, the V2 and V3 may be divided separately, and a unification venoplasty may be done to form a single large orifice. A venous patch using cryopreserved vein or saphenous vein may be sutured to make the orifice even wider (Fig. 27.3).

If the left lateral segment graft is too big (GRWR more than 5) or too thick to fit inside the recipient's abdomen, then it may be reduced further. A reduced left lateral segment graft or a hyperreduced size monosegment graft can be fashioned by in situ transection [31]. For a hyperreduced size graft based on segment 2, the initial transection is done in a manner similar to that for a left lateral graft. Intraoperative Doppler ultrasound study is performed to identify the portal branches to segments 2 and 3, as well as the position of V2 and V3. The continuation of the hilar plate in the umbilical fissure is taken down to the left of the round ligament, with the intention of exposing the vasculobiliary pedicles supplying segment 3. Each individual pedicle can be occluded temporarily and the area of ischemia noted. In such a manner, the pedicles supplying segment 3 can be identified, ligated, and divided. The parenchymal transection to reduce the left lateral segment to a monosegment then follows the line of ischemia. The hepatic vein draining segment 2 is kept intact with a cuff of surrounding hepatic tissue up to its union with the LHV.

Laparoscopic donor hepatectomy is now being performed in increasing numbers. Left lateral resection is particularly amenable for laparoscopic resection [32]. Proper selection of cases is essential to avoid complications. Laparoscopic CUSA and vascular staplers are used to perform the parenchymal transection and vascular division.

27.7 Recipient Surgery

The abdominal cavity is exposed through a bilateral subcostal incision, sometimes with a midline extension (Mercedes incision). In infants, the superior flap of the incision can be retracted using sutures passed through the edge of the anterior abdominal wall and held in place with a Bookwalter retractor [33]. The round ligament is isolated and held with a long suture for exposure of the hilar region. The suprahepatic vena cava is approached by dividing the falciform ligament and carefully dissecting the dense fascia over the diaphragm and hepatic veins in this region, using a combination of electrocautery, suture ligation, and blunt dissection. Left triangular ligament is incised and opened. The left inferior phrenic vein is usually ligated and divided just before entering the inferior vena cava. The left coronary ligament is ligated and divided. The gastrohepatic ligament is opened, taking care to preserve any arteries supplying the liver. Once the caudate lobe is exposed, it is retracted to the right, and the caudate veins entering the vena cava are double ligated or transfixed and cut. The duct of Arantius is carefully transfixed and ligated before cutting it.

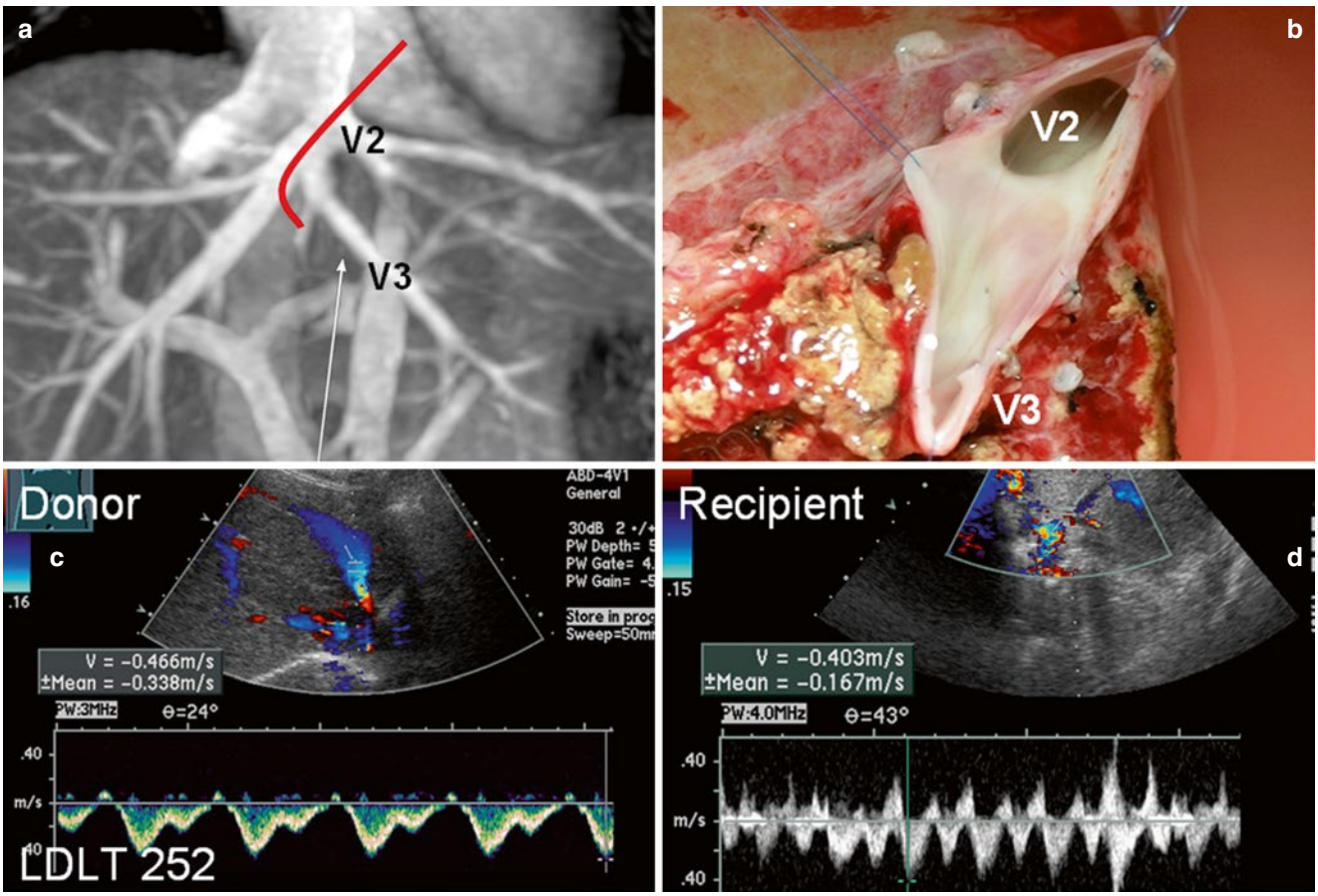

Fig. 27.2 (**a**) Separate V2 and V3. (**b**) When encountering widely separate V2 and V3, half of the MHV circumference containing both V2 and V3 is harvested. (**c**) Triphasic waveforms in the donor MHV years after donation. (**d**) Triphasic waveforms in the recipient hepatic veins after reconstruction

The right side of the liver is now mobilized. The retroperitoneal attachments to the kidney and adrenal tissues are cut, and hemostasis is achieved using electrocautery and sutures. The right triangular ligament is dissected, and the inferior vena cava is visualized. The right hepatic vein and the trunk of the middle and left hepatic vein are looped separately.

The hilar dissection is started by looking for the left hepatic artery after applying upward traction to the round ligament. It is followed down up to the common hepatic artery, dissected free from surrounding tissues, and encircled with a vascular loop. The left portal vein may be visible at this point in a deeper plane to the left hepatic artery. The cystic duct is divided to enable easier hilar dissection, and the gall bladder is left in situ. The right hepatic artery is identified at this point and dissected carefully. The portal vein is identified below the right hepatic artery and common bile duct and is dissected free and looped carefully. The hepatic arteries are dissected as high as possible and examined for quality of vessel wall and blood flow. They are occluded with atraumatic microvascular clamps before proceeding with further hilar dissection. The bile ducts are not dissected bare; the whole hilar plate containing the bile ducts, Glissonian sheath, and periductal tissues is kept intact and separated from the underlying portal veins. This hilar plate is traced as high as possible, and then the right and left hilar pedicles are cut separately. The vascularity, size, and number of bile duct openings are noted. A vascular clamp is used to prevent bleeding from the pedicles and also for retraction purposes. The cut end of the hilar plate on the hepatic side is sutured. The portal veins are now the sole vascular supply to the native liver.

Recipients with biliary atresia who have undergone Kasai procedure may have dense adhesions, and hilar dissection may be difficult in such cases. The Roux loop has to be taken down to complete the hilar dissection. Often, the atretic bile duct cannot be identified. The hepatic arteries may be large but fragile and must be handled delicately. The main portal vein may be sclerotic and hypoplastic and is traced down to the confluence of the splenic and superior mesenteric veins (splenomesenteric junction).

The bare area of the liver is a significant source of bleeding in the cirrhotic patient. While waiting for the graft to be

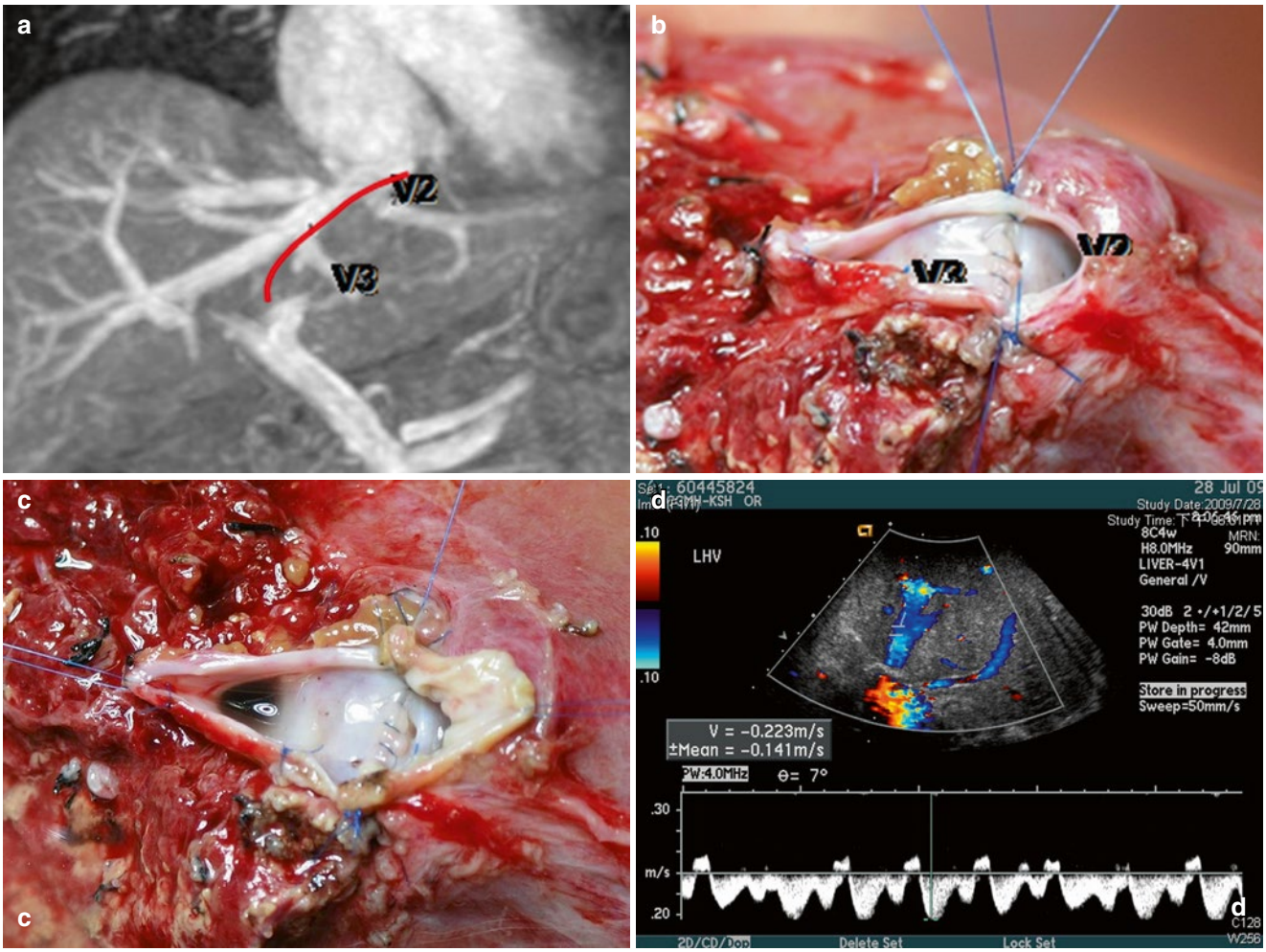

Fig. 27.3 (**a**) Separate V2 and V3. (**b**) V2 and V3 harvested individually and a graft venoplasty has been done. (**c**) A cryopreserved vein patch has been used. (**d**) Doppler ultrasound after reconstruction shows triphasic waveforms in the recipient hepatic veins

prepared, this area may be sutured and the peritoneal folds approximated to achieve hemostasis.

It is useful at this point to insert drains and connect them to suction tubing, to enable proper visualization of the surgical field.

The suprahepatic and infrahepatic vena cavae are dissected circumferentially to permit safe application of vascular clamps. In pediatric LDLT, a triple venoplasty (Fig. 27.4) utilizing the right, middle, and left hepatic vein orifices may be used to ensure a wide outflow [34]. Alternately, the venoplasty may be performed by extending the opening of the common trunk of middle and left hepatic veins to the right.

The main portal vein is clamped and the right and left portal veins are cut separately a short distance from the bifurcation. This ensures that the right, left, or main portal vein, or even a branch patch of the right and left portal vein, can be used, depending on the size of the graft portal vein. It is inspected for presence of thrombosis, and thrombectomy is done if required. It is important to keep the orientation of the portal vein in mind, in order to avoid torsion while making the vascular anastomosis. The vascular clamps are passed around the inferior vena cava, above and below the hepatic vein orifices, after communication with the anesthetist. A cross clamping time of 45 min to 1 h can be tolerated without significant hemodynamic compromise. The presence of extensive collaterals facilitates the performance of the procedure without using venovenous bypass. The hepatic veins are divided, leaving a short stump. The right hepatic vein orifice is sutured if it is not going to be included in the reconstruction. The common trunk of the LHV and MHV may be incised medially to make the opening wider and ensure adequate outflow from the graft. Although the orifice should be wide, the reconstructed hepatic vein should not be unduly long; otherwise, it might get kinked when the graft regenerates.

The graft is positioned inside the upper abdomen and oriented properly. Hepatic vein anastomosis to the IVC is done usually with 5-0 Pronova, similar to the technique in adult

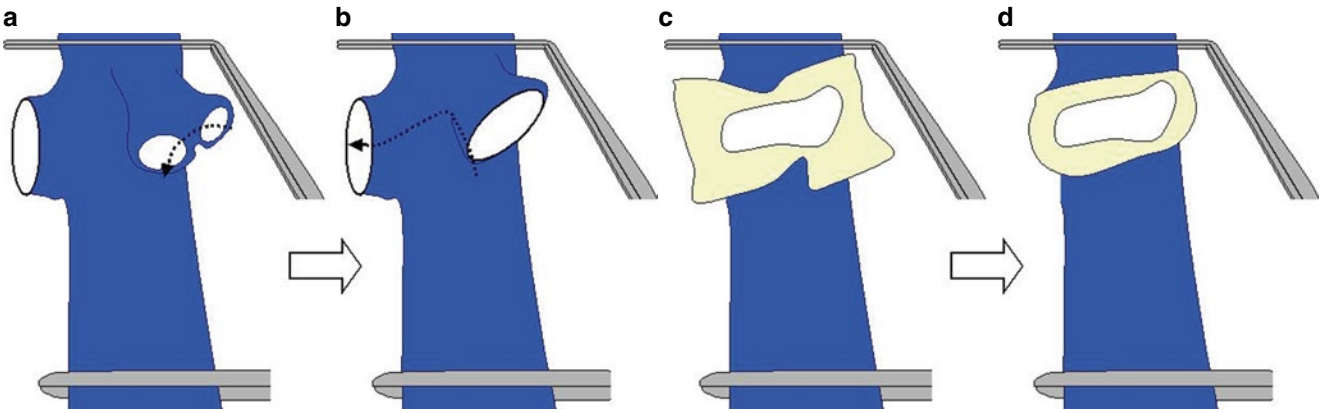

Fig. 27.4 Recipient triple venoplasty. (**a**) The septa between the middle and left hepatic veins is divided (*dotted arrow*) to perform a double venoplasty. (**b**) Triple venoplasty technique is performed by dividing all the intervening septa between the three hepatic veins (*dotted arrow*). (**c**) A single wide orifice is thus created. (**d**) The edges of the orifice-can then be suitably modified before anastomosis with the graft side outflow tract

LDLT. Portal infusion of lactated Ringer's solution is stopped after completing the anastomosis. Initial induction of immunosuppression with loading dose of methylprednisolone 10 mg/kg/day is kept ready.

The orifice of the recipient portal vein is now examined and adequate portal flow is confirmed. The reconstructed portal vein must not be redundant in order to avoid kinking. The main portal vein is flushed vigorously to remove thrombi, and anastomosis with the graft portal vein is commenced. Everted running polydioxanone (PDS® – Ethicon US, LLC) or polyglyconate (Maxon™ – Covidien AG) monofilament sutures are taken, and size disparity is managed. An "air knot" or growth factor equal to the diameter of the portal vein is kept in order to prevent purse string effect. Correct orientation is essential for avoiding stenosis.

The arterial anastomosis is ideally done using the operating microscope and microsurgical instruments by an experienced microsurgeon. The exposure of the surgical field, depth of the site of anastomosis, respiratory movements, and the mobile viscera are significant factors which are encountered in microvascular reconstruction. The size, quality, and orientation of the arteries are examined under the microscope. Usually, the arterial anastomosis is performed using interrupted 8-0 or 9-0 polypropylene sutures [35]. If the graft has two arteries, then the dominant artery is reconstructed first. The second artery is ligated if there is strong pulsatile backflow. If the recipient's hepatic artery is not suitable, then the gastric arteries, especially the right gastroepiploic artery, are suitable alternates, because of their diameter, presence in the same surgical field, and adequate length. A radial artery interposition graft can also be considered. Size disparity up to a factor of 2 can be managed by using a branch patch or obliquely cutting the artery [36].

The bile duct anastomosis is done routinely using the operating microscope at the author's center since 2006, using 6-0 polypropylene or polydioxanone interrupted sutures without a stent. A primary anastomosis of the graft bile duct with the recipient bile duct is preferable to a bilioenteric anastomosis except in cases of biliary atresia, where the Roux-en-Y loop is preferred. In cases where there are more than one bile duct openings in the graft, a ductoplasty or separate biliary anastomoses may be done, depending on the diameter of the bile duct openings and the distance between them [37].

An intraoperative Doppler ultrasound is performed after the arterial anastomosis. An ideal arterial anastomosis should demonstrate a peak flow velocity of more than 40 cm/s, a triphasic pulsatility pattern and a resistive index between 0.5 and 1. Unsatisfactory arterial flow may be due to thrombosis, stenosis at anastomosis site, kinking, etc., and may need a redo anastomosis or construction of a new inflow anastomosis. Ideally, the portal flow velocity should be more than 10 cm/s to rule out portal hypoperfusion, and the portal flow volume should be less than 250 ml/min/100 g graft weight to avoid portal hyperperfusion. If low portal flow is encountered, it is essential to rule out hypovolemia, hypotension, and outflow obstruction and perform maneuvers such as repositioning the graft, ligation of collateral veins, portal stenting under fluoroscopic guidance, and even redo of the anastomosis. A high portal flow may be managed by splenic artery ligation or splenectomy. However, it is unusual in pediatric recipients.

After the biliary anastomosis, hemostasis is checked. Areas such as the diaphragmatic surface, bare area of the liver, anterior surface of the IVC, site of the anastomoses, raw surface of the graft, etc., are specifically checked. The falciform ligament is fixed to the anterior abdominal wall for left-sided grafts, to prevent graft rotation. Abdominal incision is closed in layers. Doppler ultrasound is repeated after closure to check vascular flow. Patient is shifted to the ICU, usually without extubation.

Postoperatively, mechanical ventilation support is removed usually on the first postoperative day. Doppler

ultrasound study is performed daily for the first 2 weeks and more frequently if indicated. Anticoagulants and prostaglandins are started after stabilization and are continued in the first 2 weeks. Immunosuppression in the form of calcineurin inhibitors (cyclosporine or tacrolimus) and steroids is started with drug level monitoring. Proper ICU care with early enteral feeding, physical and pulmonary therapy, and early mobilization are essential for early recovery. Radiologic imaging, laboratory investigations, and liver biopsy as indicated are vital in diagnosing various complications in the early stage.

27.8 Complications

Various complications may lead to suboptimal outcomes after LDLT (Table 27.3). Surgical complications carry the highest relative risk with respect to long-term graft survival and patient survival [38].

Hepatic artery thrombosis (HAT) is especially likely when pediatric LDLT is associated with low body weight, small-caliber artery, and CMV infection. Incidence of HAT is above 10 % in some series [39]. It is necessary to confirm suspicious Doppler ultrasound findings by urgent CT angiography. Early HAT within 2 weeks of transplant is best managed by reexploration, revision of anastomosis, or creation of new anastomosis. Persistence of HAT or onset of graft necrosis implies need for urgent retransplantation. In the long term, HAT leads to graft dysfunction, septic complications, and ischemic biliary strictures [40].

Portal venous thrombosis (PVT) is less common than HAT (1–5 %) but is just as serious. Early PVT can be diagnosed on Doppler study, and treatment options include urokinase, transhepatic or transplenic stenting by radiologic guidance, and surgical revision. Late PVT presents with features of portal hypertension and is managed by endoscopic treatment of varices, medical therapy, and retransplantation if indicated.

Outflow obstruction due to kinking or stenosis of hepatic veins is more likely with smaller grafts and occurs in 1–2 % cases. It typically presents with ascites, altered LFT, and splenomegaly. Doppler ultrasound and CT angiography can confirm the diagnosis. Percutaneous or transjugular stenting or balloon dilatation may be curative.

Biliary complications are the most common cause of significant morbidity in the recipient, with incidence ranging from 5 to 20 % [37]. It could manifest as bile leaks or anastomotic stricture in the early postoperative phase. Bile leaks could be from the transection surface of the liver or the anastomotic site. Careful monitoring of drain output and liver function can help in deciding whether surgical exploration is warranted. Delayed biliary strictures are usually due to ischemic changes and manifest as cholangitis and jaundice. ERBD (endoscopic retrograde biliary drainage) and PTCD (percutaneous transhepatic cholangiographic drainage) are indicated to dilate and stent the biliary stricture. Surgical exploration or retransplantation may be required for long-standing biliary complications resulting in decompensated liver function.

Small-for-size syndrome results when the portal perfusion is more than 250 ml/min/100 g of functioning graft tissue and manifests as persistent jaundice and ascites for more than 2 weeks. It is associated with higher risk of morbidity and mortality. Intraoperative Doppler ultrasound study can help to alleviate the hyperperfusion by reducing the portal flow using splenic artery ligation or splenectomy. However, it is unusual in pediatric patients.

Large-for-size graft increases the chances of graft ischemia and primary graft dysfunction. This is more likely to occur with low-body-weight infants and can be ameliorated by using hyperreduced size grafts.

Biliary atresia patients have usually undergone previous surgeries and are behind in the growth curve. Their small size and dense adhesions predispose them to significant blood loss during recipient hepatectomy. Inadvertent enterotomies may occur due to the extensive bowel adhesions. If the flow in the recipient's main portal vein is unsatisfactory, then various alternative options need to be considered.

Graft portal vein could be anastomosed with:

- Recipient portal vein (if it is of adequate caliber). Large shunts such as the coronary vein may need to be ligated to achieve sufficient portal inflow.
- Recipient splenomesenteric junction. Care should be taken to avoid tension on the venous anastomosis.
- Interposition graft or venous patch on the splenomesenteric junction (if the splenomesenteric junction and the graft portal vein are distant from each other or the splenomesenteric junction is behind the pancreas).
- Coronary vein (if it is of large caliber, it can replace the native portal vein).

Patients with acute liver failure are at risk of encephalopathy, cerebral edema, coagulopathy, and sepsis. Hence, their perioperative management and anesthetic monitoring are extremely important. Similarly, patients undergoing retransplantation are extremely challenging. They carry higher risk of bleeding, bowel injury, poor wound healing, renal dysfunction, and infections such as CMV. They are also prone to PTLD, graft rejection, and lower survival rates [41].

Donor complications occur less frequently than with adult LDLT, because of the use of the left lobe or left lateral segment in pediatric LDLT rather than right lobe LDLT. Donor morbidity may be due to bile leak from the hilar plate or cut surface of the liver, as well as due to gastric stasis caused by adhesion of the stomach to the cut surface of the remnant

Table 27.3 Early and late complications after pediatric LDLT

Infection
Wound infection
Pneumonia
Surgical site infection
Cholangitis
Immunologic
Hyperacute rejection (rare)
Acute cellular rejection
Chronic rejection
Immunosuppression related
Renal insufficiency
Infections (Epstein-Barr virus, cytomegalovirus, etc.)
Posttransplantation lymphoproliferative disorder (PTLD)
Arterial
Hepatic artery thrombosis
Hepatic artery stenosis
Ischemic biliary strictures
Portal
Portal vein stenosis
Portal vein thrombosis
Hepatic vein
Outflow obstruction
Biliary
Bile leak
Biliary strictures – anastomotic and nonanastomotic
Others
Intra-abdominal bleeding
Primary graft nonfunction
Graft necrosis
Graft failure
Small-for-size graft (relative portal hyperperfusion)
Large-for-size graft (relative portal hypoperfusion)
Side effects of drugs (hypertriglyceridemia, obesity, diabetes, renal dysfunction)
Noncompliance to treatment

liver. Other causes of donor morbidity are similar to those described in adult LDLT.

27.9 Outcomes

The outcomes of pediatric LDLT are superior to those for adult LDLT in terms of survival and complication rates. Most indications for pediatric LDLT do not recur after transplantation. The regeneration of the liver graft ranges from 30 to 120 % of the original graft size within 6 months of transplant. It is significantly reduced in recipients with large-for-size grafts or low body weight.

The 5-year overall survival rate is above 90 % in some centers [42] and reported to be 75 % at 20 years [43]. The 5-year survival rate for biliary atresia children undergoing LDLT at the author's center is 98 % [6]. The survival rates for recipients aged less than 6 months when undergoing LDLT are reported to be inferior to those for older recipients [17]. The principal causes of late mortality include rejection due to noncompliance to immunosuppression regimens, PTLD, sepsis, and malignancy. The graft survival rates have improved over time, as the rates of technical complications and rejection have decreased with accumulated experience. Early retransplantation may be required due to hepatic artery thrombosis or primary graft nonfunction, while indications for late retransplantation include chronic rejection of the graft and biliary complications. Survival rates after retransplantation are inferior due to the complexity of the procedure and associated comorbid conditions.

Growth of the child after LDLT is accelerated due to optimal nutrition, anabolic effect of steroids, and treatment of liver disease. The child may get back on the normal growth curve, provided the transplant was done before the onset of severe malnutrition or growth failure. Ten to fifteen percent of recipients may have impaired cognitive functions and lag in psychosocial assessment compared to their peers. However, most children grow up and are able to study, work, marry, and have children [44]. The incidence of renal dysfunction and diabetes mellitus is less than in adults but along with the cardiovascular disease, contributes to significant morbidity by the time they reach adulthood.

Conclusion

The better long-term survival in pediatric LDLT is attributed to careful preoperative planning, better anesthesia management, meticulous surgical technique, and prompt detection and treatment of complications. The wise use of immunosuppression drugs and expert surgical management has resulted in excellent outcomes for children with end-stage liver diseases and metabolic diseases. Continuing innovations in surgical techniques and perioperative management can be expected to further improve the quality of life over the long run.

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Right Hepatectomy Without Middle Hepatic Vein in Living Donor

28

ShuSen Zheng

28.1 The History and Status Quo of Living Donor Liver Transplantation

In 1967, Thomas Starzl performed the first successful orthotopic cadaveric liver transplantation (LT) with long-term survival [1]. Over the next two decades, the exploration to LT in the medical field wounds in a zigzagging course. Advances in operative techniques, the development of immunosuppressive medications, and preservation solutions have contributed greatly to the remarkable progress of LT. Since then, LT was put into clinical practice and has become the best therapeutic option for patients with end-stage liver disease. With subsequent shortage of grafts, reduced-size livers, split livers, marginal liver, and other expansions in the donor pool failed to solve this issue. To meet the growing demand of grafts, there have been increases in donor-awareness campaigns, and the perfected donation programmes after brain death are also established in North America and Europe. In China, the system of livers donation has been perfecting in an all-round way, the demand for grafts is far greater than the supply. Living donor liver transplantation (LDLT) has developed rapidly and plays such an important role in saving the patient on waiting list when xenotransplants and cell transplants retain unsuccessful so far.

In 1988, LDLT was firstly introduced in the pediatric population by Raia and the colleagues [2]. Although the operation didn't achieve the expected outcomes, it laid the basis for the feasibility of this technology. And the first successful case of adult-to-pediatric LDLT was done by Strong et al. in 1990 [3]. It was also attempted in Japan in the same year despite the recipient death of graft rejection and multiple organ dysfunction 285 days after operation [4]. Then, news of adult-to-pediatric LDLT keeps pouring in from different parts of the world.

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In 1993, the first adult-to-adult LDLT using left lobe was performed for primary biliary cirrhosis by Hashikura et al. [5]. Thereafter, there has begun a new era for adult-to-adult LDLT. And the indications for LDLT were further extended to adult patients with HCC. When LDLT was first introduced, left-lobe grafts were used because of the lower risk the donor takes [6]. It soon became apparent that left-lobe size is insufficient for the adult recipient and may lead to the development of small-for-size syndrome.

In order to overcome this problem, right liver lobe emerged as the graft of choice and improved the surgery results in most transplant centers around the world. In 1993, Yamaoka et al. firstly used the right lobe in LDLT for a 9-year-old child [7]. In 1996, Fan et al. performed the first adult-to-adult right-lobe LDLT [8]. The first hospital of Zhejiang university took the lead in performing successfully the right lobe LDLT including MHV in Mainland China. Then right lobe LDLT has developed energetically.

In the 21st century, the number of LDLT procedures has increased rapidly around the world. With the concerns of morbidity and mortality in living donors, the number of LDLT tends to remain stable in recent years. Actually, LDLT has emerged as a valuable alternative to deceased donor liver transplantation for the increasing demand for LT. By September 2015, 30166 liver transplantation were performed in Mainland China and 2486 (8.24%) were LDLTs. Right lobe LDLT still accounts for the majority of adult-to-adult LDLT [9]. With the progress of strategy for small-for-size syndrome, there has been a resurgence of interest in the use of the left lobe in adult-to-adult LDLT [10].

28.2 Selection of Surgical Procedure for LDLT

28.2.1 Left or Right Lobe

When LDLT was early successfully introduced into clinical practice, left-lobe LDLT was widely used and gained

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acceptable survival rates of recipient, especially for children recipients. However, a few adult recipients developed small-for-size syndrome because a relative small graft, injured during operation, may not meet the metabolic demands of the recipient [11, 12]. In general, the relative large graft could be sufficient for the recipient's metabolic demands for patients with acute and subacute liver failure. Therefore, right-lobe LDLT is developed to overcome this graft-size problem, and right liver lobe is the most frequently used graft for adult-to-adult LDLT in most transplant centers around the world [13, 14]. In an analysis of graft type in 3372 graft, 85% were right lobe [15]. But right lobe donation may involve potential risks for the healthy living donor. 24 donor deaths were reported with the majority of deaths occurring within 2 months after donating [16, 17]. Portal hyperperfusion has been reported to be one of the important etiological factors of small-for-size syndrome [18]. There has been a recent trend in left lobe LDLT to employ portal inflow modulation with techniques such as splenectomy [19–21], and portosystemic shunting [22–24] to prevent small-for-size syndrome.

28.2.2 Middle Hepatic Vein Allocation

There is disagreement across different centers as to whether the middle hepatic vein (MHV) is included in right-lobe LDLT. Right-lobe LDLT graft including MHV was first performed in Queen Mary Hospital of the University of Hong Kong and achieved excellent results [8]. Then, the number of right-lobe LDLT with MHV has increased rapidly in many centers. In fact, the right lobes with MHV supply more functional graft volume to recipients, but may cause greater harm or risk to donors. Right-lobe LDLT without MHV may cause severe congestion of the right anterior sector and even early graft dysfunction despite the appropriate balance between donor and recipient liver volume allocation [25], but the safety of donor is more important.

The first hospital of Zhejiang University advocated right lobe without MHV as the first choice and usage of vein grafts for venoplasty to guarantee venous drainage of the right anterior sector. Reconstructions of MHV tributaries can solve the congestion problem of the right paramedian sector and help to improve the outcomes of the patients [26]. The necessity of reconstruction depends on the diameter of the MHV tributaries and is evaluated by intraoperative ultrasound examination. Right lobes without MHV not only guarantee donor safety, but also provide enough liver volume for recipients.

28.3 Preoperative Evaluation

28.3.1 Goals and Principles of Assessment

Donor selection is the primary issue that tops the list of concerns when planning LDLT. Most of the big transplantation centers across the world agree on the major points regarding principles of assessment:

- Donor safety must be guaranteed during graft harvest.
- Graft should at least meet the metabolic demands of the recipient.

28.3.2 Donor Selection and Evaluation

28.3.2.1 Preliminary Screening

Preliminary screening aims to check whether the potential donors really meet the inclusion criteria of liver donation. Donor safety and health is the major concern of LDLT. Therefore, the potential donors should be carefully evaluated under the following principles.

Contents of screening: blood types, age, body size, body mass index, relationship to the recipients, medical history, and other general conditions. The potential donors should be characterized by compatibility/similarity of blood type, the age bracket 18–65 years, and the lack of history of the operation or severe illness. However, the long-term effect of advanced age on grafts and recipients need to be evaluated through a comprehensive and long-term in-depth observation. Donation contraindications include hypertension, hypercholesterolemia, obesity, and peritoneal cavity operation. The donors without the abovementioned contraindications will be further examined by the blood routine test, routine urinalysis, the liver and kidney function tests, electrolyte analysis, and virus's hepatitis tests.

Actually, more than half of all potential donors are excluded in this phase mainly due to not close relative or other important relationship, blood type incompatibility, and potential health problems (e.g., HIV, HBV hepatitis, severe obesity, and drug abuse).

28.3.2.2 Systematic Evaluation

The potential donors selected from the preliminary screening phase will undergo a complete history and physical examination, psychosocial evaluation, preoperative filter, and anesthesia assessment. Avoiding influencing by emotions or personal prejudices of surgeon planning the transplantation, history and physical examination should be performed by the physician who will not take part in operation.

In this phase, the graft volume estimate and vascular anatomy are very important and will be detailed in the next section. Those with anatomical variation thought to be detrimental to donor safety should be rejected.

28.3.2.3 Exclude Potential Diseases

This phase is devoted to further special assessments required to investigate potential diseases discovered during the previous two phases. This may include biliary stones, occupying lesions, fatty liver, heart disease, and so on. The donors with

focal or diffuse liver disease should be excluded, which can be confirmed by biopsy. Finally, on the premise of the donors' wishes to donate, when to transplant is determined according to the recipient' conditions.

All patients should be in the waiting list for cadaveric grafts before receiving living-donor livers.

28.4 Graft Volume Estimation

Donor safety is an important ethical prerequisite for LDLT. The larger volume the recipient receives, the higher risk the donor will have to take. It is generally acknowledged that the risk of left lateral donation is lesser than that of right donation. The surgical mortality risk is estimated at 0.1 % for left lateral donation and 0.5 % for right liver donation [27]. The liver function recovery is slower for right than left lateral liver donation; operation time and hospital stay are also longer for right liver donation. The smaller residual liver volume would lead to slower liver function recovery, and postoperative complications (e.g., bile leakage, infection, bleeding) even may threaten donor life. With modern medical imaging, estimation of remnant liver volume (RLV) to total liver volume (TLV) ratio in each donor is therefore important to warrant donor to recover completely without complications. Accurate estimation of TLV and lobe volume is necessary for optimizing graft harvest strategy and operation success.

The residual liver or graft, if too small, either could lead to small-for-size syndrome, even the donor also requires liver transplantation to save life. Fan et al. [28] suggest that 27 % of RLV/TLV ratio is the lowest limit that can support donor survival, if the liver itself is normal. To allow safety margin, residual liver volume of 30 % of total liver volume is probably the lowest limit. Currently, it is widely accepted that for the donor, 30 % of total liver volume could meet basic metabolic demand (more than 40 % of total liver volume is much better); for the recipient, the ratio of graft volume/standard liver volume is not less than 40 %, or graft-recipient body weight ratio > 0.8 % is sufficient for survival. With the experience of about 180 LDLT patients who underwent in the first hospital of Zhejiang University, to keep the enough residual liver volume for donor, the right liver graft without MHV could also meet the metabolic demand of the recipient.

Multispiral computed tomography (MSCT) has been proven to be useful and accurate for determining the liver volume and is the most commonly used method in many liver transplant centers [29]. Other methods such as ultrasound and semiautomated MR volumetry are also used for liver volume estimation [30]. Through the image analysis package, the surgeon draws the outer margin of the liver or right lobe on CT images, excluding large vessels such as the portal vein at the porta hepatis and the inferior vena cava, as well as hepatic fissures. Using a summation-of-area method, the hepatic volume is then calculated. Various technical factors contribute to accurate volumetric measurements, such as phase of contrast enhancement, CT thicknesses, software, and formula [31]. Besides, it has been assumed that weight and volume of the liver are equivalent at 1 g/mL. However, a conversion factor of 1.15 mL/g is also adopted in some other publications. The transection plane of standard right lobe without MHV is 1 cm away from the right side of MHV, this could contribute to less bleeding during operation. If the right liver without MHV is too small to meet recipient demand, and at the same time donor has a bigger left liver, the right liver with MHV should be considered.

28.5 Specific Anatomical Features Related to Right Hepatectomy in Living Donor

28.5.1 Hepatic Arterial Anatomy

Variants of hepatic artery (HA) are very common, which play the important roles in liver surgery [32–34]. Usually, the liver receives its total arterial inflow from a common hepatic artery of the celiac trunk, occurring in 55–75 % of cases in general [35–37]. The main classification of HA variants was described by Michels in 1966 [35] and modified by Hiatt et al. in 1994 [36]. Anatomic variations of the HA in right liver living donors were classified into five types by Varotti et al. [38] (Fig. 28.1). Other extremely uncommon variations of HA, not listed, could be found in Soin's and Koops's observations [39, 40].

The dominant artery of segment IV (quadrate lobe) is also the vital screening content for LDLT using right lobe. It may arise from left hepatic artery, right hepatic artery, proper hepatic artery, even at the same time from left and right hepatic artery. If the artery of segment IV is from right hepatic artery, the distance between it and right hepatic artery origin should be determined, and the transection plane should avoid affecting its blood supply for segment IV.

28.5.2 Portal Venous Anatomy

Anomalous branching pattern of the portal vein (PV) at the hepatic hilum is less frequent than those of the hepatic arteries, hepatic veins, and biliary ducts [41]. And their incidence has been reported about 30 % in previous publications [42, 43]. The normal PV anatomy is defined as a division of the main portal vein into two branches: the left (supplying segments II, III, and IV) and right portal veins. The right portal vein divides secondarily into two branches: the right anterior portal vein feeding segments V and VIII and the right posterior vein feeding segments VI and VII. Any deviation from this anatomy is considered an anatomical variant. The anatomical variations of the portal

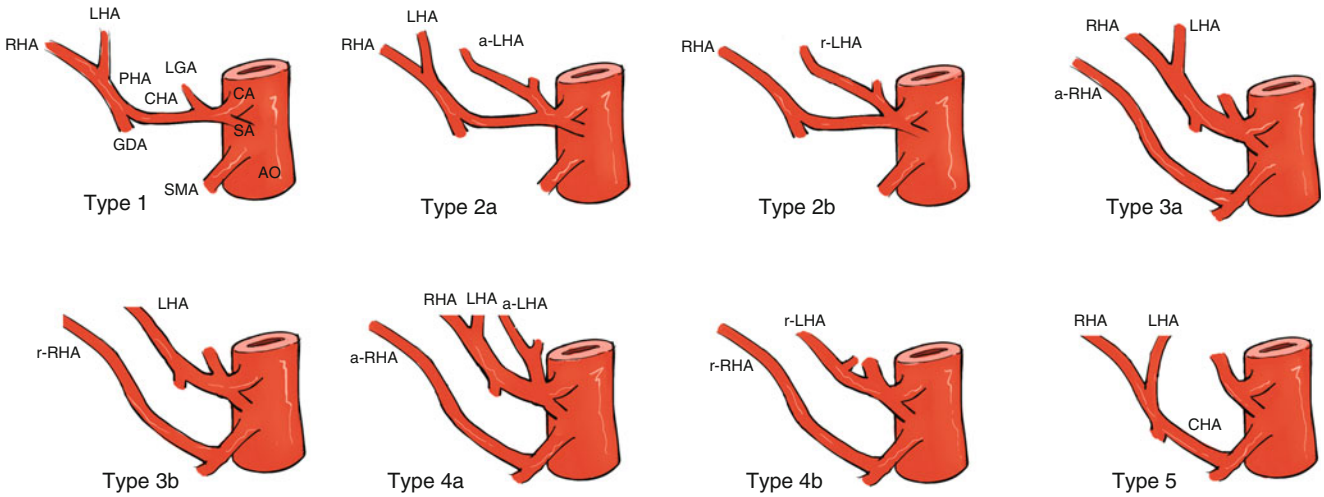


Fig. 28.1 Classification and incidence of the hepatic artery anatomy: type1, 71 %; type2a, 6 %; type2b, 6 %; type3a, 3 %; type3b, 10 %; type4a, 0 %; type4b, 2 %; type5, 1 %. *AO* aorta, *CA* celiac axis, *CHA* common hepatic artery, *GDA* gastroduodenal artery, *LGA* left gastric artery, *LHA* left hepatic artery, *PHA* proper hepatic artery, *RHA* right hepatic artery, *SA* splenic artery, *SMA* superior mesenteric artery

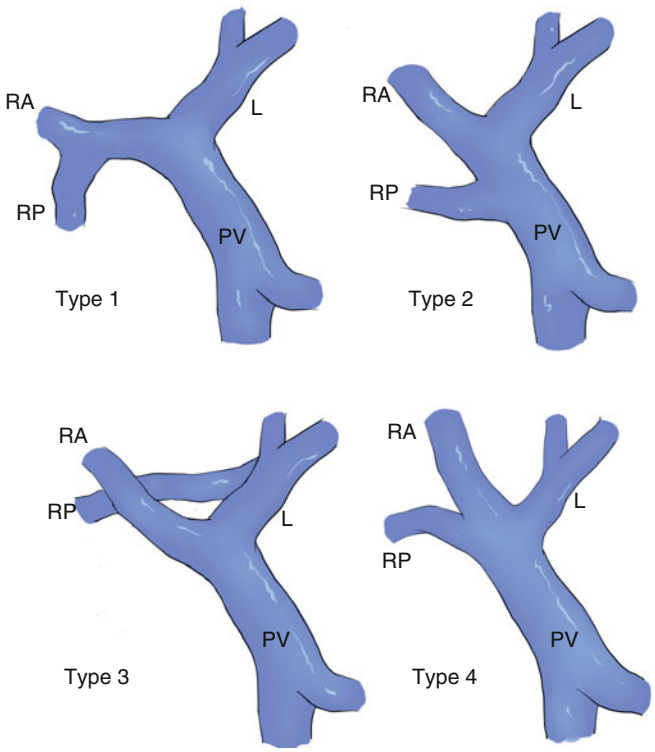


Fig. 28.2 Schematic guide for assignment of categories of conventional and variant portal venous anatomies: type1, 81 %; type2, 11 %; type3, 2 %; type4, 4 %; others, 2 %. *RA* right anterior branch, *RP* right posterior branch, *L* left branch, *PV* portal vein

vein are shown in Fig. 28.2 according to Chen et al. [44] and Covey et al. [45] classifications. Presurgical awareness of portal vein anatomy is utmost important for operation strategy. For example, RP form main and trifurcation, the two portal veins of right graft should be reconstructed during transplantation.

28.5.3 Biliary Anatomy

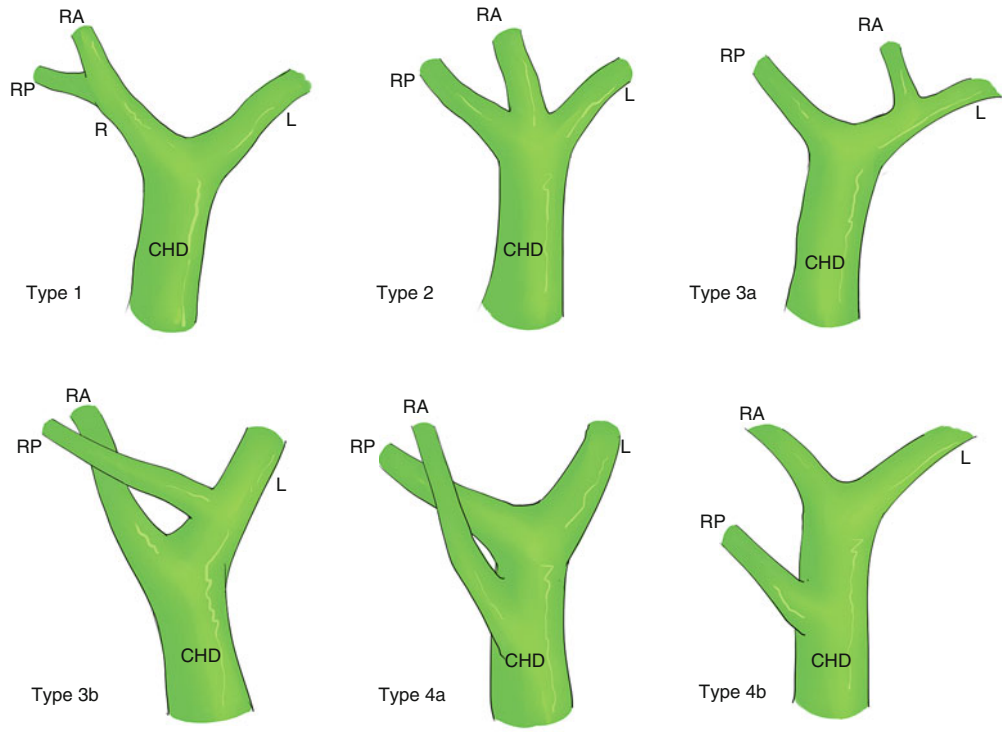
Variations in biliary anatomy are not uncommon, with the classical branching pattern present only in about 60 % of the normal population; right hepatic duct drains from the right anterior or posterior sectoral duct [46]. The anomalies of right hepatic duct result in multiple graft bile duct openings and require more complicated biliary anastomosis in the recipient. Information regarding their biliary anatomy can guide appropriate surgical strategies or help in the selection of the optimal donor when multiple donor candidates are available. The anatomical variations of the biliary anatomy were described according to Choi et al. [47] and Varotti (Fig. 28.3) classifications.

28.5.4 Hepatic Vein Anatomy

Generally, the middle and left hepatic veins converging a common trunk, which open into the inferior vena cava, account for majority. The middle and right hepatic veins sharing the common trunk are not fit for right-lobe LDLT. Based on the presence or absence of significant segment V and VIII accessory hepatic veins and one or more accessory short hepatic veins, Varotti proposed four anatomic patterns [38] (Fig. 28.4). Inferior right hepatic veins and the tributaries of middle hepatic vein with diameter >5 mm should be kept for reconstruction during transplantation in case of severe congestion.

28.6 Preoperative Preparation

Under the guidance of doctors, the donors are on liquid food the day before the planned transplantation and fast after midnight. The bowel preparation is also undergone the



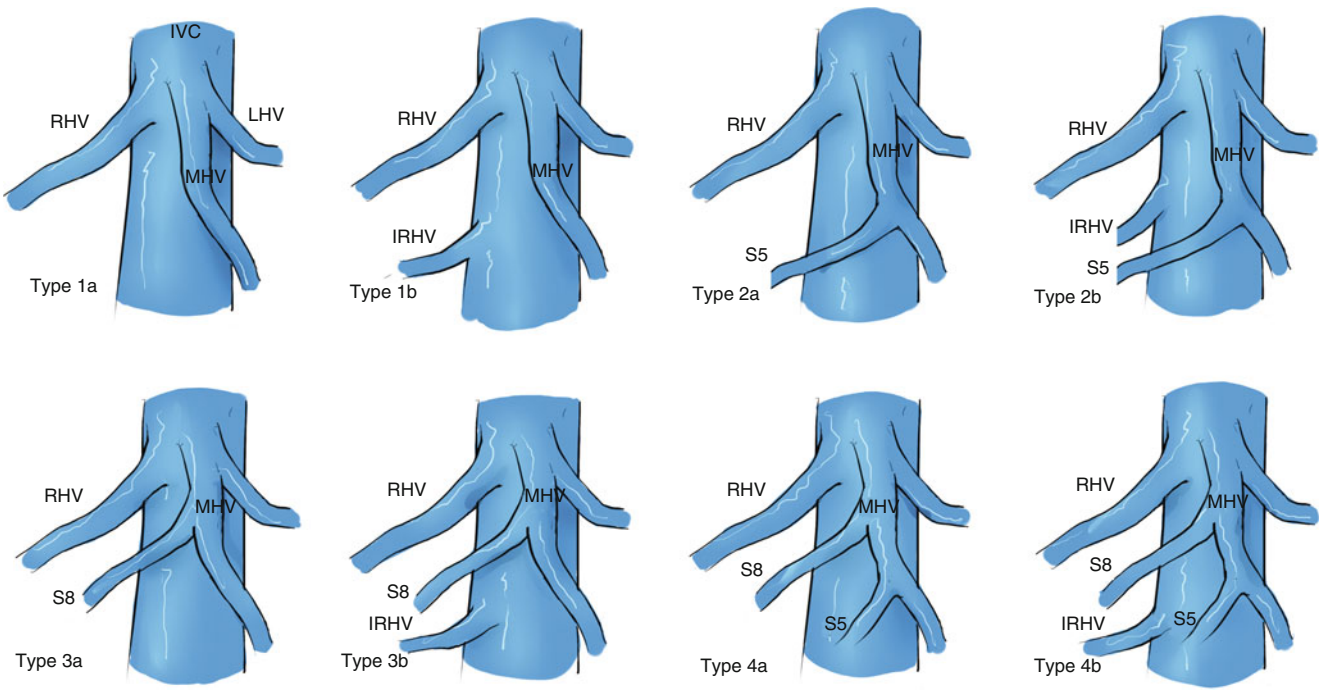


Fig. 28.3 Classification and incidence of the biliary tree anatomy: type1, 56 %; type2, 14 %; type3a, 5 %; type3b, 16 %; type4a, 3 %; type4b, 7 %. *CHD* common hepatic duct, *L* left hepatic duct, *R* right hepatic duct, *RA* right anterior hepatic duct, *RP* right posterior hepatic duct

Fig. 28.4 Classification and incidence of the right liver hepatic venous anatomy. *Type1*: Absence of S5 and S8; absence of IRHV (type1a, 14 %), or presence of IRHV (type1b, 8 %). Type2: Presence of S5; absence of IRHV (type2a, 20 %), or presence of IRHV (type2b, 9 %). Type3: Presence of S8; absence of IRHV (type3a, 17 %), or presence of IRHV (type3b, 19 %). Type4: Presence of both S5 and S8; absence of IRHV (type4a, 11 %), or presence of IRHV (type4b, 3 %). *IRHV* inferior right hepatic vein, *IVC* inferior vena cava, *LHV* left hepatic vein, *MHV* middle hepatic vein, *RHV* right hepatic vein

night before the planned transplantation. All these should keep the donor at his/her best without any health problems.

At the operative day, the transplant surgeon and the anesthesiologist review the donor data for the last time just before the operation. And the donors should receive an epidural patient-controlled analgesia for postoperative pain management.

To prevent deep venous thrombosis, the compressing equipment around lower extremities is applied immediately

before general anesthesia with endotracheal intubation. After general anesthesia, urethral catheterization with Foley catheter and nasogastric tube drainage are performed. Antibiotic prophylaxis, the central venous pressure, and arterial blood gas analysis are usually necessary.

Preoperative autologous blood donation or intraoperative salvaged autotransfusion sometimes would be considered for special situations.

28.7 Operation Procedure

28.7.1 The Key Points of Graft Harvest

1. A cavitron ultrasonic surgical aspirator (CUSA) is recommended for parenchymal dissection, particularly along the hepatic veins and major vessels. When closing with hepatic veins, the power of CUSA should be reduced, and division is carried with more caution. Sometimes intraoperative ultrasound evaluation of the vascular structures is needed for reconfirming liver transection plane and the anatomy of hepatic veins and inferior vena cava. CUSA with the higher power or rough action would easily cause rupture of the hepatic vein and massive hemorrhage.
2. In principle, during the graft harvest, parenchymal transection is performed without the Pringle maneuver to reduce liver ischemia-reperfusion injury.
3. The clamping site of atraumatic forceps on the vessels is very important. It cannot be too close to the main trunk of the portal vein when clamping its branches, in order to avoid portal vein stenosis and subsequent portal hypertension of the donor. Similarly, for hepatic veins, the forceps cannot be placed too close to the common trunk of the left hepatic vein and middle hepatic vein in case Budd-Chiari Syndrome occurs.
4. Large inferior right hepatic veins are preserved and reconstructed in implantation; otherwise, adequate drainage of graft would be affected.

28.7.2 Laparotomy

A J-shaped right subcostal incision is firstly used for exploration. If liver texture is normal, the incision is expanded to a bilateral subcostal incision with the right longer than the left. Whether an upper midline extension (Mercedes incision) is necessary depends on donor's costal arch angle, body type, and operative fields. Generally, Mercedes incision provides excellent access to liver but may delay or prevent healing at the junction of the vertical and horizontal incision then prolongs hospitalization.

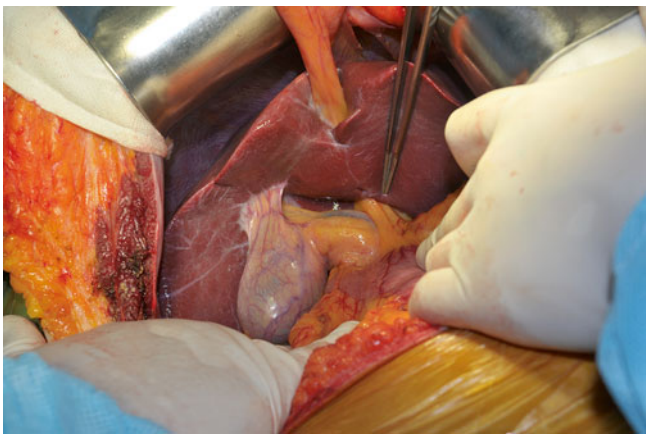


Fig. 28.5 Exploration after laparotomy

Therefore, we advocate finishing donor's surgery through the bilateral subcostal incision if possible.

After entering the peritoneum, pathological condition and anatomical variations of the liver and surrounding tissues need to be carefully explored again (Fig. 28.5). Special attentions should be paid to anomalous bile ducts and hepatic arteries, abnormal enlargement of the lymph nodes and mass, varicose veins, left- and right-lobe size, surrounding ligaments, and liver texture and color. When necessary, intraoperative biopsy is required to determine whether the donor's liver suits donation. Intraoperative ultrasound examination is performed to identify the major vascular structure of the liver. The anatomical variants of left and middle hepatic vein are common and usually present as a common trunk of the two veins before entering the inferior vena cava. The dissection begins until finishing these evaluations.

28.7.3 Cholecystectomy and Biliary Duct Assessment

After careful separation of the cystic artery and the cystic duct, the gallbladder is retrogradely removed. During this procedure, the surgeon should preliminarily understand the anatomy of extrahepatic bile ducts, including the distribution of the common bile duct and the left and right hepatic duct, and their bifurcations.

Cholangiography through the cystic duct stump for evaluation of the biliary tree is performed after cholecystectomy. We usually use the epidural catheter and put it into the common bile duct through cystic duct. However, due to a helical structure of the duct, the catheter is difficult to intubate and may cause the common bile duct injury in the donor. Therefore, we usually preserve Hartmann's pouch for binding the catheter at the entrance of cystic duct with silk suture (Fig. 28.6). The routine intra-operative cholangiography is helpful to clarify

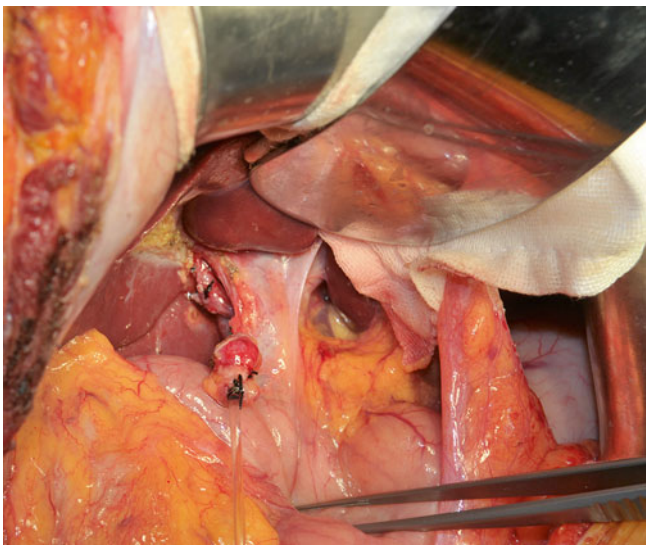


Fig. 28.6 Preserved Hartmann's pouch for putting the catheter into cystic duct

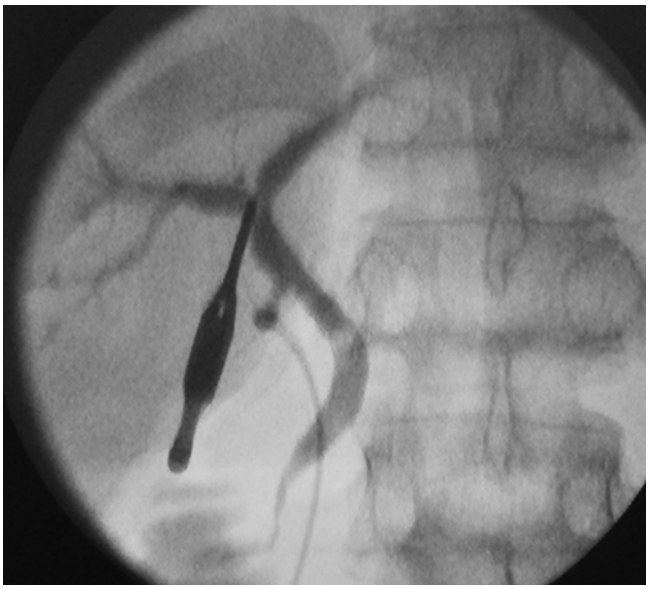


Fig. 28.7 Cholangiography before the separation of liver

the division line of the hepatic duct, reducing the biliary complication rate [48].

The cholangiography using C-arm X-ray system is performed to delineate the biliary tree and second-order biliary duct branches (Fig. 28.7) as well as the variants.

28.7.4 Separation of Right Hepatic Artery

Anatomic variations of hepatic artery are the most common among variations of hilar structures. In the presence of any variations, the principles of graft surgery conclude:

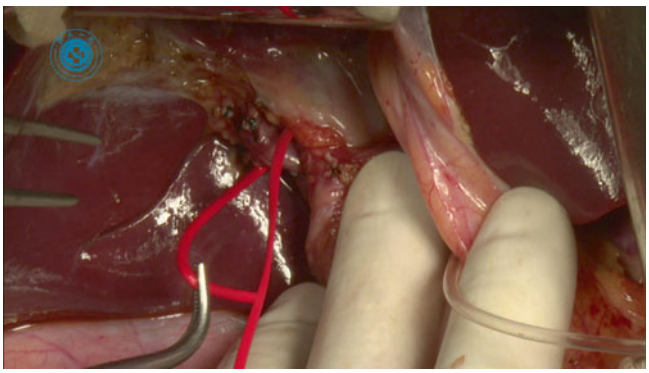


Fig. 28.8 Separation of right hepatic artery

1. The arteries of the right-lobe graft must be preserved with appropriate length and size.
2. No harm to the arteries and blood supply of the donor's remnant liver.
3. Variant hepatic arteries must be preserved as well as possible, since each hepatic artery dominates a specific area and their terminal branches doesn't communicate with each other.

The right hepatic artery generally is located on the right side of the common bile duct. Originating from the proper hepatic artery, the right hepatic artery goes into the right liver through the backside of the common bile duct. Generally, it is lower than the bifurcation of the common hepatic duct and the portal vein. The classic anatomy is reported in about 55–75 % of the population. Separation is performed along the right hepatic artery until reaching the right lobe. And then label the right hepatic artery with a red rubber band (Fig. 28.8). Caution that directly clamping the artery and using electrocautery near the arteries should be avoided, in case of arterial injury.

During the procurement of right-lobe graft, the surgeon should identify and preserve any artery branches supplying blood to the segment IV. The artery of segment IV frequently arises from the left hepatic artery. But a few cases present the so-called middle hepatic artery from proper hepatic artery to supply segment IV and V, the middle hepatic artery should be retain for the donor. Beyond this, the artery of segment IV of some cases branches from the right hepatic artery; this branch sometimes supplies blood to the segments II and III. Therefore, the injury to this artery during donation would cause partial left liver ischemia, even leading to biliary leakage and liver atrophy. In this situations, the right hepatic artery should be separated enough long, and dissection of right artery should be after the origin of this branch. However, excessive dissection of biliary duct system and proximal right hepatic artery should be avoided to prevent biliary duct ischemia.

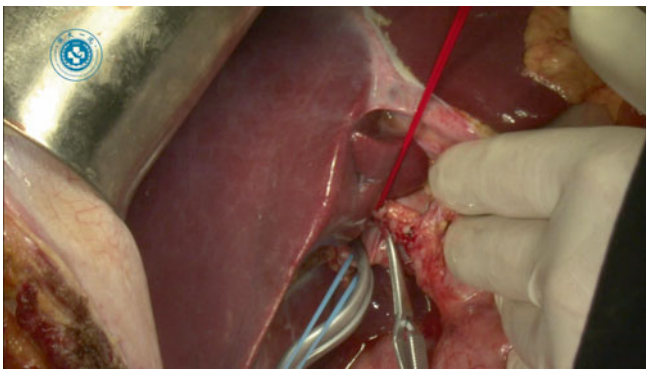


Fig. 28.9 Separation of right portal vein

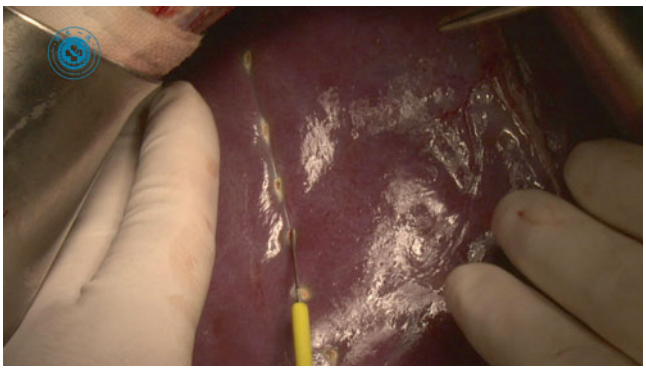


Fig. 28.10 Mark the transection line by electrocautery

28.7.5 Separation of Right Portal Vein

The separation continues to the medial side of the hepatoduodenal ligament. By stripping a little connective tissue, the portal vein trunk and the right portal vein are present with the bluish purple side wall. Carefully ligate the superficial lymphatic ducts to prevent postoperative chylous leakage.

After confirming the right branch of the portal vein, surgeons use a blunt rectangular forceps to separate it from the bifurcation and confirm its extension direction. And then label the right branch of the portal vein with a purple rubber band (Fig. 28.9). Generally, right portal vein has relative long extrahepatic segment and is easy to be dissected free. But the surgeons should preserve adequate long stump for closure at the donor side to prevent stenosis in the main trunk of portal vein after the suture.

Sometimes, in order to acquire enough length of free right portal vein, the dissection could be extended into the liver parenchyma during the operation, cutting off the veins originating from the right portal vein and supplying blood to the caudate lobe. Transecting small branches will not lead to death of the caudate lobe or biliary leakage.

Portal vein anomaly generally doesn't require any modification during liver transection. The plasty of portal vein is performed using cryopreserved iliac and/or saphenous vein grafts in back table procedure, which is relative easy to dissolve.

The portal blood of the segment IV may come from the branch of the right portal vein. Although these abnormal branches to segment IV are rare, it is still important to clarify the branches and direction of right portal vein and be aware of such branches.

28.7.6 Right Lobe Separation and Parenchymal Transection

The dissection of liver ligament begins after the separation of right hepatic artery and portal vein.

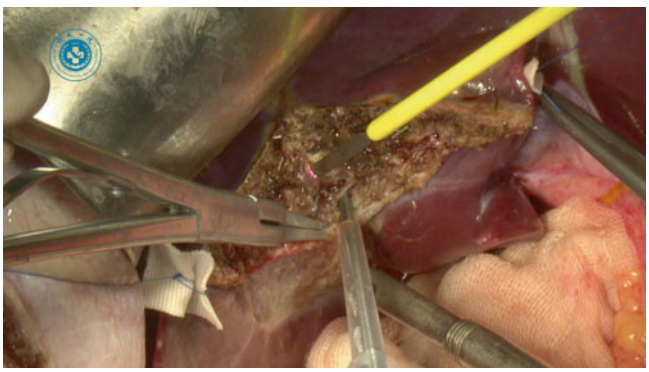


Fig. 28.11 Liver parenchyma transection by CUSA

Dissect the falciform ligament and the right triangle ligament, turn the donor liver to the left, and expose the posthepatic inferior vena cava. Separate the right adrenal gland from the liver, and transect and ligate the short hepatic veins. Separate the right hepatic vein and label it with a blue rubber band. During the process, surgeons may see some posthepatic veins and short hepatic veins draining segments VI and VII. The veins >5 mm in diameter need to be preserved. The approach is not to cut them until the transection of major vessels. This may cause some degree impact on the exposure of posthepatic structures, but most cases could be finished successfully. It is also feasible to transect the veins after seizing with atraumatic clamps. That depends on surgeon's demands and preferences.

Until now, the right hepatic artery and portal vein of the first porta hepatis and the right hepatic vein of the second porta hepatis and the third porta hepatis have been successfully separated. After blocking right portal vein and right hepatic artery with atraumatic clamps, Cantlie's line forms between left and right lobes. Mark the line by electrocautery and transect the liver (Fig. 28.10). The most common method for transection is CUSA (Fig. 28.11). The vessels are clipped or ligated and subsequently cut. The tributaries of middle hepatic vein >5 mm should be retained for reconstruction during transplantation in case of severe congestion (Fig. 28.12).

28.7.7 Time Point for Bile Duct Transection

In the process of LDLT, transection of donor bile duct basically suggests that the donation cannot be aborted. This is the so-called point of no return.

Usually, donors' operation begins ahead of recipients'. However, if the recipients died during the operation, or a variety of situations happen, such as severe adhesions, bleeding, and other conditions, the operation cannot proceed or eventually abort. Once these unexpected situations happen and the donor liver has already been cut, it will become an orphan donor. That means the graft will be taken by no recipient or someone else, resulting in the difficult-solved ethical issue. Therefore, it is necessary to determine an appropriate time point after which the donor's liver must be transected. Currently, transection of the bile duct is believed to be such a time point.

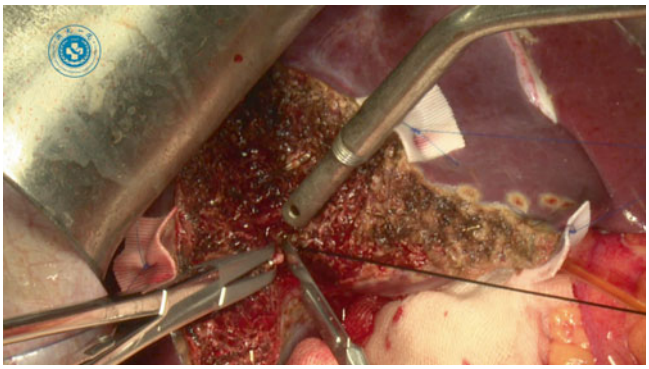


Fig. 28.12 The tributaries of middle hepatic vein >5 mm are preserved

The order of living-donor graft harvest is transection of most part of liver parenchyma, cholangiography and transection of the bile duct, transection of hepatic artery and portal vein, and transection of hepatic vein in the First Affiliated Hospital of Zhejiang University. Cholangiography is performed before and after dissection of right biliary duct (Fig. 28.13). Its advantages are good exposure of portal vein and hepatic artery, feasibility of sharp cutting the hepatic plates around the hepatic duct, and ensuring the blood supply to hepatic duct and the ideal section.

But such order is based on the premise that the operations of donor and recipient are conducted at the about the same time. Thus the operation of recipient usually begins half an hour later than that of the donor. That ensures that the risk and feasibility of recipient surgery are clear before the transection of donor's bile duct (point of no return). The only disadvantage is prolonged anesthesia time of recipient because the operation of recipient would be completed and need to wait for the graft for 10–20 min.

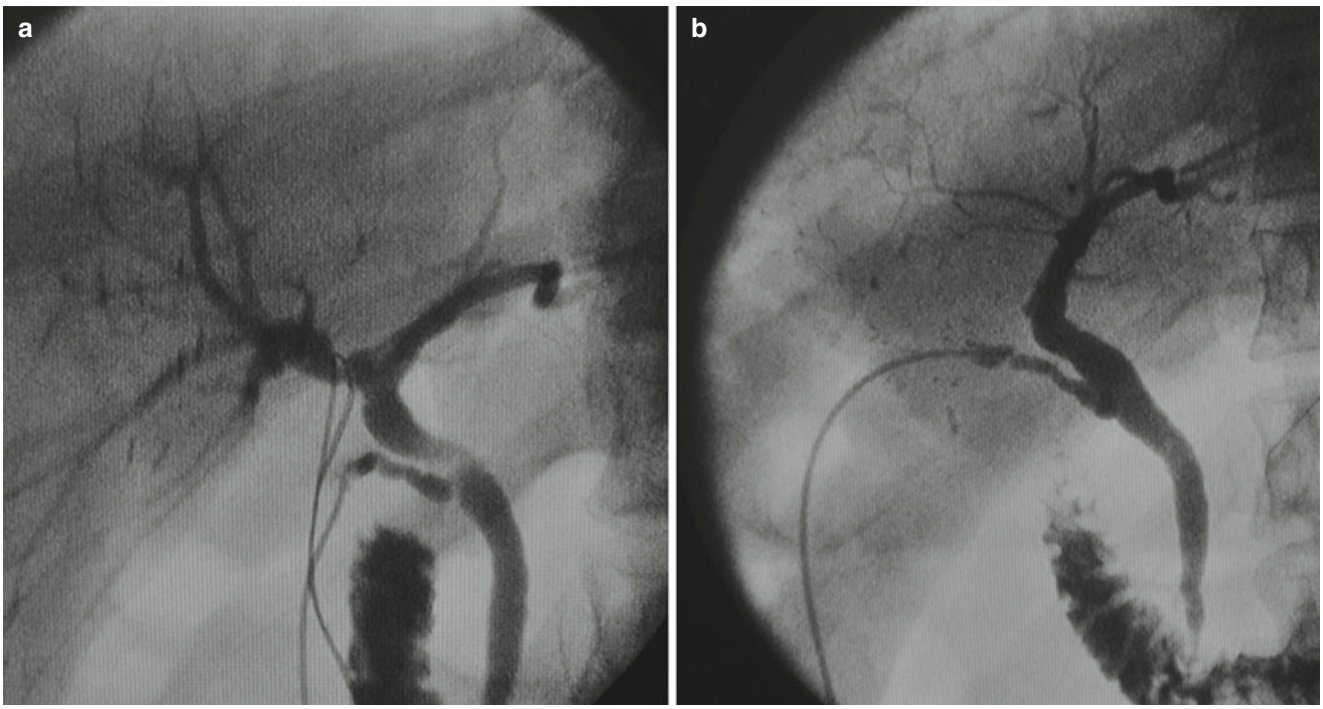


Fig. 28.13 Cholangiography before (**a**) and after (**b**) dissection of right biliary duct

28.7.8 Perfusion of Graft

1. Prepare items in advance.

   Sterile crushed ice, 4 °C HTK solution 4,000 ml, 2×4 °C normal saline solution 1 L, 2×sterile basins, 1×hammer, 2×sterile liver bags, 2×blood transfusion devices, 1×syringe (50 ml), 1×syringe (20 ml), 2×18 G trocar, 2×three-way stopcocks.

   Put adequate sterile crushed ice in the two sterile basins. Cover the basins with sterile liver bags. Each bag is injected with 1,000 ml of 4 °C HTK solution. Drain off the air in the perfusion system.
2. Steps:

   Suspend preservation solution and maintain the vertical distance between preservation solution and table at 150 cm. Add 2,000 U low molecular weight heparin into 1,000 ml HTK for perfusion. The volume of HTK perfusion is about three times of the graft volume. Because right portal vein contains right anterior and right posterior branches, it usually needs two blood transfusion apparatuses for perfusion of the two branches at the same time.

   Put the graft in a basin immediately after being removed from the body, intubate into the portal vein, and start perfusion (Fig. 28.14). During the perfusion, small branches of the middle hepatic vein are temporarily clamped by big titanium clips; the surgeon should pay attention to the fluid outflow and perfusion in liver parenchyma. The congestion area size and position can render important reference for subsequent reconstruction or not. Biliary duct also will be perfused by HTK solution via 18 G trocar. If the donor is treated with systemic heparinization (1,000 units), the hepatic artery wouldn't need perfusion. Otherwise, HTK containing heparin sodium is given through the artery to prevent microthrombus and be careful not to injure the inner lining of the artery. Venoplasty is usually performed in the ice basin after the perfusion.

Fig. 28.14 Perfusion of graft

28.7.9 Venous Plasty of the Graft

Reconstruction for branches of the middle hepatic vein

In LDLT using right lobe without middle hepatic vein, the reconstruction of branches of MHV and IRHV, draining segments V, VIII, and VI, will reduce the congestion area of grafts, the damage to hepatic cells and help the recipient early recover. These branches are usually reconstructed together or separately (Fig. 28.15). Generally, the branches of middle hepatic vein >5 mm in diameter should be reconstructed. In the practice of the First Affiliated Hospital of Zhejiang University, only the diameter of veins as the criteria for reconstruction is not enough; smaller veins without reconstruction also may cause severe congestion after implantation. If the branches lead to congestion in more than 30 % area of right anterior sector, these also need to be reconstructed. Thus, the branches >5 mm need to be reconstructed, and whether the branches between 3 and 5 mm need reconstruction depends on the intraoperative ultrasound examination for blood congestion.

28.8 Complications and Treatment

The complication rate of living donors is about 20–30 %[9, 49, 50]. Except bleeding and infection, biliary complications constitute the majority of the clinically donor complications [49, 51], including hyperbilirubinemia, biliary leakage, bilomas, and biliary strictures. Abdominal effusion and abscess and vascular complications also require a lot of attention. The most serious are unexpected re-explorations. These usually occur because of potentially life-threatening complications such as hemorrhage and portal vein thrombosis.

28.8.1 Biliary Complications

Majority of biliary complications occur in the early period after operation; other delayed biliary complications are also observed in 7–65 weeks postoperation. Most of biliary complications are mild and self-limited, and the minority requires treatment with drugs or even the intervention in the form of drainage, ERCP, and reoperation. Biliary strictures usually present at the hilum where left and right hepatic ducts converge. Biliary leakage, biliary peritonitis, or cholangitis need external drainage and drug treatments. If donors present with hyperbilirubinemia, ultrasound or MRCP is the useful tool for diagnosis. ERCP is used for confirming the stegnosis location and treating sacculus dilatation, stent placement, or nasobiliary drainage. Percutaneous transhepatic cholangial drainage (PTCD) is another method for biliary strictures, but cautions the damage to liver parenchyma and intrahepatic

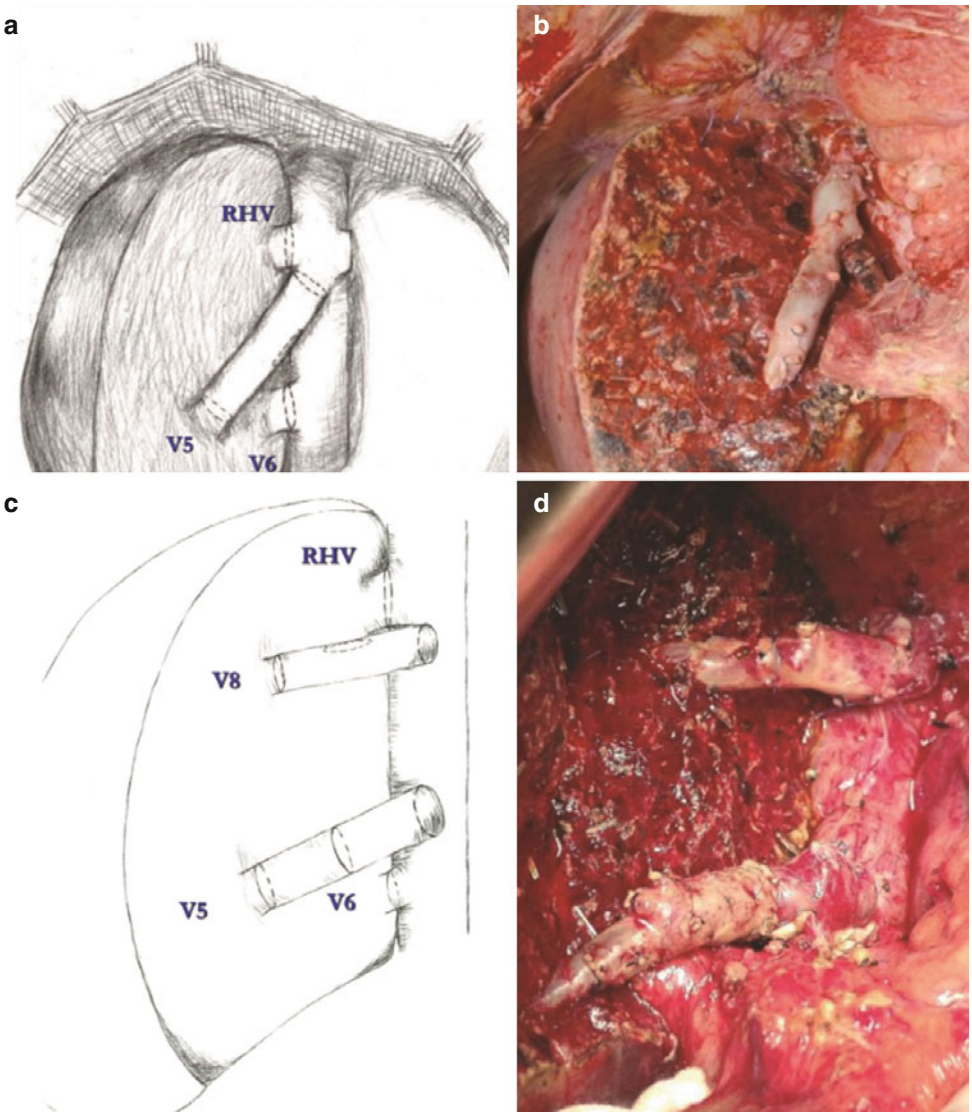


Fig. 28.15 Reconstruction for branches of the middle hepatic vein: V5 and V6 (**a**, **b**), V5, V6 and V8 (**c**, **d**), *RHV* right hepatic vein

large vessels. If biliary leakage leads to the biloma, that is a bilirubin-rich intra-abdominal fluid collection as proved by aspiration and/or placement of percutaneous tube drainage under sonographic control.

28.8.2 Abdominal Fluid and Abscess

Abdominal ascites are common among the donors after operation and most of them are self-limited. When the drainage tube is removed depends on the specific situation. Routine drainage examination or biochemical analysis should be performed: bilirubin quantitative determination for identifying biliary leakage, chylous quantitative determination for identifying chylous leakage, and bacterial culture for infection. If abdominal abscess is found, effective drainage and sensitive antibiotics are necessary.

28.8.3 Vascular Complications

Intra-abdominal bleeding is a very common complication of the donors, mostly occurs within 1 week postoperation. Monitoring the change of hemoglobin in the blood and the drainage and ultrasound examination is essential for identifying abdominal bleeding in the early period after the operation. When the bleeding results in serious hypovolemic shock, relaparotomy should be adopted for hemostasis. Also, radiological interventional treatment may be another good method for finding the active site and performing artery embolization.

Portal vein stenosis or distortion may be present intraoperatively or postoperatively, especially for the donor having the right posterior vein arising from the trunk of the portal vein. Usually, routine ultrasound examination could find the portal vein stenosis or distortion, laparotomy can remove and reconstruct the vein.

In conclusion, the donation operation for LDLT is feasible and relatively safe; the accompanied complications mostly occur in the perioperative period and are also self-limited. In order to reduce the rate of complications, the graft harvest should be given more attention with precise procedure; perioperatively close monitoring is also needed. When complications occur, drug treatment or the intervention even reoperation is considered if necessary.

28.9 The Results of Long-Term Follow-Up in Donors

LDLT offers many advantages: reduced waiting time for transplantation, possibility to schedule the timing of surgery, better-quality organ, and reduced cold ischemic time. Despite the positive aspects of the technique, donor safety must be considered to be a priority in LDLT. It is reported that LDLT have shown a donor mortality of 0–0.3 % [52], possibly reaching 0.5 % when using the right lobe [53]. The percentage of adverse events is 20–30 %, including 10 % that are serious requiring intervention [50, 51, 54]. Actually, most of them could have complete recovery by itself or via active intervention.

There are few information about the long-term results of LDLT donors. The donors are of overall well-being during long-term follow-up in the first hospital of Zhejiang University. Whether there might be long-term negative effects of donation for donors needs further studies. Regarding with the psychosocial aspects of LDLT donors, some studies reported that the quality of life for living liver donors was comparable to a healthy control group [55, 56], whereas Fukuda found that the donors with the time to donation >4 weeks or pre-donation self-oriented concern require enhanced pre- and post-donation psychological care [57]. The center of liver transplantation must maintain long-term contact with the donors and ensure that the donor is free from adverse donation-related effects regardless of medical or psychosocial aspects, is receiving adequate treatment if such effects are present.

Although LDLT is a safe procedure for donors and an effective therapeutic approach for patients with end-stage liver disease, many living donors still experience various postoperative morbidities. Low morbidity rates of living donors can be expected when preoperative donor evaluation and clinical monitoring are adequate, and the surgeon has gained meticulous technique.

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Resection and Procurement of the Right Hemiliver in Adult-to-Adult Living-Donor Liver Transplantation (LDLT)

29

Wentao Wang, Jianyong Lei, and Jiulin Song

The first living-donor liver transplantation (LDLT) was performed by Dr. Raia in Brazil for a 4-year-old child who had died 6 days postoperatively. Then, in 1989, Dr. Strong from Australia successfully transplanted a mother's left lateral liver into her child. In 1993, Dr. Makuuchi from Shinshu University in Japan completed the first adult-to-adult LDLT with a left liver graft. Dr. Sheung Tat FAN of Queen Mary Hospital of Hong Kong successfully used the right hemiliver, including the middle hepatic vein (MHV), for an adult-to-adult LDLT in 1996.

Compared with the left liver graft, the right hemiliver is sufficiently large to compensate for the recipient's metabolic requirement and decreases the risk of small-for-size syndrome (SFSS) postoperatively. Adult-to-adult LDLT with the right hemiliver has gradually become a standard treatment for patients with end-stage liver disease, which presents similarly to whole-liver transplantation.

29.1 Indications and Contraindications of Adult-to-Adult LDLT

29.1.1 Indications for the Recipient

(1) Chronic end-stage liver disease, (2) fulminant hepatic failure, (3) inherited metabolic liver disease, and (4) unresectable hepatic malignancy without distant metastases. However, the hepatic carcinoma is supposed to meet the international Milan criteria or UCSF criteria.

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29.1.2 Contraindications for the Recipients

(1) Severe infection: sepsis, AIDS, extrahepatic malignant diseases, or drug abuse; (2) severe diseases of the heart, lung, and brain, severe hypertension, and diabetes mellitus; (3) severe renal failure; (4) intrahepatic biliary infection; (5) psychiatric history; and (6) portal venous thrombosis or embolus

29.2 Evaluation of the Donor Liver Graft

See the section above for more details.

1. Volunteer donors must be between 18 and 60 years old. The relationship between the donor and recipient must accord with ethical principles.
2. All donors must undergo liver function tests, routine blood tests, coagulation function tests, and transfusion-associated contagion tests.
3. An ultrasound test for evaluation of the donor liver quality and hepatic vascular patency must be conducted.
4. With 3-D reconstructive computed tomography (CT), the volume and weight of the donor liver must be estimated and the graft-to-recipient weight ratio (GRWR) or right hemiliver-to-standard liver volume (SLV) ratio must be calculated. It is typically believed that the GRWR should be more than 0.8 %, and the right hemiliver-to-SLV ratio should be more than 40 %.
5. With CT to evaluate the distributions, the areas and quantity of hepatic venous tributaries should be collected, as should the branches and variations of the portal vein and hepatic artery in the donor right hemiliver.
6. With CT, the quantity and caliber of the large tributaries of the MHV collecting segments V and VIII in the donor right hemiliver should be evaluated; once found, the large inferior right hepatic veins and tributaries of the MHV collecting segments V and VIII (≥5 mm) in the donor right hemiliver must be preserved and reconstructed during the liver resection.

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7. With preoperative magnetic resonance cholangiopancreatography (MRCP) and intraoperative cholangiography, the branches and variations of the biliary ducts in the donor right hemiliver should be evaluated.

29.3 MHV Allocation in Adult-to-Adult Right Hemiliver Living-Donor Liver Transplantation

Controversy exists regarding the determination of whether the MHV is included or retained by the donor in adult-to-adult right hemiliver living-donor liver transplantation [1–6]. A satisfying venous outflow tract is of great importance for maintaining the graft's normal function in the early stages. MHV-harvested right hemihepatectomy can resolve the issue of venous outflow obstruction in V5 and V8 for the recipient. However, it may simultaneously cause venous outflow obstruction in V4 for the donor and affect liver function and regeneration, threatening the donor's health. To ensure the donor's safety and improve the venous outflow of V5 and V8 for the recipient, many transplantation centers propose a strategy of MHV-retained adult-to-adult right hemiliver living-donor liver transplantation and vascular reconstruction for the tributaries of the MHV for the recipient's V5 and V8. However, MHV vascular reconstruction requires strong technical skills. The source for vascular bridge is another problem, and the criteria for reconstruction remain controversial.

For the safety concerns of donors, many transplantation centers in the world choose MHV-retained adult-to-adult right hemiliver living-donor liver transplantation. Among the globally recognized living-donor transplantation centers, Hong Kong University mainly uses the MHV-harvested adult right hemiliver for living-donor liver transplantation [1], Chang Gung Hospital in Taiwan mainly uses MHV-retained adult right hemiliver for living-donor liver transplantation [5], and Kyoto University in Japan determines the MHV allocation according to the subtype of the donor's MHV and the estimated remnant-to-recipient weight ratio and GRWR [6, 7].

29.3.1 MHV-Retained Right Hemihepatectomy

Advantages Short operation time for the donor, large remnant liver volume, and safe for the donor

Disadvantages Venous drainage of V5 and V8 may be damaged; delayed recovery time for the graft; the requirement for MHV reconstruction; excessive operation time; the possibility of tortuosity, angulation, or embolism of bridging vessels; and other factors that also could cause the venous outflow obstruction

Selection Criteria Less adipose degeneration in the donor, right lobe liver without an MHV-to-recipient ratio (GRWR) $\geq$ 0.8, and V5/V8 $\geq$ 5 mm with or without outstanding right inferior hepatic vein

29.3.2 MHV-Harvested Right Hemihepatectomy

Advantages Large graft volume; graft's venous drainage of V5 and V8 are adequate; and the recovery is good; avoids the possibility of angular or twisted bridging vasculature that causes venous outflow obstruction.

Disadvantages Strong technical skills are required for donor hepatectomy; excessive operation time for the donor; the possibility of venous outflow obstruction of V4; potential risk for donor regarding liver function and regeneration.

Selection Criteria Less adipose degeneration in the donor; right lobe liver without an MHV-to-recipient ratio (GRWR) $<$ 0.8; preoperative CT estimated remnant of the left liver with a volume $\geq$ 30 %; intraoperative ultrasound confirms MHV to be the major drainage vessel for V5 and V8; and the tributaries of MHV in V4 are outstanding.

In summary, MHV allocation in adult-to-adult right hemiliver living-donor liver transplantation depends on various transplantation centers and the doctor's experience. Factors to consider are the donor-to-recipient weight ratio, the graft-to-recipient weight ratio, the right hemiliver volume-to-estimated standardized liver volume ratio, the remnant liver volume, the venous drainage area for the MHV, and the caliber of the MHV tributaries [4, 6].

29.4 Hepatectomy and Procurement of Right Hemiliver Excluding MHV

29.4.1 Surgical Position and Incision

The patient is typically placed in the supine position. An L-shaped incision is made in the upper abdomen (see Fig. 29.1).

29.4.2 Exploration and Mobilization of the Donor Liver

The normal liver is bright red and sharp edged (see Fig. 29.2). A few liver tissue samples are typically taken for intraoperative biopsy.

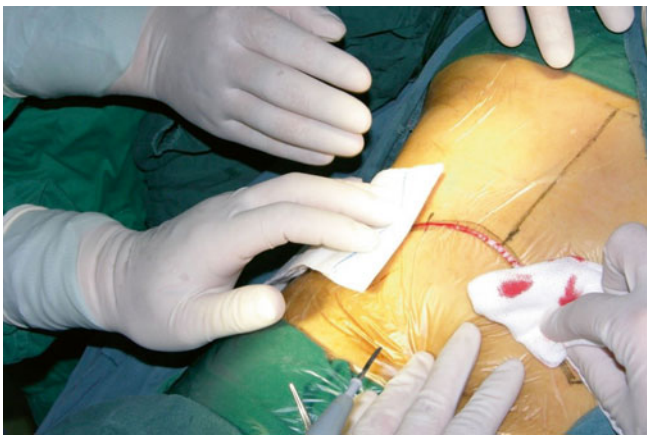


Fig. 29.1 Shows the donor's incision

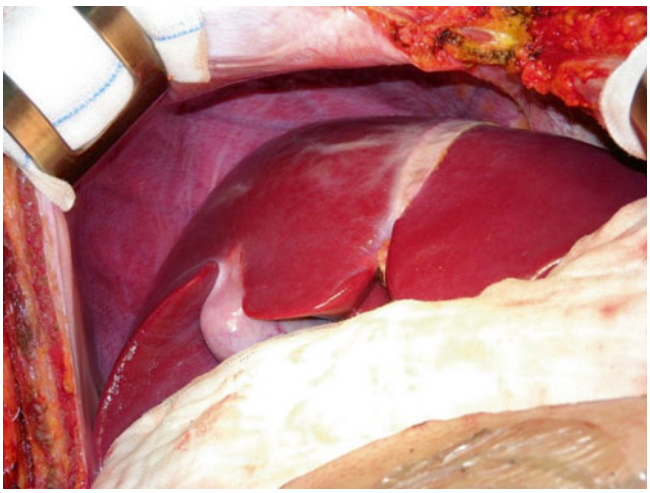


Fig. 29.2 Shows the normal donor's liver

29.4.3 Dissection of the First Porta Hepatis

29.4.3.1 Intraoperative Cholangiography

The gallbladder is excised, and then, intraoperative cholangiography is conducted through the cystic duct with clamping of the common bile duct with a biliary clip at the superior border of the duodenum to explore the intrahepatic bile ducts (see Figs. 29.3 and 29.4). A titanium clip is used to clamp the hilar plate tissue at the junction of the common hepatic and right hepatic ducts. The confluence of right hepatic bile duct is located, and the resection line at hilar plate is marked (see Fig. 29.5).

29.4.3.2 Separation and Dissection of Vessels and Ducts

Dissections must be performed carefully to avoid electrocoagulation and additional injuries and to prevent the capillary network from supplying the bile ducts. The right

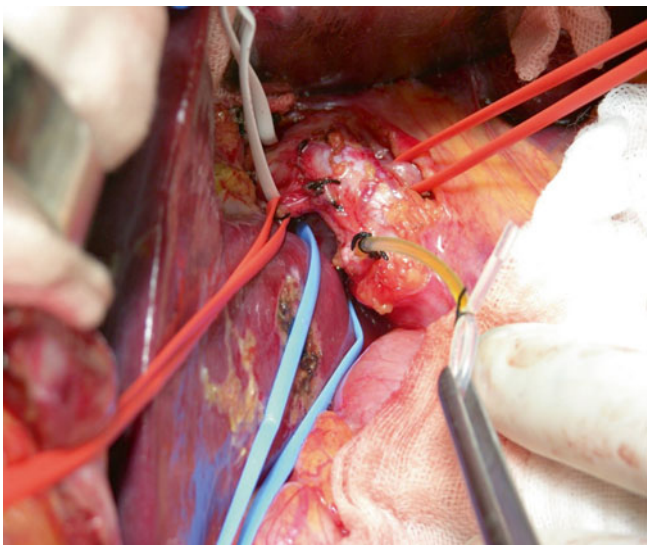


Fig. 29.3 Shows intraoperative cholangiography by intubation of cystic duct

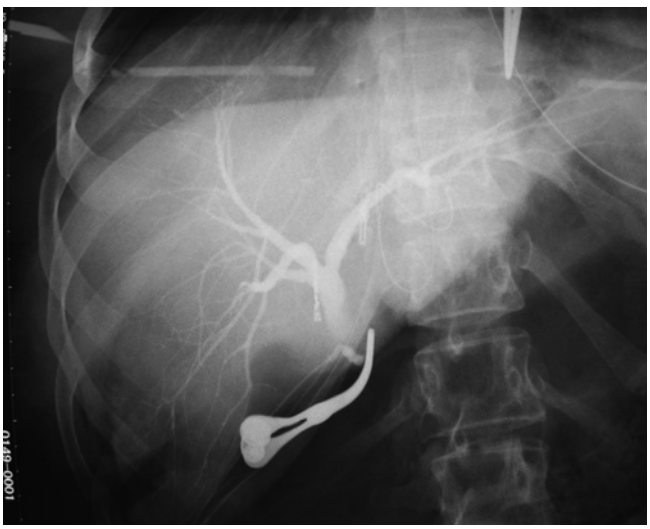


Fig. 29.4 Shows the titanium clip located at the junction of the common hepatic and right hepatic ducts

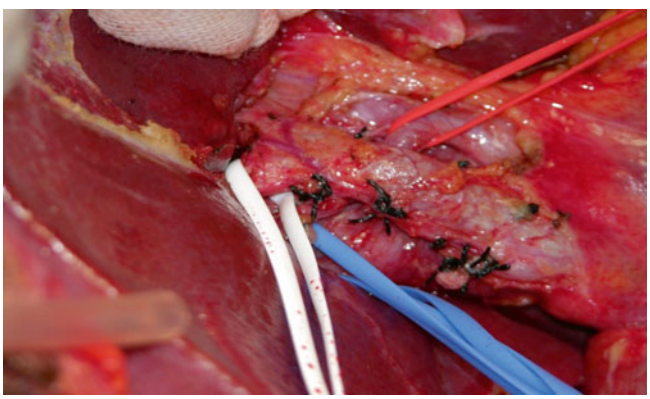


Fig. 29.5 Shows the structures of the first porta hepatis (right hepatic artery with *red sling*, right hepatic duct with *white sling*, and the right portal vein with *blue sling*)

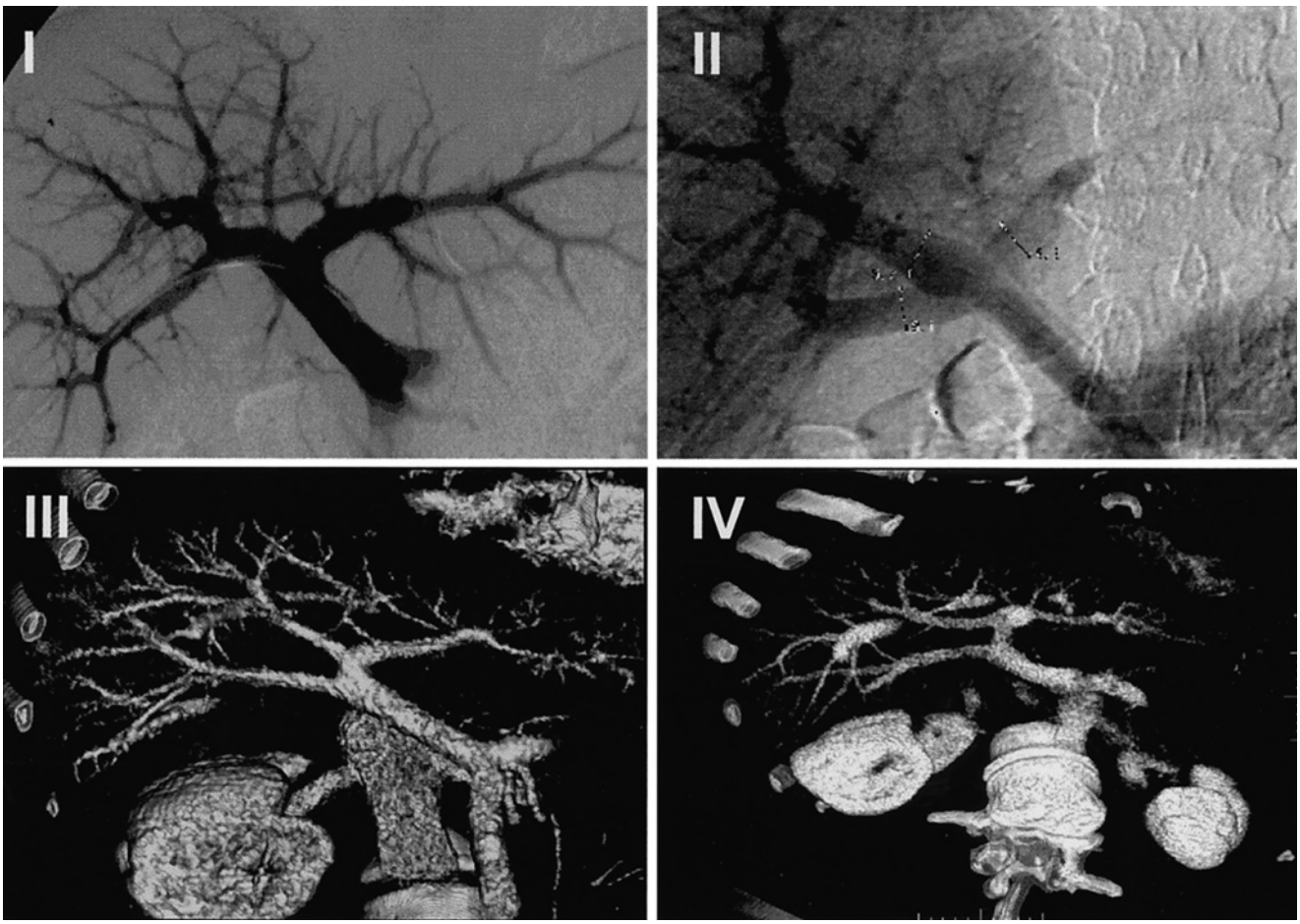


Fig. 29.6 Shows the four types of portal vein

hepatic artery and right portal vein are dissected. If the right hepatic ducts are converged by 2–3 hepatic bile ducts, they are typically transected with the right hilar plate at the same time after splitting the liver parenchyma rather than dissecting it at the beginning.

There may be variations of the portal vein, as four types often occur (see Fig. 29.6). Types I and II are suitable for LDLT. However, types III and IV are difficult for bile duct reconstruction [8].

The figures below show the preoperative CT imaging and intraoperative finding of a donor with type II portal vein (Figs. 29.7 and 29.8, 29.9, 29.10, and 29.11).

29.4.4 Separation of Perihepatic Ligaments

The hepatocolic ligament, right triangular ligament, and right coronary ligament are successively resected, exposing the right adrenal gland and right margin of the posthepatic inferior vena cava (IVC).

29.4.5 Dissection and Transection of the Third Porta Hepatis and Right Hepatic Vein

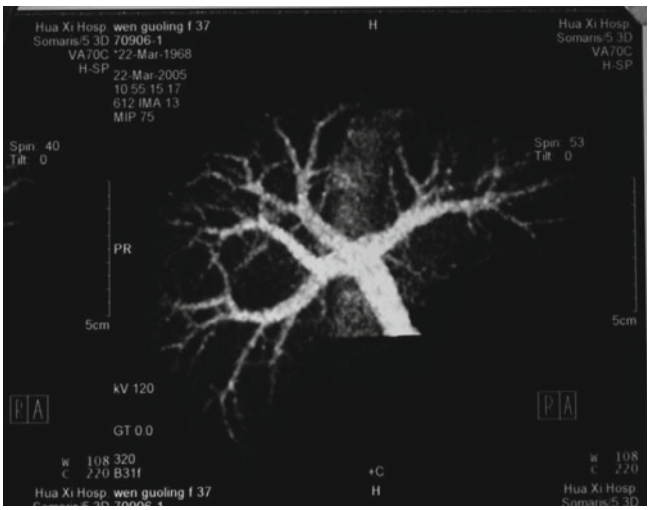
The assistant helps push the liver to the left without force. All of the short hepatic veins on the right side of the posthepatic IVC are transected. If the short hepatic vein or accessory right hepatic vein is more than 0.5 cm in diameter, it should be preserved and reconstructed (Fig. 29.12).

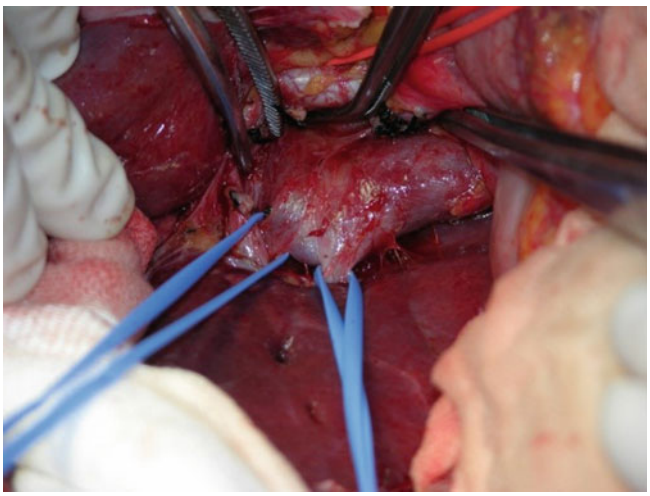
The right liver is intermittently lifted to avoid compressing and occluding hepatic inflow that might result in liver injury when handling the short hepatic veins.

29.4.6 Transection of the Liver Parenchyma

29.4.6.1 Prediction of the Resection Line of the Right Hemiliver Excluding the MHV by 3-D Reconstructive CT (Figs. 29.13 and 29.14, 29.15 and 29.16)

The resection line is conformed intraoperatively in three ways: (1) the ischemia line of the left and right livers is used





Figs. 29.7 and 29.8 Show preoperative CT imaging and the intraoperative finding of the right portal vein with right anterior and right posterior branches

Fig. 29.9 Shows openings at the right anterior and right posterior branches of the type II portal vein

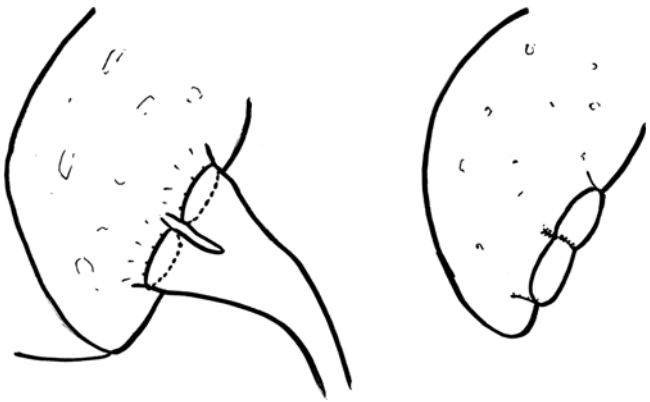


Fig. 29.10 Shows two types of reconstructions of the type II right portal vein with right anterior and right posterior branches. The *left picture* shows an anastomosis of the recipient's left and right portal veins with the donor's two right portal vein branches. The *right picture* shows reshaping of the donor's two right portal vein branches as a common opening to anastomosis with the recipient's main portal vein when the two branches are adjacent

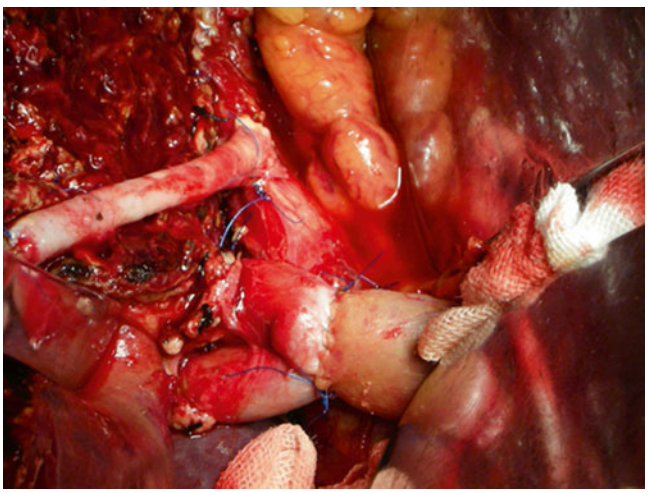


Fig. 29.11 Shows that the author used a cadaveric iliac U-shaped artery to reconstruct and form an anastomosis with the recipient's portal vein

by temporarily occluding the right hepatic blood inflow as the resection line, (2) the Cantlie line (which is the connecting line at the liver surface stretching from the middle of the gallbladder fossa to the midpoint of the right and MHVs at the second porta hepatis) is used, and (3) the intraoperative ultrasound is used to confirm the resection line (Figs. 29.17, 29.18, and 29.19).

29.4.6.2 Transection of the Liver Parenchyma

The liver capsule is cut with an electrotome along the resection line, and the cavitron ultrasonic surgical aspirator

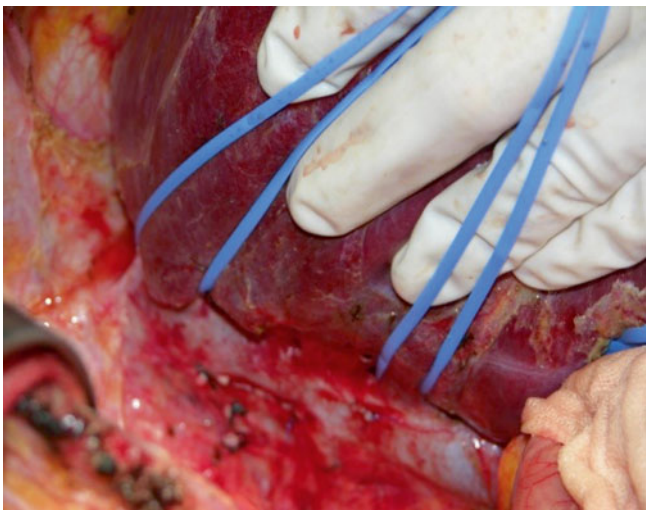
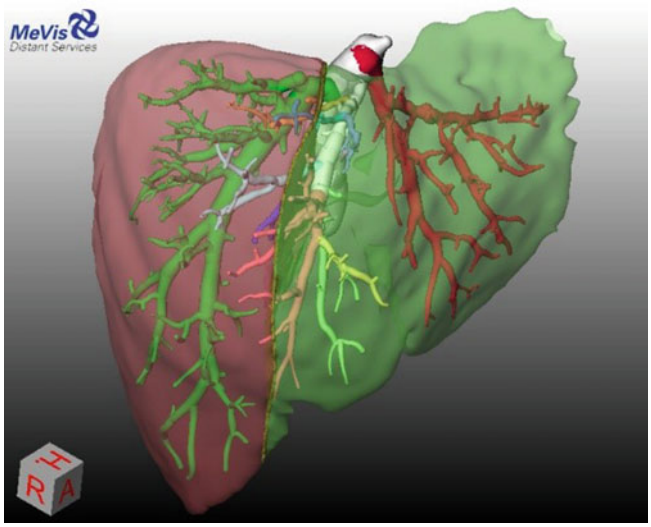
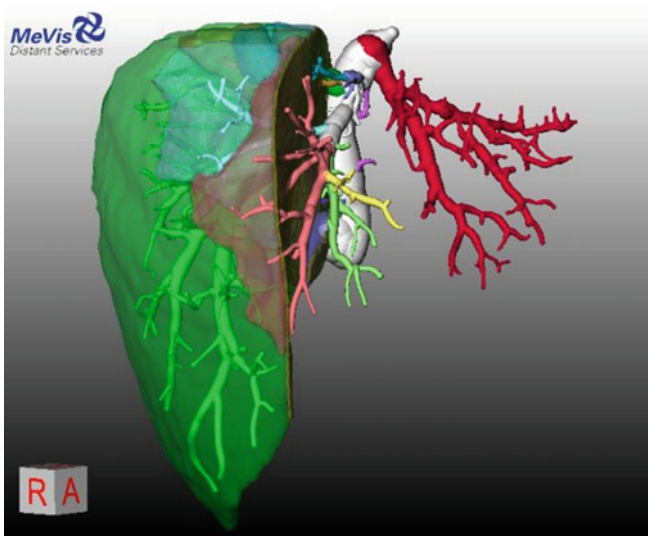


Fig. 29.12 Shows the right hepatic vein with the left sling and the large inferior right hepatic vein for reconstruction with the right sling





Figs. 29.13 and 29.14 Show the 3-D images of the donor's whole and right liver, respectively

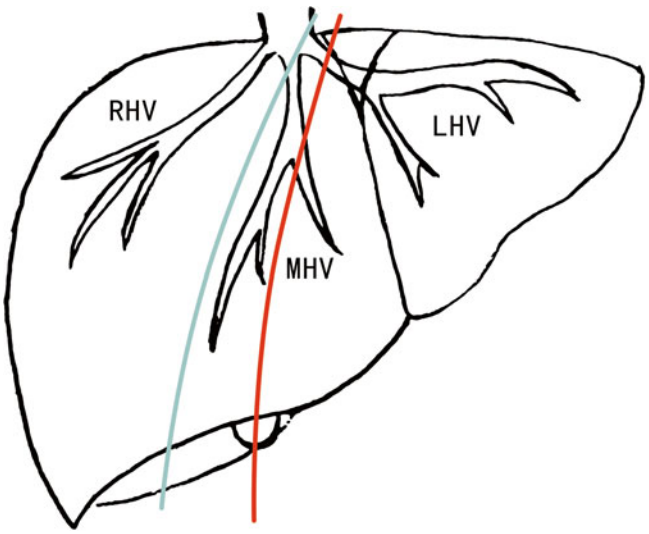


Fig. 29.15 Shows the predictive resection line of the right hemiliver including and excluding the MHV. LHV: Left hepatic vein; RHV: Right hepatic vein

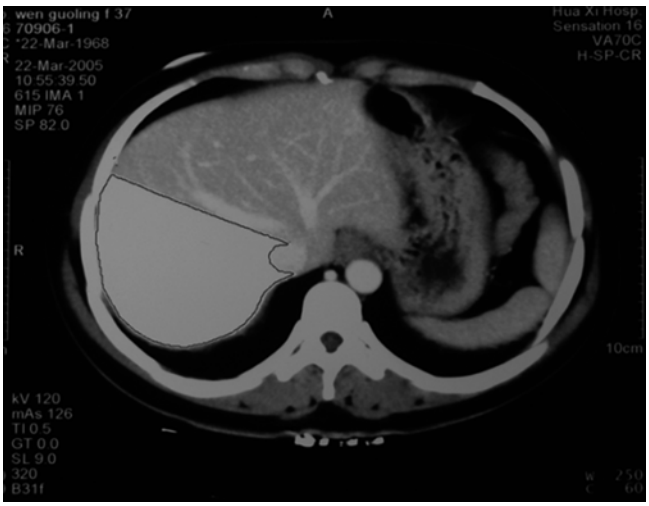


Fig. 29.16 Shows the right hemiliver excluding the MHV during CT imaging

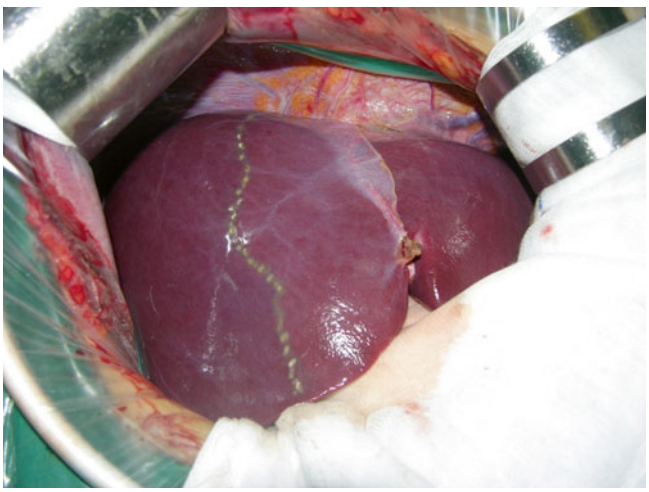


Fig. 29.17 Shows the donor ischemia line

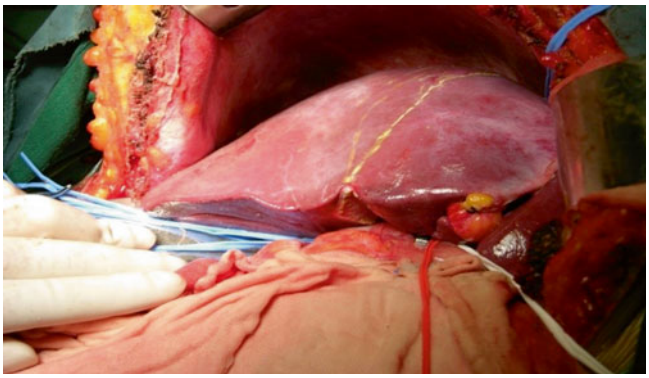


Fig. 29.18 Shows the Cantlie line at the surface of the liver

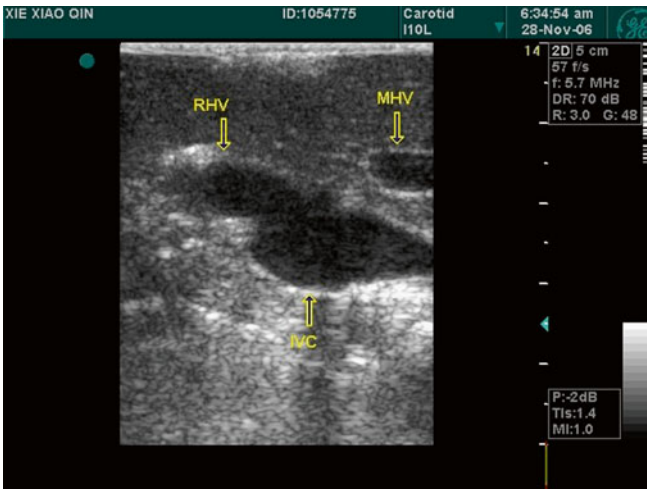


Fig. 29.19 Shows the intraoperative ultrasound confirming the resection line

(CUSA) is used to skeletonize the intrahepatic vessels. The assistant uses the bipolar coagulator or electrotome to coagulate the bleeding points at the liver cross-section and to expose the operation field by using scissors to compress the liver cross-section. The vessels at the liver section less than 3 mm in diameter are resected after clamping with a titanium clip, vessels between 3 and 5 mm in diameter are cut off after ligation, and vessels more than 5 mm in diameter should be preserved and reconstructed. A rubber sling is placed between the back of the liver and the front of the IVC through the left side of the right hepatic vein and the internal side of the portal bifurcation. The sling can pull the liver up when transecting the liver tissue adhering in front of the IVC to prevent the IVC from unexpected surgical injuries and to increase surgical field exposure (Fig. 29.20).

29.4.6.3 Procurement of the Right Hemiliver Excluding the MHV

All of the hepatic vessels and ducts must be well dissected and recognized before removing the right hemiliver.

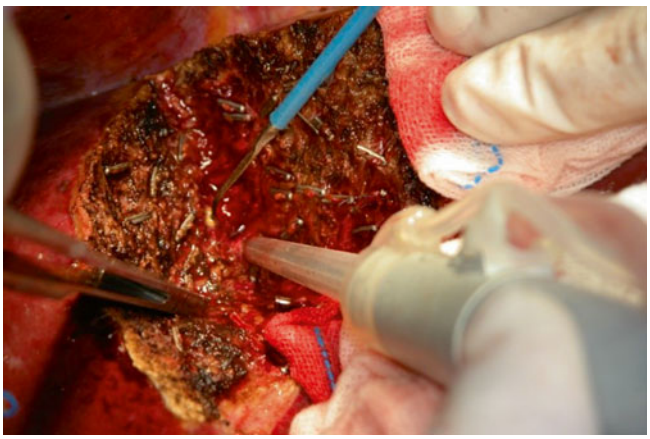


Fig. 29.20 Shows CUSA being used to transect the donor liver

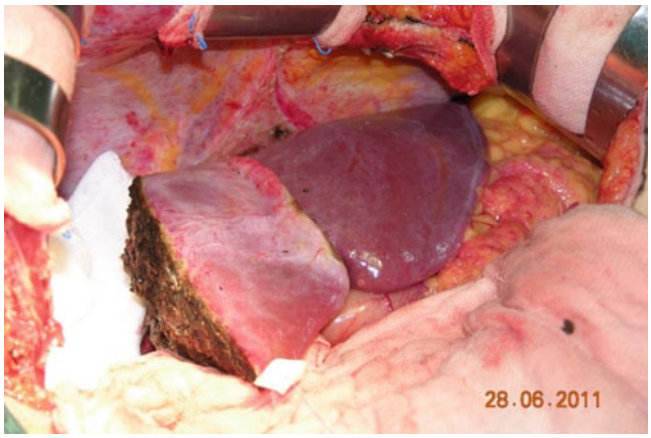
Intravenous injection of heparin at 0.5 mg/kg weight is used after completely transecting the liver parenchyma for the donor. The right hepatic artery is clamped with two microvascular clips at the distal end and then transected. The portal occlusion clip is used to clamp the right portal vein several millimeters distant to the main portal vein. The other clip clamps the distal end, and then, the right portal vein is cut off. If the right portal vein is type II and has three openings at the bifurcation of the main portal vein, the right posterior and right anterior branches must be clamped separately. If an accessory right hepatic vein exists, the right liver is pulled up slightly, and the wall of the IVC is clamped to retain a sufficient amount of the long end for reconstruction. To neutralize the heparin in the donor, 1:1 protamine is used after removal of the right hemiliver.

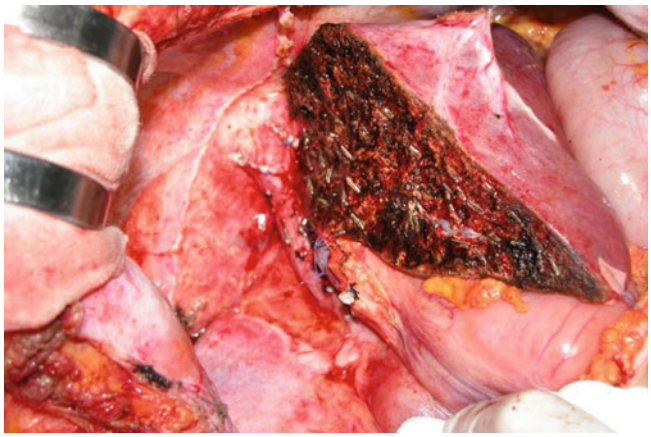
The excised right hemiliver should be put into 0–4 °C icy saline solution immediately and perfused with organic preservation solution before being prepared for modulation.

29.4.7 Management of Remnant Hepatic Vessels and Cross-Section

The break end of the donor's hepatic vein, the right hepatic duct, and right portal vein are continuously sutured with 5-0 Prolene, and a 3-0 silk line is used to doubly ligate the stump of the right artery. The break end of the bile duct can also be continuously sutured with 6-0 Prolene or 5-0 PDS.

The bleeding is stanched and the clean gauze is covered at the liver cross-section to check whether a bile leakage exists. The liver cross-section should be covered with hemostatic materials. One drainage tube is placed at the space inferior to the right diaphragm, and the graft is fixed with interrupted suturing of the falciform ligament (Figs. 29.21 and 29.22).





Figs. 29.21 and 29.22 Show the donor remnant left liver cross-section and hilar structures, including the MHV

29.4.8 Preparation and Modulation of the Graft on the Back Table

29.4.8.1 Preparation and Modulation of the Graft Portal Vein

There is no need for further management for the portal vein because of careful dissection during liver resection and procurement. The inferior mesenteric vein or left ovarian vein is required for vein transplantation when the left portal vein is not sufficiently long to transplant. These veins can be prepared in the process of preparing the graft. The vascular septum of the bifurcation of the right anterior branch and right posterior branch of the portal vein or right portal vein and branches that are close to the opening should be trimmed and sutured continuously with 5-0 Prolene to extend the length of the cuff. The same procedure can be used when the right anterior branch and right posterior branch of the right portal vein are sufficiently close and separated. Separated anastomoses are required in the opposite situation.

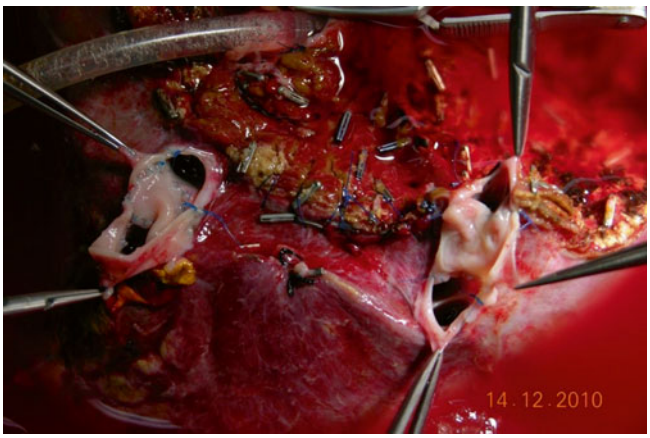


Fig. 29.23 Shows the patch by the great saphenous vein co-fusing the two right hepatic veins and two inferior right hepatic veins as common trunks

29.4.8.2 Modulation of the Graft Hepatic Artery and Bile Duct

The main purpose to modulate the graft's hepatic artery and bile duct is to identify the incomplete intima, thrombosis, and obstruction. Reconstruction of the variation is based on the condition of the recipient.

29.4.8.3 Modulation of the Hepatic Vein of the Liver Donor

The independent hepatic vein of the liver donor with a large diameter and sufficient outside length is adequate for transplantation. The branches of the left hepatic vein include the superior left hepatic vein, middle left hepatic vein, inferior hepatic vein, left superior posterior branch, and right branch. The main branch of the left hepatic vein consists of 2–3 of these veins. Angioplasty is not needed if the co-trunk of the MHV and left hepatic vein (LHV) is sufficiently long. In the opposite situation, the septum should be dissected to extend the length of the cuff. The right wall of the LHV and the left wall of the MHV should be sutured with continuous 5-0 Prolene to extend the diameter of the outflow track, while the MHV and LHV converge into the inferior vena cava. Otherwise, they should each be anastomosed. The vascular septum between the LHV and its superficial branches is close to the opening and should be trimmed, with the sutures being made continuous with 5-0 Prolene to extend the length of the cuff (Fig. 29.23).

A venous bypass achieved using a property vein graft is required when those branches with a diameter over 5 mm of MHV are not sufficiently long to be anastomosed with the IVC (Figs. 29.24 and 29.25).

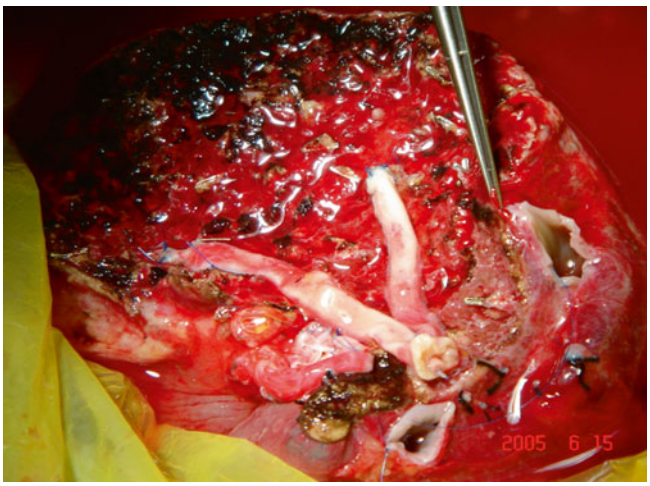


Fig. 29.24 Shows two tributaries of the MHV (more than 0.5 cm in diameter) collecting segments V and VIII, lengthened with bypass vessels at the back table and co-fused as a common opening at the lengthened ends

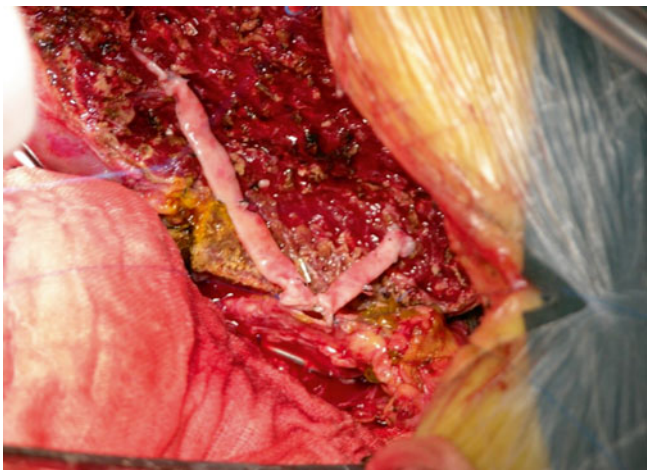


Fig. 29.25 Shows two reconstructive bypass vessels anastomosed with the recipient's IVC

29.5 Resection and Procurement of the Right Hemiliver Including the MHV

The method and process are highly similar to those presented in "resection and procurement of the right hemiliver, excluding the MHV." The resection line can be determined by the three aforementioned methods. After determining the resection of the right hemiliver, including the MHV, transection of the liver on the left side of the gallbladder fossa is conducted. Concurrently, the surface of the liver resection line is ensured on the side of the portal vein and hepatic artery ischemia line.

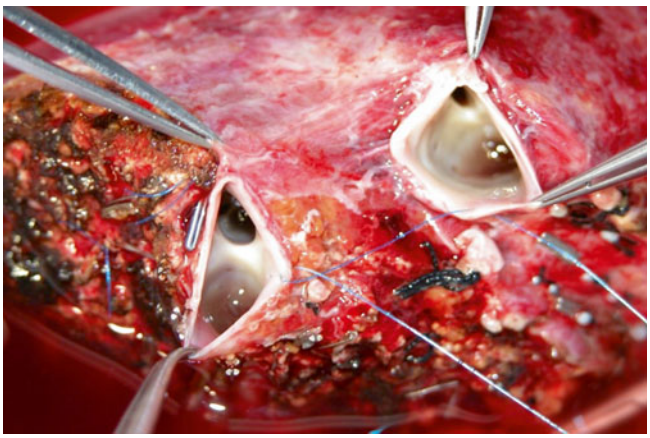


Fig. 29.26 Shows the RHV and MHV in the liver cross-section when preparing the right hemiliver including the MHV

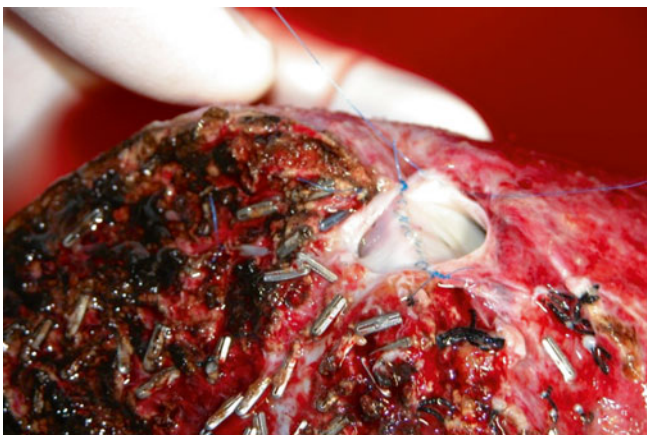


Fig. 29.27 Shows the RHV and MHV merge into a common cutout in the liver section

When it reaches the confluence of the IVa hepatic vein, the MHV trunk can be seen along this section to the confluence of the inferior vena cava vein. In this process, the decision of whether to retain the MHV branches depends on the aperture size (Figs. 29.26, 29.27, 29.28, 29.29, 29.30 and 29.31).

29.6 Outcomes and Complications After Donor Resection of the Right Hemiliver

The majority of studies suggest that there is no difference in the postoperative complication morbidity between the donors with and without the MHV in grafts. Mancero et al. [9] compared the influence of grafts including or excluding MHV

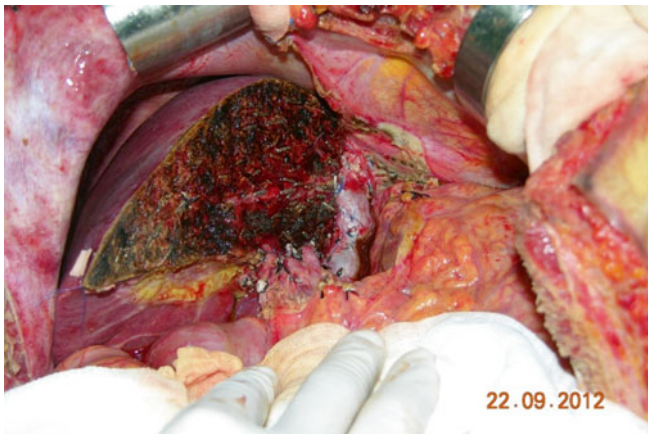


Fig. 29.28 Shows no congestion in the edge of 5 and 8 segments of the liver when the expanded right semiliver is implanted with the MHV

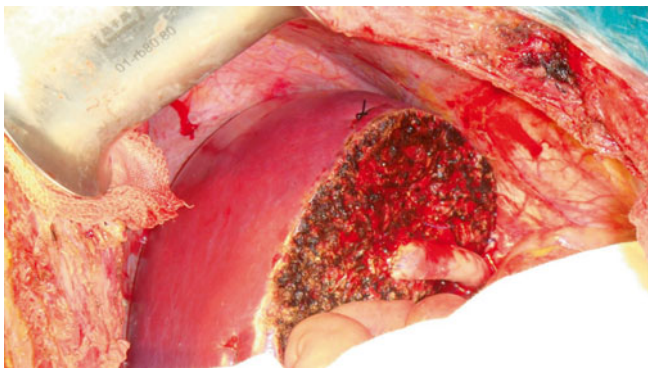
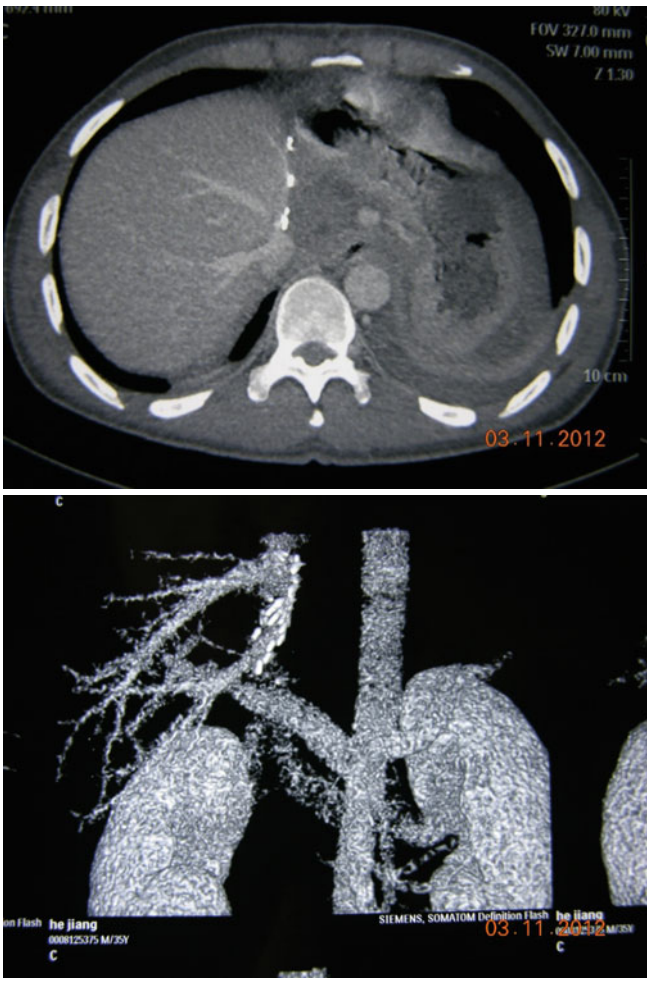


Fig. 29.29 Shows no congestion in the edge of 5 and 8 segments of the liver when the expanded right hemiliver is implanted without the MHV after using cryopreserved vascular bypass liver drainage flowing into the vascular hepatic vein on section



Figs. 29.30 and 29.31 Show the liver section of CT and hepatic vein angiography 1 month after the expanded right hemiliver was implanted with the MHV

on one single center's donors' postoperative complication morbidity and concluded that there is no distinction between these two groups. In the group of donors without MHV in grafts, the postoperative complication rate was approximately 25.6 %, and approximately 17.5 % of donors had severe complications (≥ level III). Whereas in the group of donors with MHV in grafts, the complication rate was 24.1, and 15.3 % of donors have severe complications. There were no deaths in either group, and the biliary complication was the most common type of adverse outcome, in which bile leakage could occur easily. Moreover, there was no distinction in the postoperative assessment of the experiments between two groups. Dayangac et al. [10] suggested that there were no difference in either group if the residual liver volume was more than 30 %. However, when the residual liver volume was less than 30 %, the complication could reach 57.1 % in the donors with MHV in grafts, and some donors showed a consistent jaundice resulting in liver dysfunction.

In brief, whether the MHV could be contained in the right hepatectomy in adult-to-adult living-donor liver transplantation depends on the experience of the surgeon and the transplantation center. However, for the safety of the donors, it is rather preferable to resect the right hemiliver without the MHV than with the MHV [11–18].

The major complications in the donor after right hepatectomy include:

1. Postoperative hemorrhage: Unrelenting hemostasis and liver tissue necrosis are the main reasons for this complication. Blood transfusions, correction of shock, and laparotomy should be conducted to ensure the safety of the donor.
2. Biliary complications: The prevalence of these complications is approximately 2–15 % in right hepatectomy, and bile leakage is the most common of these complications.

Dropping off sutures or the titanium clip in the lobe section could lead to bile overflow. Although bile peritonitis rarely results when the drainage occurs, secondary formation of bile leakage could result.

3. Abdominal infection: Intraperitoneal effusion, hemorrhage, or poor drainage in the postoperative period might lead to secondary pyogenic infection or even septic shock. Drainage should be performed if the size and location of the effusion is identified.
4. Complications associated with the liver itself: Ascites or hepatic dysfunction (and even liver failure and hepatic encephalopathy) often occurs due to insufficient residual liver volume, which typically occurs 2 weeks after the operation. Liver-protecting treatment should be positively managed.
5. Other complications: Such as atelectasis, pneumonia, etc.

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Right Posterior Sector Graft for Living-Donor Liver Transplantation

30

Qiang Xia

30.1 History and Current Status

In Australia in 1989, Strong et al. [1] reported the first case of a living-donor liver transplantation (LDLT), a procedure that has been subsequently heavily promoted in Asia due to scarce donations in this region. At first, to ensure the safety of the donations, LDLT was only undertaken in children, who received a left lateral liver or left lobe transplant. However, for adults with end-stage liver diseases, the left lobe was insufficient as a graft and was only used in low-weight patients. In 1994, Kyoto University [2] reported the first liver transplantation using a right lobe graft, which was donated to a 9-year-old patient with biliary atresia. Although the right lobe was selected due to a variation of the left hepatic artery rather than a consideration of donor liver volume, this report provided strong evidence for the safety of a right lobe graft. Adult patients comprised the majority of patients with end-stage liver diseases many years; thus, LDLT with a right lobe graft between adults decreased the mortality for these patients waiting for livers. For this reason, LDLT has become important in the context of liver transplantations in adults. Nonetheless, the risks of surgery for donors increased, while the complication rate decreased in the recipients when a right lobe instead of left lobe hepatectomy was undertaken. Some cases have even reported donors with liver failure or death. For example, Surman et al. [3] reported seven cases of donor mortality. Moreover, two donors accepted liver transplantation after resection due to the deficiency of the residual liver volume.

Particularly for patients with a proportionally large right lobe, a hemihepatectomy of the right lobe can increase the risk to donors. Many special procedures have been promoted to decrease such risks, such as auxiliary liver transplantation, "dual grafts for one recipient" liver transplantation, and right posterior sector (RPS) graft liver transplantation. Among these methods, an RPS graft including segments VI and VII could be used in donors whose right lobe comprises more than 70 % of the whole liver volume. This procedure avoids resecting the right lobe while guaranteeing sufficient liver volume for metabolism in recipients. Therefore, RPS grafting has been promoted in some experienced transplantation centers. In 2001, the University of Tokyo [4] transplanted the right lateral sector from a living donor to her granddaughter, which was the first published RPS graft procedure. RPS resection met the requirement for the remaining liver proportion in the donor but increased the technical difficulty of the procedure due to the special anatomical characteristics of the RPS. Even in some large transplantation centers, only a small proportion of transplants are RPS grafts. For example, only 1 % of 2,234 LDLT patients received an RPS graft in Japan as of 2005. Currently, the reports of RPS resection are from centers in Asia, such as in Japan and Korea [5–11]. Moreover, some centers have recently reported "dual grafts for one recipient" liver transplantation and cases using RPS for LDLT in children in mainland China.

30.2 Anatomical Characteristics

30.2.1 The Classification of the Portal Vein in RPS Resection

Variations in the donor portal vein are classified into three types (Fig. 30.1). Type I is a bifurcation and is observed in 79.7 % of donors. In this variant, the main portal vein branches into a left and right portal vein, which supply the left and right lobes of liver, respectively. When the right vein branches into a posterior and anterior portal vein, the donor is not suitable for an RPS graft procedure. Type II is a trifurcation and is found in 7.6 % of donors. In this variant, the main portal vein branches into left, right posterior, and anterior portal veins, with the trifurcation occurring in the hilar

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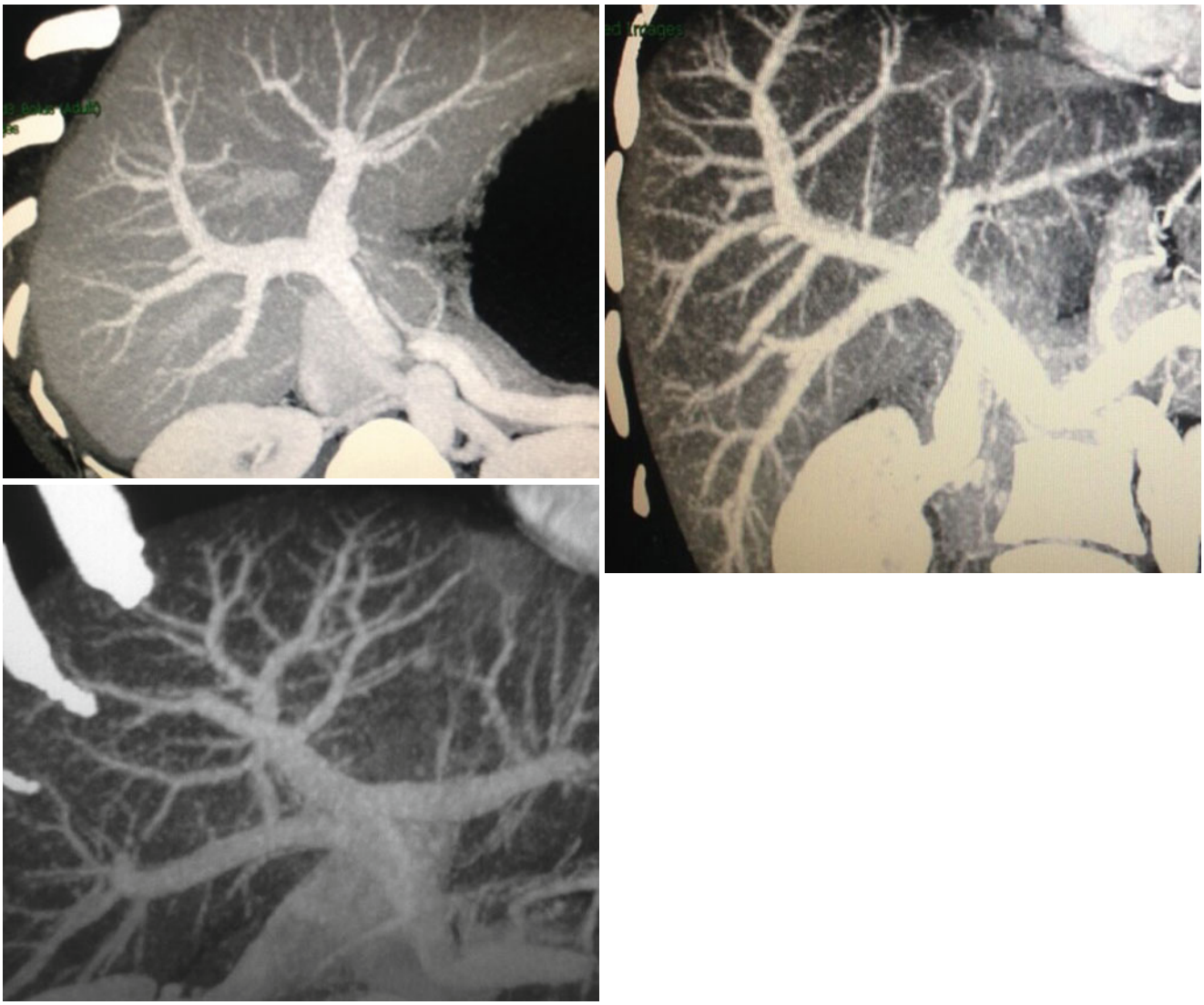

Fig. 30.1 Portal vein variations (including type 1, 2, 3)

plate. Type III portal veins are the primary portal vein variant and present an independent RPS portal vein that branches from the main PV (12.7 %). In this variant, the left portal vein gives rise to branches for the left lobe and the right anterior segment (RAS) of liver, whereas the right portal vein is the independent right posterior branch. Among these types, types II and III are suitable for RPS resection, and the latter is the best choice [5].

30.2.2 The Classification of Hepatic Ducts in RPS Resection

Hepatic ducts can be classified into the four following types (Fig. 30.2). In the type I variant, the right hepatic duct (RHD) exhibits the usual bifurcation of the hilar bile duct and is found in 62.9 % of the population. In the type II RHD variant, the hilar bile duct trifurcates (12.2 %). Type III is the RHD variant with a Y-shaped union of the RAS and the left hepatic duct, with the RPS duct bent behind the RAS (13.2 %). Type IV is the RHD variant with a separate low-branching RPS duct (11.7 %) [5]. If the portal vein is suitable for RPS resection, the requirement for the hepatic duct is not strictly limited; however, the most suitable type of hepatic duct is type IV.

30.2.3 Selection of the RPS Artery

Based on the origin of the RPS artery, the branching patterns of right hepatic artery are classified as extrahepatic and intrahepatic (Fig. 30.3). The extrahepatic type occurs when the

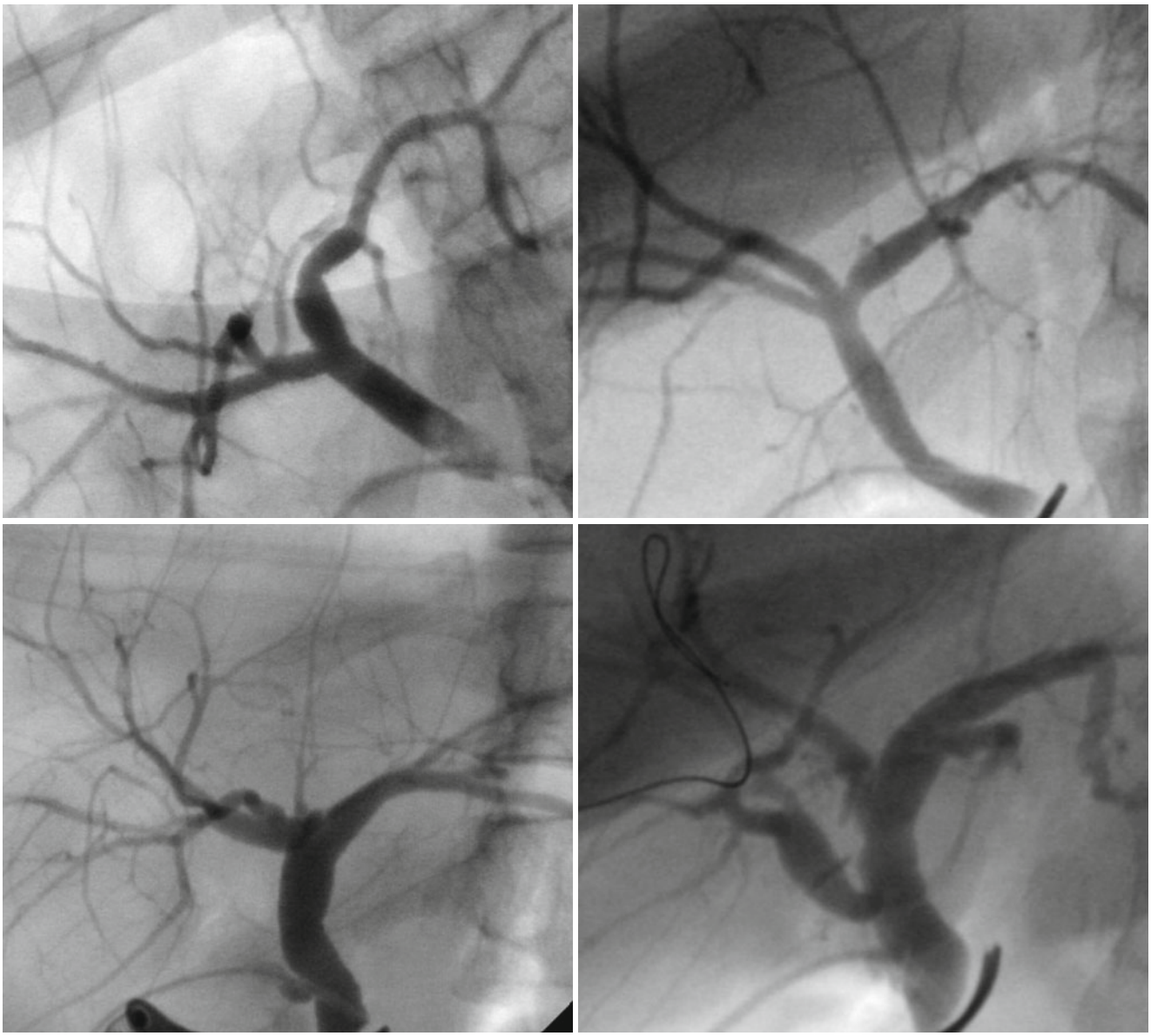

Fig. 30.2 Hepatic duct types (including type 1, 2, 3, 4)

RPS artery branches outside of the liver parenchyma. In this situation, the RPS is easy to liberate during a liver resection; therefore, it is the more suitable variant and is found in 78.7 % of the population. The other branching pattern occurs when the intrahepatic right hepatic artery is long and divides into a right posterior and anterior artery; in this case, liberation is difficult (21.3 %) [5].

30.2.4 Technical Difficulties in Resection and Implantation of RPS

Both RPS resection from the donor and implantation in the recipient demand a developed surgical technique; therefore, the RPS graft is an uncommon type of transplantation. First, the vessels of the RPS usually come from the secondary vessel and increase the complexity of the anatomy. The stump of the RPS would not be sufficient for anastomosis when the portal vein is the bifurcation variant. Thus, donors with this variant are not suitable for RPS. Second, variation in the hepatic duct, such as bifurcation in the RPS with the RHD running behind the portal vein, increases the difficulty of resection and anastomosis of the bile duct. Moreover, the split plane between the RPS and RAS is broad, and a tiny shift when dealing with the split plane during an RPS resection can lead to a dramatic deviation between the actual volume and the preoperative estimated volume of graft. Thus, the assessment of liver volume may be less accurate.

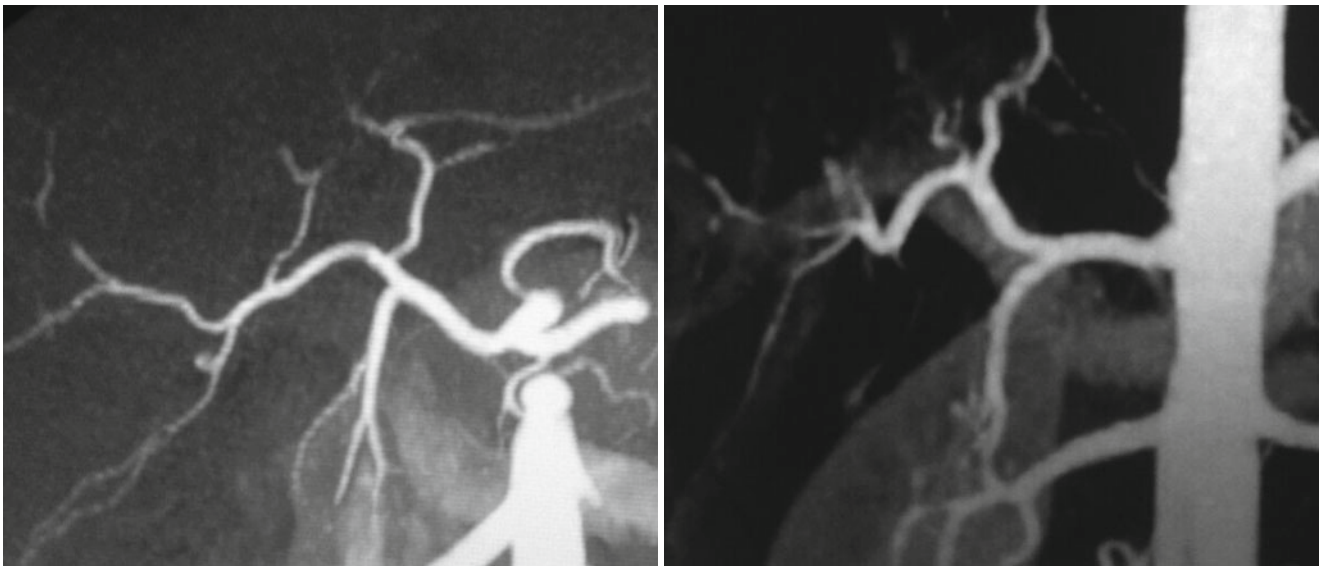

Fig. 30.3 Type of RPS artery (including extrahepatic and intrahepatic)

30.3 Preoperative Assessment

30.3.1 Routine Assessment Before Surgery

The safety of the donor is the most important principle in donor assessment. Additionally, the amount of hepatic issue should meet the metabolic needs of the recipient. The preoperative assessment should contain routine tests, including history collection, physical examination, assessment of the key organ function, imaging examination, mental condition assessment, determination of anesthetization risk, and an ethics review. Ages from approximately 18–55 years are most suitable, and the blood type should be compatible. Diabetic patients who are being treating with insulin and patients with unmanageable hypertension, physical diseases, or a history of malignancies and serious abdominal surgery should be excluded. Moreover, obese patients should be avoided due to the increased risk of cardiovascular disease, especially in patients with body mass indexes (BMIs) above 25, which significantly increases the operative risk during the perioperative period.

30.3.2 Measurement of the Liver Volume of RPS

A three-dimensional reconstruction using computer tomography angiography (CTA) of the liver can be used to measure the volume of the liver grafts. Experts from the University of Ulsan in Korea recommend that the residual liver without hepatic steatosis in donors who are 20–30 years of age should be more than 30 % of the whole liver volume. For those who are 30–50 years of age or exhibit mild or mid-stage hepatic steatosis, the residual liver volume should be more than 35 % [12]. In healthy adults, the right lobe of liver occupies an average of 67 % of the whole liver volume (Table 30.1). However, this figure is greater than 70 % in approximately one quarter of the donors [13]. In this situation, hepatectomy of the right lobe increases the risk to donors, whereas the left lobe is too small to transplant. RPS resection could be an approach for liver transplantation. The resection of the RPS requires that its volume be more than the sum volume of the left lobe and the caudate lobe, and the excess portion should be more than 3 % of the whole liver volume. At the same time, the estimated liver volume should be 40 % of a standard liver volume (SLT), or the graft-to-recipient weight ratio (GRWR) should be more than 0.8 %.

Table 30.1 The proportion of different parts in the whole liver [13]

Lobe	Volume (cm^3)	Percent (%)
Left lobe	395 ± 91	31 ± 4
Left lateral segment	220 ± 57	17 ± 4
Left medial segment	175 ± 65	14 ± 4
Caudate lobe	25 ± 7	2 ± 1
Right lobe	854 ± 151	67 ± 4
Right anterior segment	473 ± 97	37 ± 5
Right posterior segment	382 ± 84	30 ± 4

30.3.3 Assessment of the Anatomy of the Hepatic Vessels

The assessment of hepatic vessels includes the three-dimensional reconstruction of the artery, portal vein, and hepatic vein using hepatic CTA. The hepatic duct should

be visualized using magnetic resonance cholangiopancreatography (MRCP). Most studies have reported that the choice of RPS should consider the anatomy of the vessels. As mentioned above, the most suitable variant types are type III for the portal vein and type IV for the hepatic duct and extrahepatic RPS artery branches. Due to the lack of an independent branch, type I is not suitable for RPS grafts. However, research from Korean experts in 2011 recommended that if the RPS volume is suitable for transplantation, the vessels should not be considered. These authors performed 13 cases of RPS graft resection in 65 LDLTs, showing excellent results [6]. Nevertheless, based on the experience of many transplantation centers, the anatomy of the portal vein is still an important factor in RPS resection [5, 7, 14].

30.4 Surgical Approach

Incision Perform a routine incision for hepatectomy, with the specific manner being adjusted based on the experience of the surgeon and the body size of the donor. The J-type incision is usually used.

Cholangiography Detach the gallbladder to the cystic duct in a retrograde manner along the gallbladder bed. Insert and affix a Phycon tube into the cystic duct, into which 20 % diatrizoate meglumine is injected for cholangiography (Fig. 30.4).

Anatomy of the First Porta Hepatis Detach the proper hepatic artery up to the RPS artery branch and dissect the RPS duct. At the same time, detach the RPS portal vein behind the RPS artery (Fig. 30.5).

Addressing the Right Hepatic Vein Dissociate the right triangular ligament and expose the junction of the right and middle hepatic veins. Detach the veins and pull the liver to the left to expose the back of the right hepatic vein. Then, perform the liver hanging maneuver in preparation for next step (Fig. 30.6).

Split the Liver Parenchyma Due to the ischemic penumbra that can result from blocking the RPS portal vein and artery, the split-liver surgical plane is defined using the left side of the right hepatic vein from the diaphragmatic to the visceral surface behind the RPS duct. A cavitron ultrasonic surgical aspirator (CUSA) is used for hepatic resection. After dividing the RPS duct, the liver hanging maneuver is used across the right hepatic vein to the hepatoduodenal ligament. Resect the remaining liver parenchyma with the hanging maneuver (Fig. 30.7).

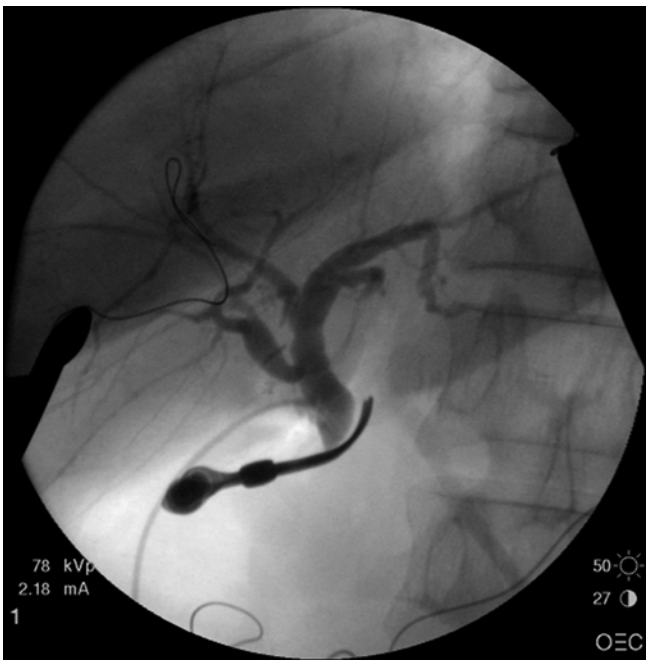

Fig. 30.4 Cholangiography during the surgery

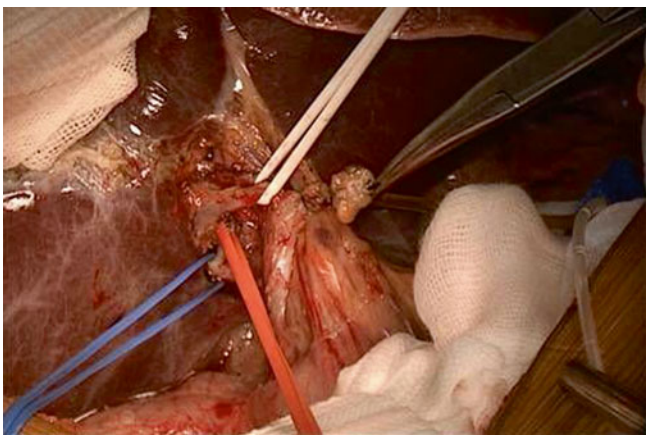

Fig. 30.5 Anatomy of the hilar plate (*red*, RPS artery; *blue*, RPS portal vein; *white*, RPS duct)

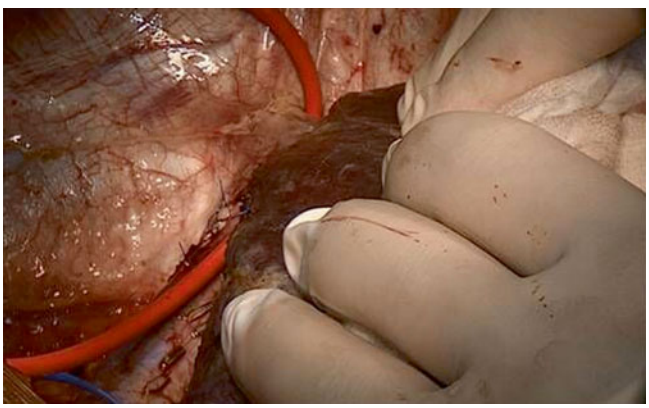

Fig. 30.6 Dissociation of the right hepatic vein

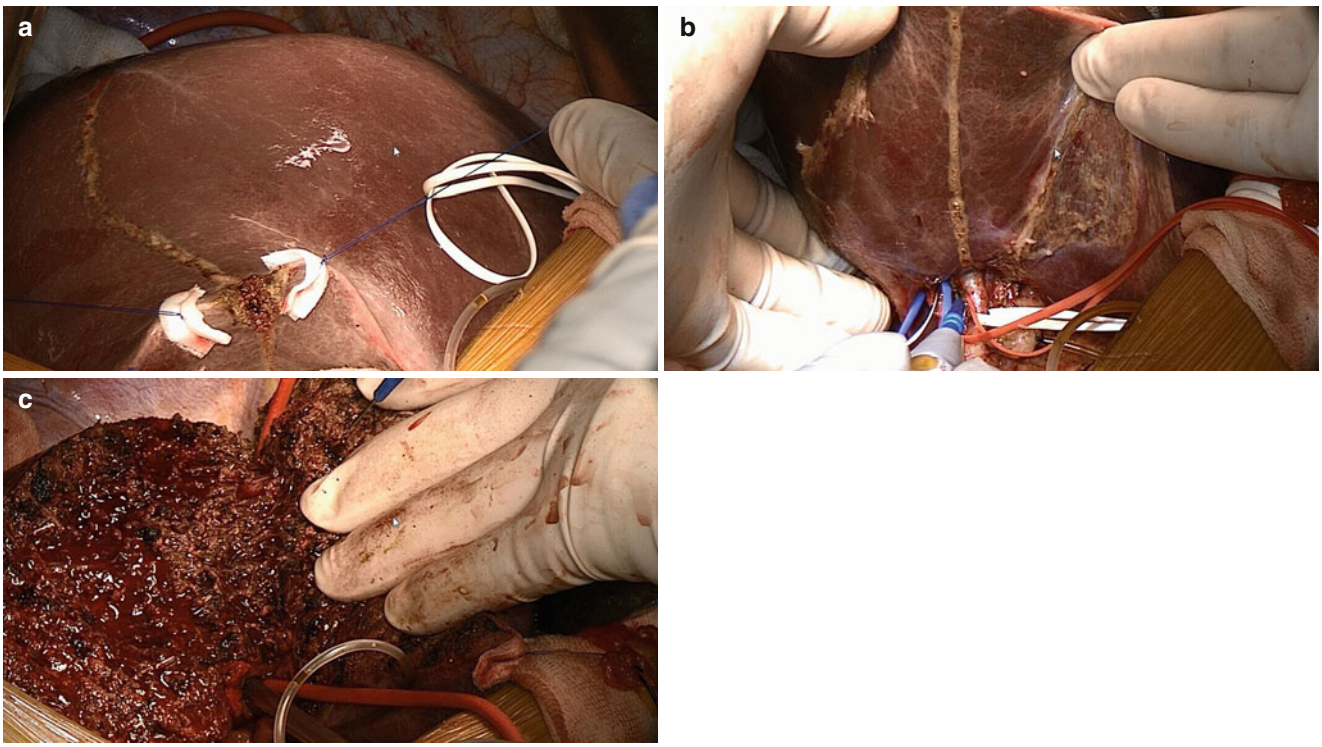

Fig. 30.7 Split the liver parenchyma. (**a**) Mark showing the split-liver surgical plane (anterior). (**b**) Mark showing the split-liver surgical plane (visceral surface). (**c**) The liver hanging maneuver for traction

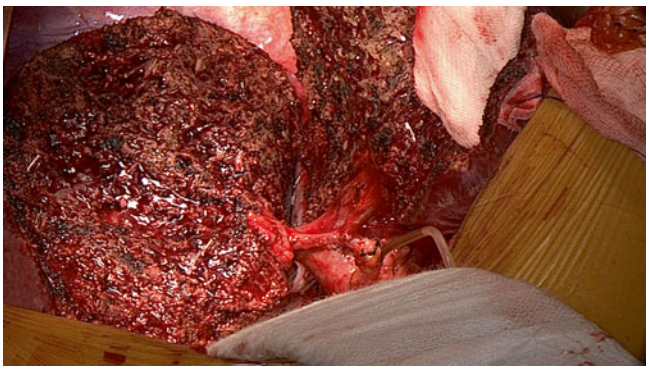

Fig. 30.8 Dividing the RPS duct

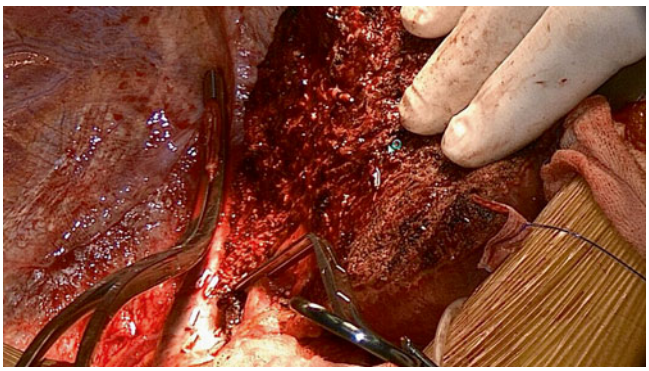

Fig. 30.9 Cutting surface of the donor liver

Dividing the RPS Duct Split the liver parenchyma to the hilar plate, noting the location of the RPS duct. Perform a second cholangiography, and resect the liver parenchyma if the RPS is ensured correctly (Fig. 30.8).

Management of the Cutting Surface of Donor Liver Suture the vessels in the cutting surface with Prolene line. Check for bleeding or bile leakage. Mild bleeding can be covered with stanching gauze, and human fibrin sealant can be sprayed over the whole cutting surface. Abdominal drainage is not necessary (Fig. 30.9).

30.5 Matters That Need Attention during Surgery

1. Generally speaking, the RPS duct traverses in front of the right portal vein and the RPS artery, so that the duct is easy to separate. However, the RPS duct can also stretch into the back of the right portal vein in certain duct variations (Fig. 30.10), increasing the difficulty of the surgery. In this condition, the RPS and RAS portal vein should be detached first. Then, track the branches of the portal vein and the hepatic artery in front of the duct with a rubber cord. At

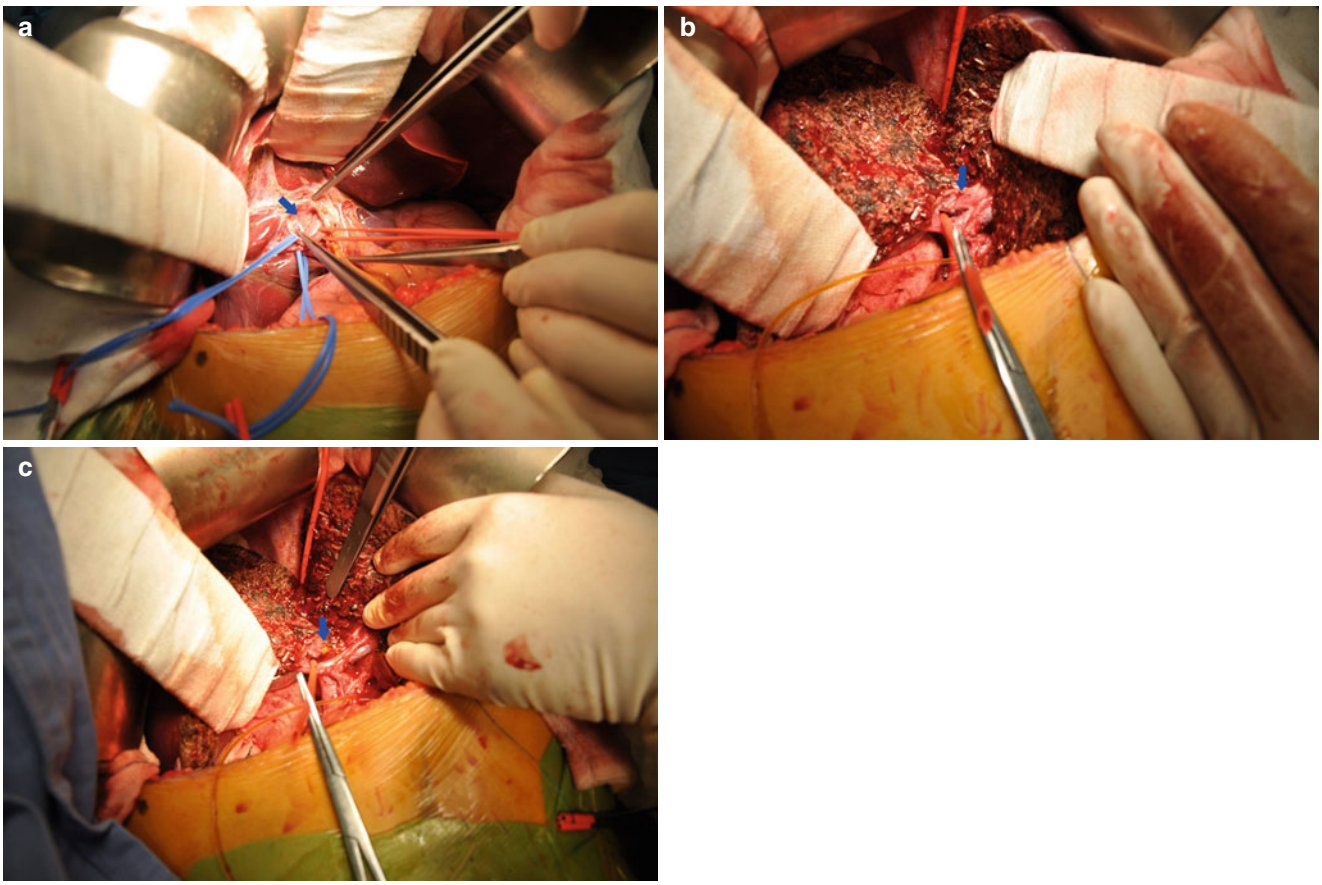

Fig. 30.10 An RPS duct stretching into the back of right portal vein. (**a**) An RPS duct stretching into the back of the right portal vein (*blue arrow*). (**b**) An RPS duct before dissection (*blue arrow*). (**c**) An RPS duct after abruption (*blue arrow*)

this point, the RPS duct is exposed, can be detached gradually, and can finally be separated at the hilar plate.
2. The split-liver plane is broad, which can lead to large deviations between the actual volume and the preoperative estimated volume of the graft. This fact should be considered in cases of small-for-size syndrome.
3. RPS grafts can contain a large branch of the middle hepatic vein in segment IV. In case of congestion, the bypass and anastomosis should be undertaken between the segment IV branches and the hepatic vein of the recipient [15].

30.6 Complications

In experienced transplantation centers, the general complication rate is usually less than 15 % for RPS graft LDLTs. Possible complications include bleeding in the abdomen, delayed liver function recovery, bile leakage at the cutting surface, thrombosis in the hepatic artery, wound infection, and pulmonary infection. Moreover, some donors cannot tolerate high-fat food and have diarrhea to different degrees due to the resection of the gallbladder [16].

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Procurement of Liver Graft

31

Ming-Qing Xu, Shi-Feng Li, and Lei Li

Hepatic procurement should follow two principles: cooling the central part of the liver quickly, and insuring the integrity of the liver, including abnormal blood vessels.

The primary steps in DBD donor liver procurement are as follows:

1. The anesthesiologist maintains vital signs of the donor.
2. Make a midline of the thoracic and abdominal region. Using a sternum saw to perform a sternotomy to open the chest, using an abdominal retractor for abdominal wall support. Avoiding to damage the heart, lung, and abdominal organs (Fig. 31.1).
3. Resect the pericardium and perform heart decompression. This procedure can promote the blood of the abdominal organs to flow into the heart and reduce organ congestion and edema. Keep the diaphragm intact (Fig. 31.2). Cut off the falciform ligament to the second hepatic portal.
4. Check the condition of the liver: whether the color is normal, the texture is soft, the edge is sharp, and whether the presence of nodule. Fig. 31.2). If the liver is swelling, a dose of 50-100 g of 20 % Mannitol should be intravenously infused; if blood pressure is stable, a dose of 20-100mg of Lasix should be intravenously infused at the same time.
5. Carefully check the branches at the first hepatic portal. Any variations of the right hepatic artery [usually originating from the superior mesenteric artery (SMA)] should be protected. If the variant artery is located behind the pancreas, the pancreas graft can be used. If the variant hepatic artery transverses the pancreas, do not use the pancreas graft and protect the liver graft.
6. Free and remove the left hepatic ligament; then, ligate the gastrohepatic ligament. The upper edge of pancreas is seen near the lesser curvature of the stomach. If there is any variant left hepatic artery (usually from the left gastric artery), it needs protection. Ligate the gastrocolic ligament. The entire pancreas is revealed behind the stomach. Check whether the pancreas is pink, soft, smooth, and without nodules. Check whether the pancreatic head is big and the pancreatic body and tail is thin and short. Cover the pancreas with wet gauze to avoid mechanical extrusion.
7. Open the pelvic peritoneum on the upper edge of the pelvic, expose the end part of the abdominal aorta and place 0-silk suture for traction. (Fig. 31.3).
8. Reveal the inferior mesenteric vein (IMV) at the left abdomen and place traction sutures to retract it (Fig. 31.4). Along the retroperitoneum, find and isolated the initial portion of the SMA and set into the traction. Do not ligate the peripheral vasculature of the SMA to avoid affecting the blood supply and venous drainage of the pancreas.

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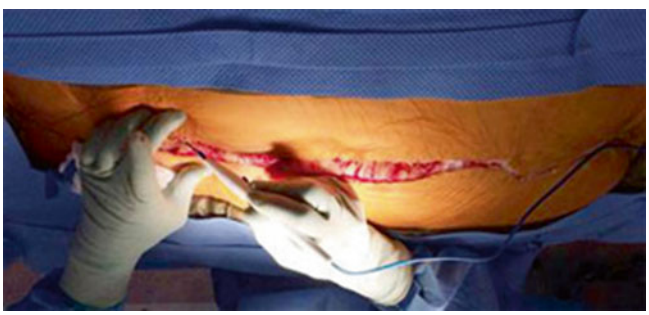

Fig. 31.1 The midline incision on the chest and abdominal wall

L. Yan (ed.), *Operative Techniques in Liver Resection*, DOI 10.1007/978-94-017-7411-6_31

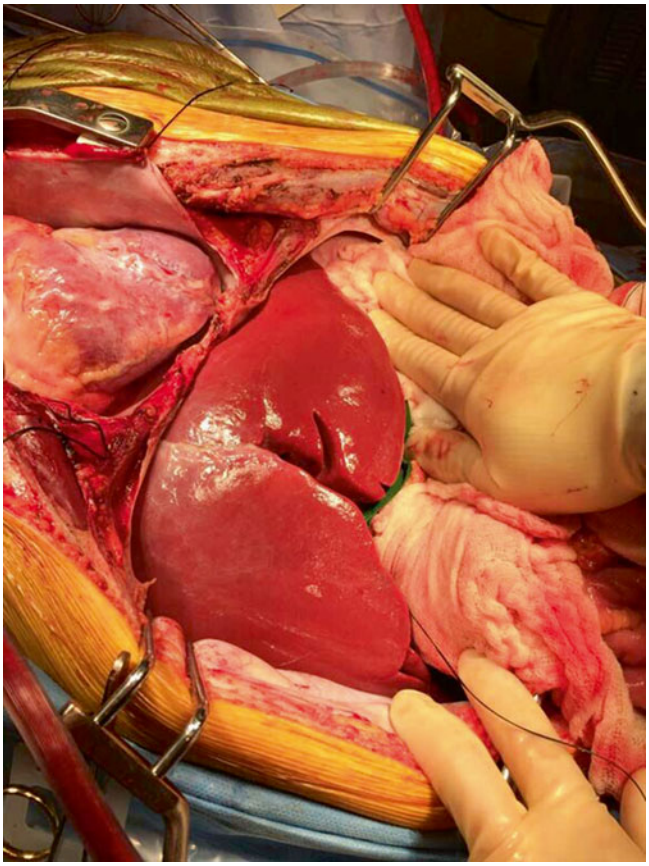

Fig. 31.2 Revealed heart, lungs, and liver

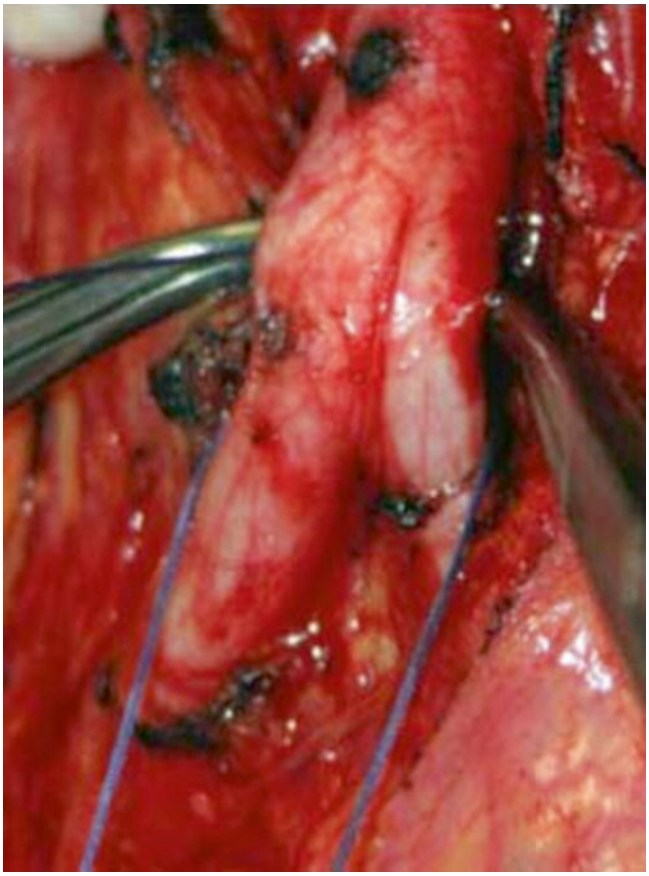

Fig. 31.3 The inferior segment of the abdominal aorta

9. Dissect the trunk of the celiac artery on the upper edge of the pancreas. Isolate the splenic artery and place traction sutures on the initial section (Fig. 31.5). Isolate the gastroduodenal artery (GDA) at the end of the common hepatic artery and place traction sutures behind the initial section of GDA (Fig. 31.6).
10. Isolate and cut off the common bile duct near the pancreatic head (Fig. 31.7).
11. Make a Kocher incision of the peritoneum along the lateral duodenal edge, separating the duodenal loop (avoiding an extrusion to the duodeum and pancreas). Reveal the abdominal aorta and inferior vena cava behind the pancreatic head. Separate the inferior vena cava under the right liver and place traction sutures (Fig. 31.8).
12. Open the bottom of the gallbladder. Flush the gallbladder and bile duct (For the DCD donors, this operation should be done during the organ perfusion).
13. Cut a small incision on the inferior mesenteric vein wall, and insert the perfusion tube centripetally into the IMV with 0-silk sutures fixation (Fig. 31.9). Clamp off the end of the abdominal, and insert the perfusion tube centripetally into the abdominal aorta with 0-silk sutures

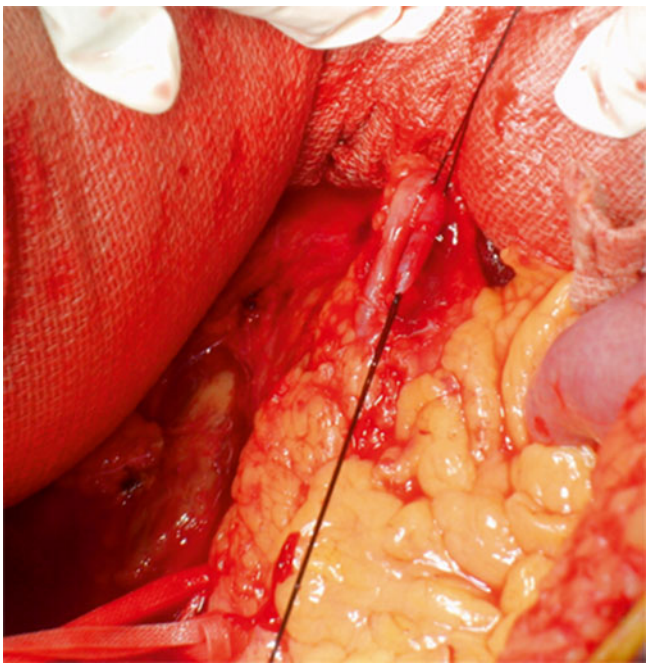

Fig. 31.4 The inferior mesenteric vein

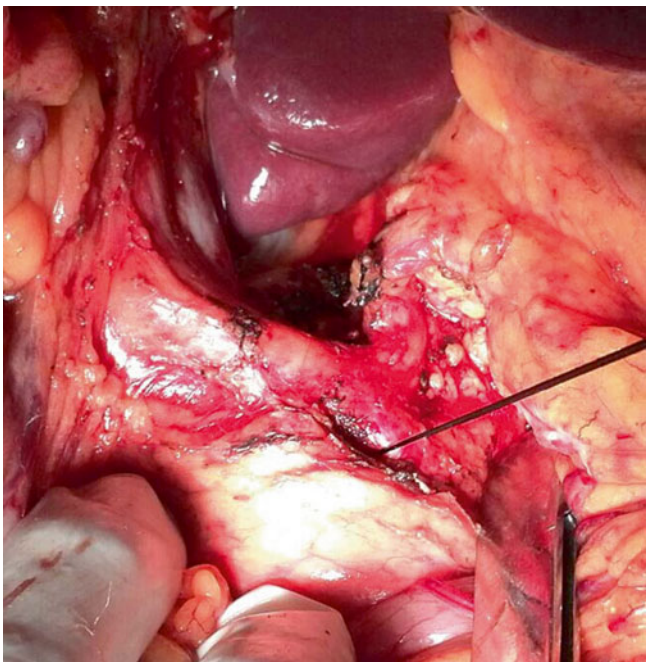

Fig. 31.5 The origin of the splenic artery

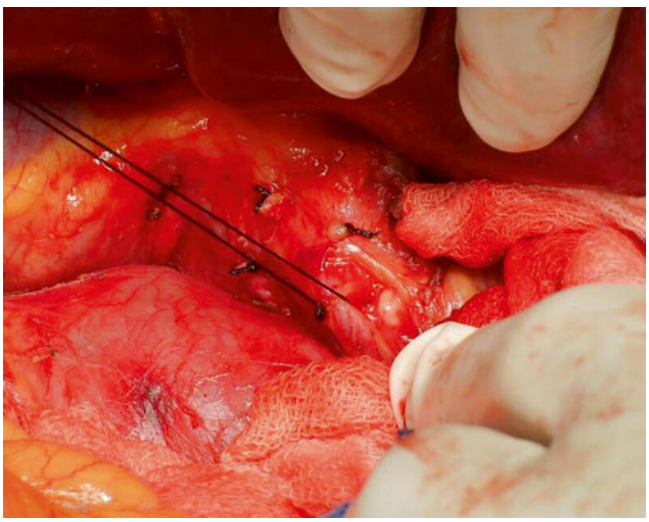

Fig. 31.6 Separation of the GDA and placement of the traction sutures

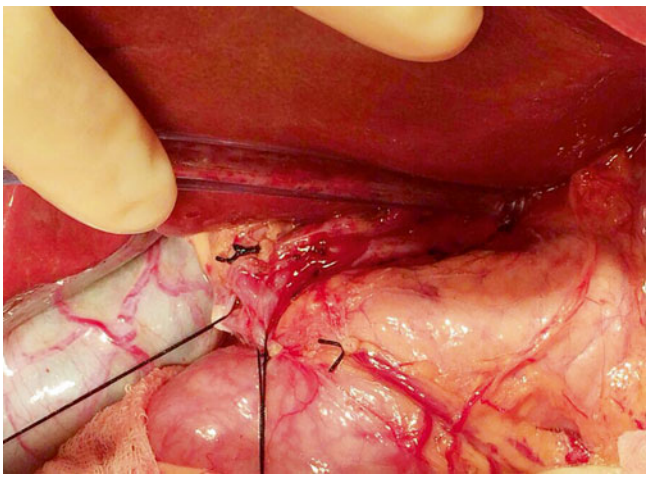

Fig. 31.7 Separation and ligation of the bile duct near the head of the pancreas

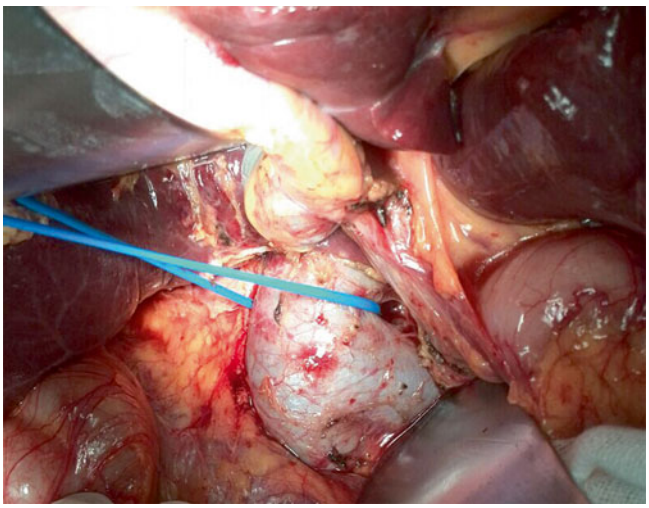

Fig. 31.8 Separation of the infrahepatic vena cava

fixation (Fig. 31.10). The upper end of the perfusion tube should not exceed the level of the renal artery to avoid adverse renal perfusion.

14. If the heart and lungs are to be procured, the perfusion tube should be placed at the same time, and the abdominal aorta should be blocked between the diaphragm and celiac artery (Fig. 31.11). If the heart and lung are not to be procured, we can use a thoracic clamp to block the thoracic aorta.
15. Cut off the vena cava at the junction of atrium and vena cava (the junction of the red auricle muscle and white vascular). Begin abdominal organ perfusion and heart-lung perfusion. Place a large amount of crushed ice to protect the liver, pancreas, and kidney from warm ischemia injury. Perfuse the liver with approximately 4,000 ml UW solution; maintain the perfusion pressure at about 100 mmHg (1 mmHg = 0.133 kPa) that is the mean arterial pressure level. Infusion quantity for the artery and portal vein needs to be 2,000 ml UW solution.
16. Tighten the traction line preplaced for SMA and splenic artery as well as GDA when approximately 1,000–1,200 ml UW solution has been perfused. Preset the splenic artery and the origin of the GDA with traction.

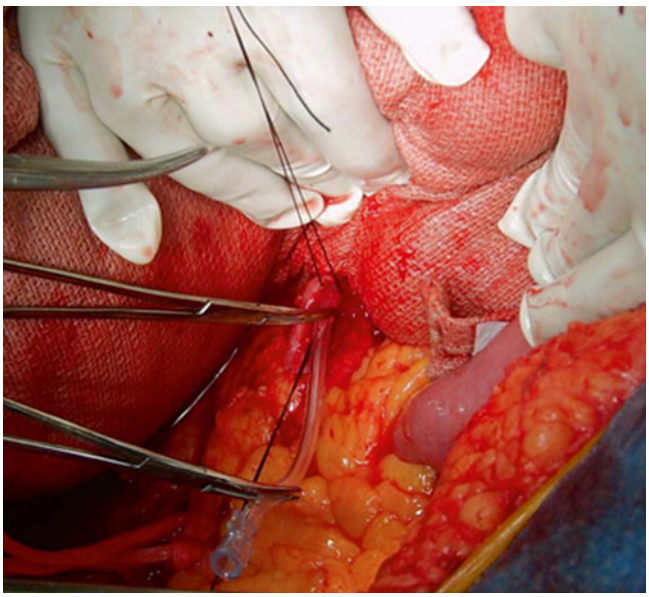

Fig. 31.9 Inserting the perfusion tube into the IMV

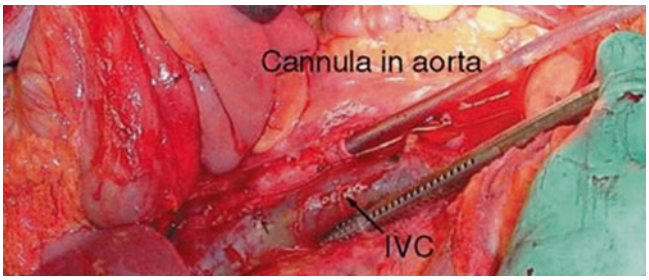

Fig. 31.10 Inserting the perfusion tube into the abdominal aorta. *IVC* inferior vena cava

Stop pancreatic perfusion to avoid excessive perfusion and pancreatic edema.

17. Procure the lungs and heart from the pleural cavity.
18. Procurement of the liver graft: Open the side peritoneum along the ascending and descending colon. The colon as well as the small intestines are placed on the lower left side of the abdominal cavity to expose the abdominal organs. Isolate and cut off the right gastric artery. GDA is then to be cut off; then, stitch the GDA incision with a 6/0 Prolene suture as a marker (Fig. 31.12). Cut off the left gastric artery at its initial part near celiac artery. The variant left hepatic artery originating from the left gastric artery should be protected. Then, cut off the splenic artery near the celiac artery. Mark the distal incision with a 6-0 Prolene suture as a marker (Fig. 31.13). Isolate the common hepatic artery. Figure 31.14, and the small vessels around the pancreatic should be ligated. Separate the celiac trunk from the abdominal aorta and visualize

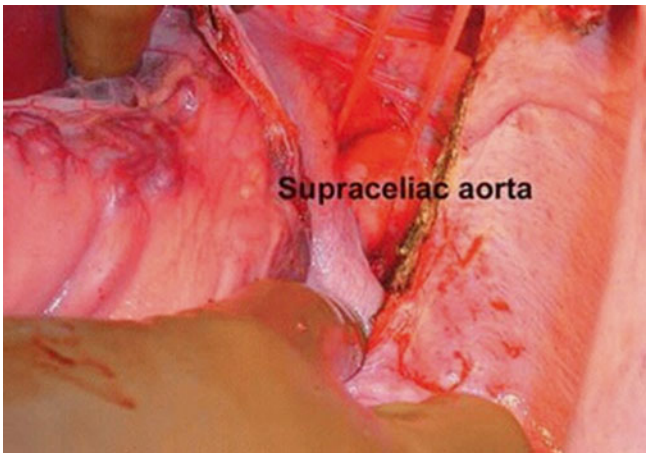

Fig. 31.11 The block parts of abdominal aorta

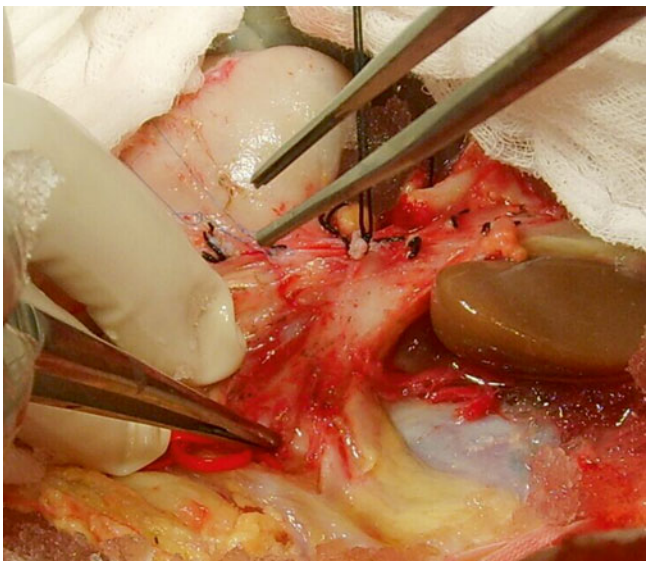

Fig. 31.12 GDA incision

the SMA on its underside. Cut off the celiac artery from the abdominal aorta (Fig. 31.15). The celiac and common hepatic arteries are completely free. Now, cut the portal vein with a 1.5 cm length from the upper pancreatic margin (Fig. 31.16). Cut the infrahepatic vena cava near the upper edge of the right renal vein (Fig. 31.17). Excise the diaphragm around the vena cava. Pay attention to prevent damage to the upper edge of the right kidney (Fig. 31.18). Thus, the donor liver is procured with the inferior vena cava and the diaphragmatic adhesions. Place the liver in a sterile basin filled with crashed ice, and then pour 1000 ml UW solution into the portal vein and hepatic artery (Fig. 31.19). Cut the bilateral iliac artery (including

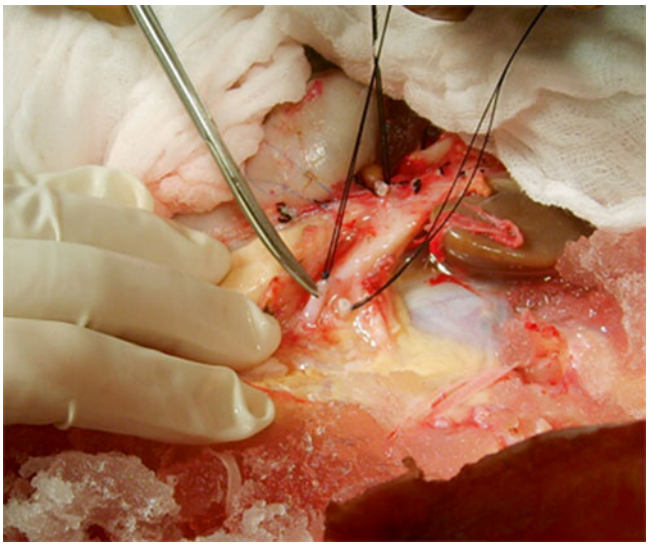

Fig. 31.13 Splenic artery incision

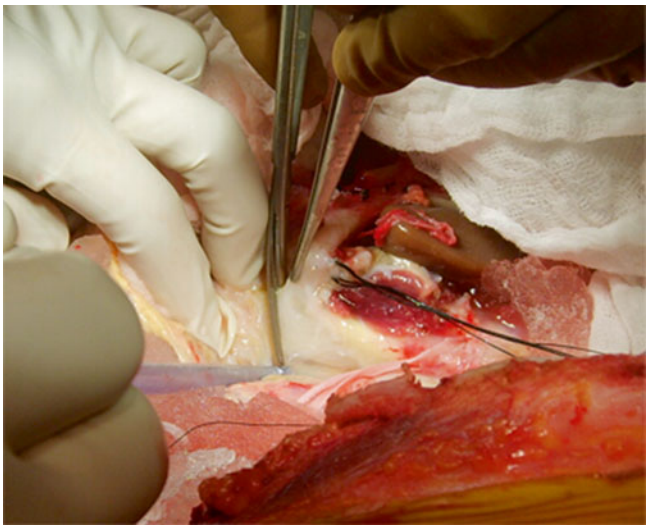

Fig. 31.15 Celiac artery and common hepatic artery incision

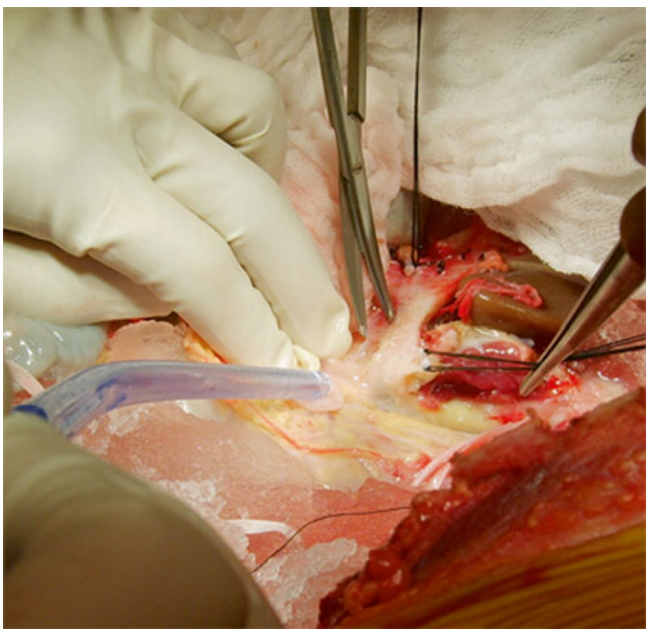

Fig. 31.14 Free of common hepatic artery

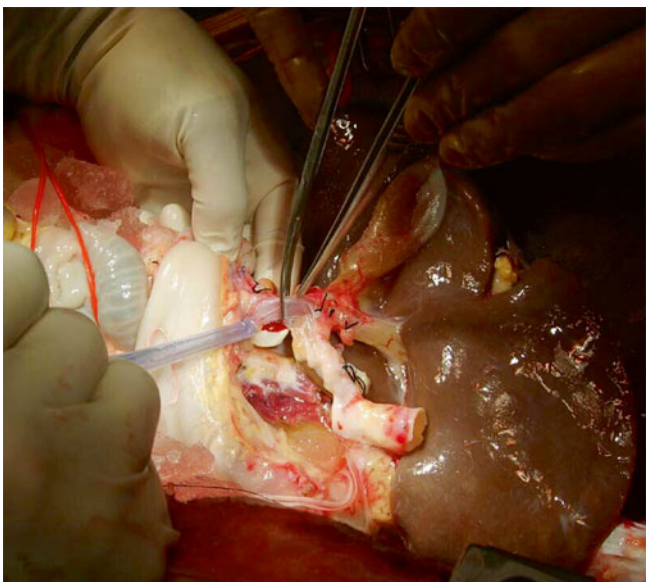

Fig. 31.16 Portal vein incision

the external and internal iliac arteries) and iliac vein for reserve.

The donor liver is to be packeted based on the principles of three layers of organ preservation: (the donor liver with the 1,000 ml UW solution in the inner layer; 0–4 °C cold water in the middle layer; and the outer layer packet for the further pollution prevention. At this moment, the donor liver and iliac artery and iliac vein can be carried to the transplant center.

19. For the procurement of liver from the DCD donor, most transplant centers have the principles of the warm ischemia time not exceeding 30 min, and firstly perfusion followed by in situ anatomy of organs. Procure the liver, pancreas and kidney in turn after finishing the perfusion. Lastly, cut the bilateral iliac artery (including the external and internal iliac arteries) and iliac vein for reserve.

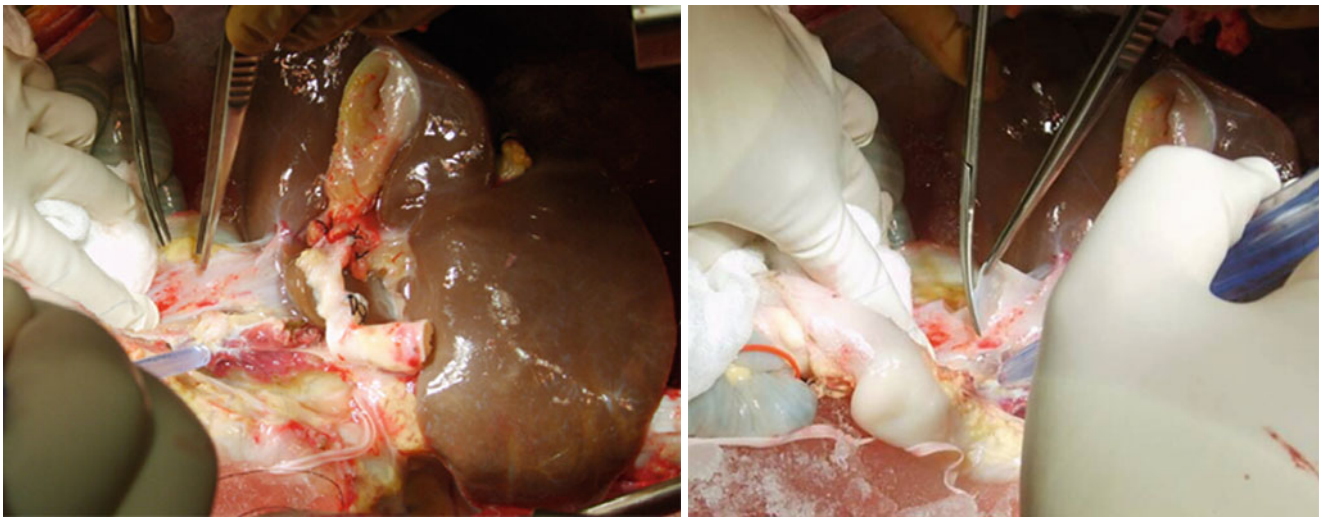

Fig. 31.17 (*1*) (*2*) Infrahepatic vena cava incision

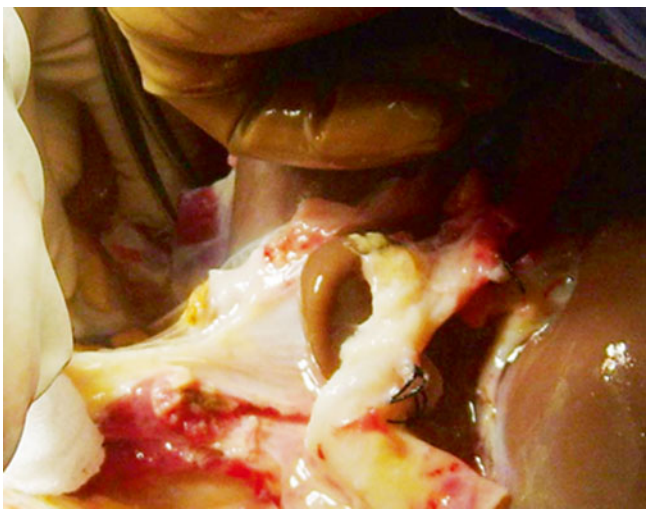

Fig. 31.18 Cutting off the diaphragm near the right liver

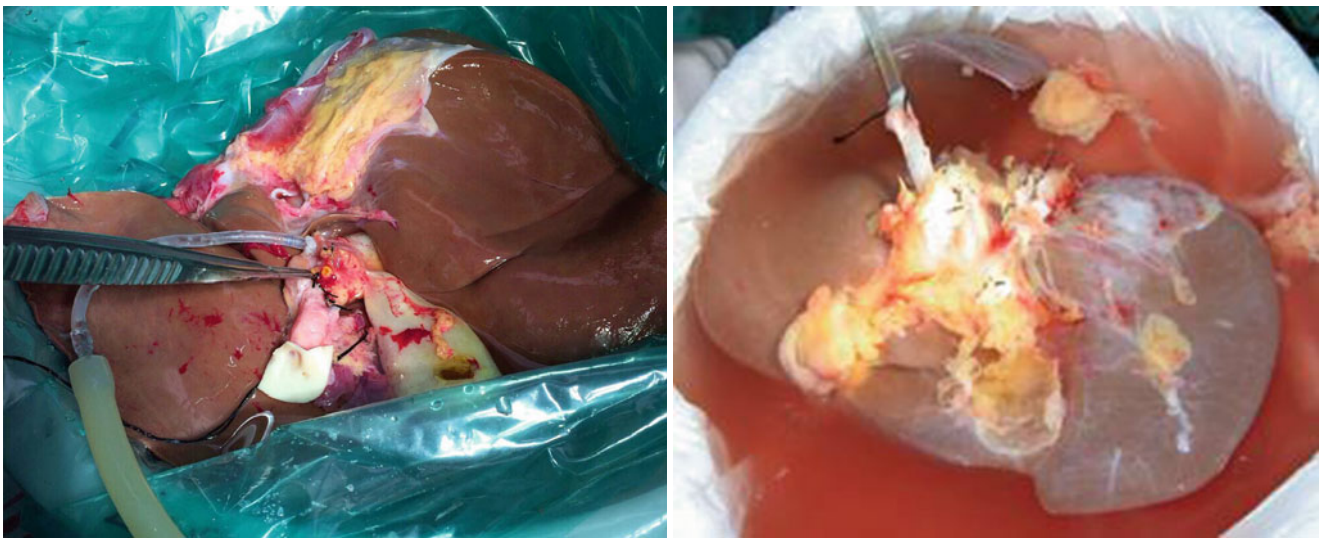

Fig. 31.19 (*1*) (*2*) The procured liver

Laparoscopic Donor Liver Resection

32

Kezhou Li, Jiayin Yang, Xiaowu Zhang, and Wei Gao

32.1 History of Laparoscopic Donor Liver Resection

Since 1988, Raia et al. of Brazil [1] have conducted living-donor liver transplantation as an important supplement to cadaveric liver transplantation. The procedure is becoming increasingly prominent worldwide.

Cherqui et al. [2] of France successfully implemented the first laparoscopic donor left lateral lobe resection in 2002. Laparoscopic techniques have been gradually implemented and successfully applied to liver resection in living-donor liver transplantation.

In 2006, Koffron et al. [3] reported the first laparoscopic-assisted living-donor right liver resection. This was mainly a hand-assisted laparoscopic dissection using minilaparotomy liver parenchymal transection hybrid technology.

In 2009, Baker et al. [4] further confirmed the safety and feasibility of the hybrid technology in their report of a group of 33 cases of assisted in vivo laparoscopic right hepatectomy.

Suh et al. [5] reported a group of nine cases of laparoscopic living-donor liver resection in 2011. In this group of patients, the first two cases of right liver resection were accomplished by hand-assisted laparoscopy, whereas the other seven cases were switched to laparoscopic laparotomy. The surgeons noted that hand-assisted laparoscopic liver resection has no greater advantage than laparoscopic-assisted, minimally invasive abdominal surgery, although the difficulty of the surgery and the surgical time are increased.

In the recent past, laparoscopic donor liver resection began to be more widely used and has developed rapidly since then. The procedure has been developed and promoted in a number of transplant centers around the world. Laparoscopic right liver resection technology is continually developing and technologically matured. Our center has completed more than 35 cases of laparoscopically assisted right hepatectomy since July 2011. Compared with open liver resection, laparoscopic liver resection involves less trauma, less postoperative pain, and a shorter hospital stay [6–22]. The problems that result from traditional open donor liver resection, such as a long incision (which leaves a significant abdominal scar), significant abdominal injury, postoperative pain, and slow postoperative recovery, emerged gradually. These issues affected potential donors, particularly the younger volunteers. Therefore, the development of laparoscopic liver resection carries major significance for organ transplant.

32.2 Surgical Types of Laparoscopic Liver Resection

32.2.1 Complete Laparoscopic Donor Liver Resection

The left lateral lobe is currently reported to be the most appropriate complete laparoscopic resected living-donor liver graft. Due to the anterior location of the left hepatic lobe (along the elongated section of the hepatic vein fissure), it is relatively simple to laparoscopically reveal the left hepatic ligament; therefore, the first step is to perform a laparoscopic liver resection of the left hepatic lobe. Due to the superficial location of the left lateral lobe, the first step of the complete laparoscopic liver resection is its removal. In 2002, Cherqui et al. [2] of France successfully completed the first entirely laparoscopic donor live resection of the left lateral lobe, with the graft being removed through a small incision above the pubis. This was the first time the laparoscopic technique was used in living-donor liver transplantation. In

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2006, Soubrane et al. [23] reported 16 cases of laparoscopic living-donor left lateral lobe resection, of which only one was converted to a laparotomy because of hepatic vein injury, whereas the other 15 cases were successful. Compared with the previous 14 cases of open surgery, the surgeons found that although the laparoscopic surgery time increased significantly, there was substantially less blood loss. In 2011, Kim et al. [24] also confirmed that complete laparoscopic living-donor left lateral lobe resection was safe and feasible. By comparison with 11 cases of open surgery conducted during the same time period, no significant differences in operative time or blood loss were reported, and the postoperative hospital stay and recovery were significantly shorter in the laparoscopic group. In addition, the above two studies showed that there is no significant difference between laparoscopic living-donor left lateral lobe surgery and open surgery in terms of the complication rate or graft survival.

It is difficult to dissect the right liver laparoscopically because of its complex surrounding ligaments and structures. Although complete laparoscopic anatomical right liver resection has been successfully completed in liver cancer patients, considering the complexity of living-donor liver surgery and donor safety, no complete laparoscopic living-donor hepatectomy has been reported.

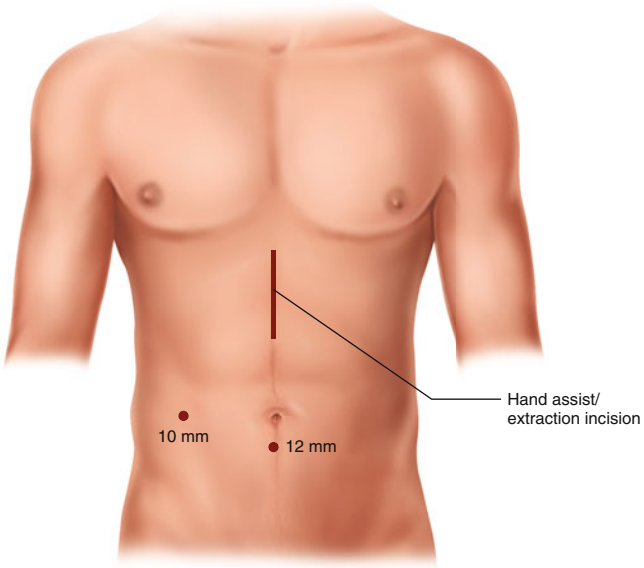

Fig. 32.1 Koffron maneuver

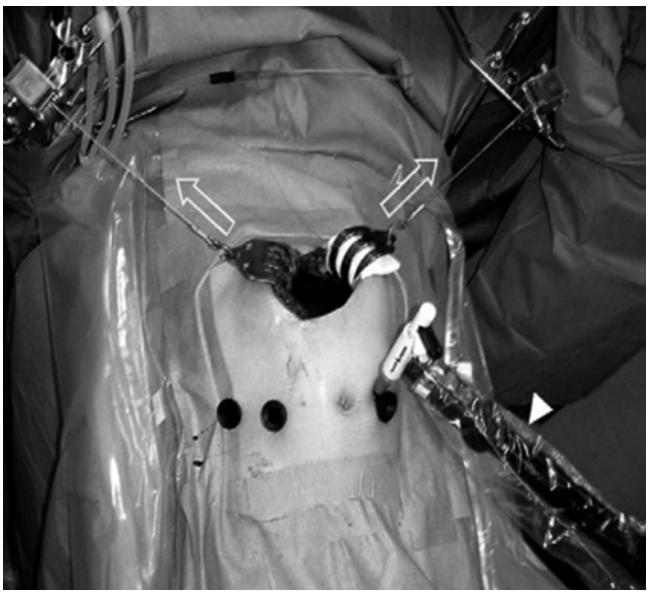

Fig. 32.2 Kurosaki maneuver

32.2.2 Laparoscopically Assisted Open Graft (Right/Left Liver) Resection

Considering that a sufficiently large abdominal incision is needed to remove the implants even in a successful full laparoscopic liver resection, the advantage of total laparoscopic liver resection has been questioned. In addition, the current total laparoscopic liver resection is technically difficult, requiring the surgeon to be simultaneously proficient in laparoscopic liver resection techniques and open living-donor surgery. Therefore, laparoscopic liver resection is currently reported only in left lateral lobe grafts. With the recent development of laparoscopic liver resection techniques, combined laparoscopic and open surgical hybrid techniques are successful in living-donor liver transplant surgery. Laparoscopic liver resection technique was further extended to the right liver graft/left-lobe living-donor liver transplant.

In 2006, Koffron et al. [3] successfully performed the first laparoscopic living-donor right liver resection. The surgical procedure included the establishment of a laparoscopic channel navel area of 12 mm, a 10 mm right abdominal laparoscopic instrument channel, and a 5 cm incision placement xiphoid hand-assisted device (Fig. 32.1). After establishing a pneumoperitoneum, the laparoscopic surgery assistant dissected the right liver and adjacent structures by hand by inserting auxiliary devices into the abdominal cavity, and the second and third hilar dissection was performed. Finally, the surgeon removed all of the hand-assisted laparoscopic instruments and extended the 5 cm xiphoid incision into an approximately 12 cm vertical incision, completing the first hilar dissection. Transection of the liver parenchyma was then conducted, and the implants were removed. In the same year, Kurosaki et al. [25] reported a group of 13 cases of laparoscopically assisted open living-donor liver resection, including three cases involving the right liver and 10 cases involving the left liver. Unlike its predecessor, the study used abdominal wall suspended gasless laparoscopy (Fig. 32.2). Compared the same open surgery, laparoscopic surgery was found to be associated with significantly reduced postoperative pain. The surgery time, intraoperative blood loss, postoperative complications, and donor graft survival were not significantly different.

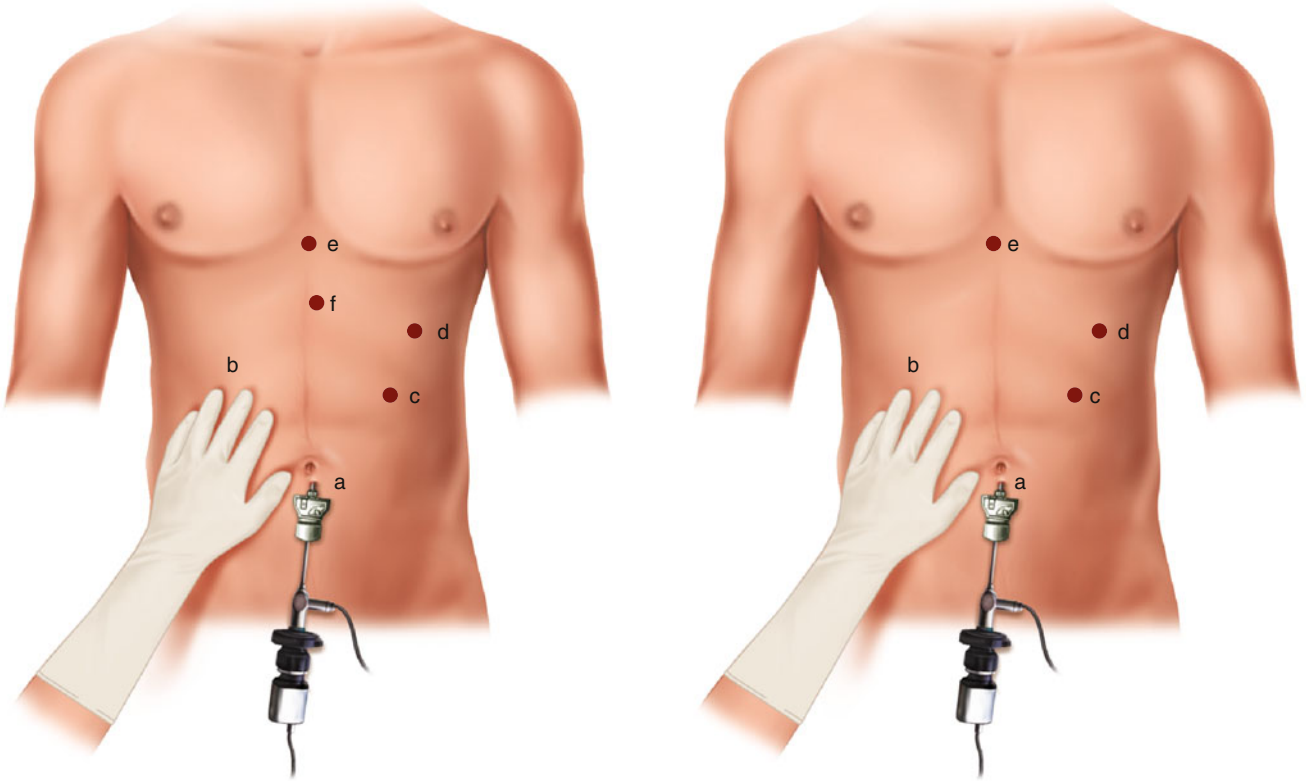

Fig. 32.3 Hand-assisted laparoscopic liver resection

In 2009, Baker et al. [4] further confirmed the safety and feasibility of assisted laparoscopic living-donor liver resection on a group of patients. From 2006 to 2008, 33 cases of continuously conducted laparoscopically assisted open living-donor liver resection were reported. Among them, two cases were converted to open procedures to ensure the safety of the donor. Another two cases have undergone reoperation: one case developed damage from intestinal perforation, whereas another case developed a biliary fistula associated with incision dehiscence. The overall incidence of complications was 21 %, and there were no cases of perioperative death or serious complications. Compared with the earlier 33 cases of open surgery, the average duration of laparoscopic surgery was significantly shorter, whereas blood loss, postoperative hospital stay, complications, and graft survival were not significantly different.

32.2.3 Hand-Assisted Laparoscopic Liver Resection

In 2011, Suh et al. [5] reported a set of nine cases of laparoscopic living-donor liver resection. The first two cases involved hand-assisted laparoscopic liver resection, whereas the other seven cases involved laparoscopically assisted open surgery. In contrast with the Koffron reports, the transverse incision of the auxiliary device is approximately 9 cm in the right upper quadrant (Fig. 32.3). Although nine case operations were successful, two cases of hand-assisted laparoscopic surgery took 765 and 878 min, respectively, which is considerably longer than the duration of the laparoscopically assisted surgery cases (range, 310–575 min). In the report, they noted that although surgeon hand-assisted laparoscopic liver resection is feasible and safe (compared with laparoscopically assisted open surgery), laparoscopic liver resection with minimally invasive surgery has no greater advantage but does involve increased difficulty of operation and operative time, thus indicating the advantage of laparoscopically assisted open surgery over hand-assisted laparoscopic surgery.

32.3 Anatomical Points of Laparoscopic Liver Resection

1. Combined with preoperative radiographic evidence of clear structural anatomical features of the liver donor to develop an accurate donor liver resection program.
2. Determine the variation and diameter of the bile duct branch.
3. Determine the variation and diameter of the portal vein.
4. Determine the variation and diameter of the hepatic artery.

5. Determine the variation and diameter of the hepatic vein.
6. Determine the variation and diameter of the right hepatic veins when the graft is the right liver.

32.4 Preoperative Assessment

1. General assessment of the donor

   Donors older than 18 years and less than 60 years must be informed and healthy and voluntarily decide to donate.

   Donor's height and weight are consistent with those of the recipient's.

   Living organ donor and recipient's relationship must be in line with relevant laws and regulations.

   Blood tests: ABO blood group and Rh blood group (matched or compatible).

   Donor must have no history of any upper abdomen operations.
2. Medical assessment of donor

   Detailed history taking and physical examination, routine electrocardiogram, chest radiograph, and abdominal B ultrasound. Surgery can increase the risk of various acute and chronic diseases.

   Blood (e.g., general testing, biochemistry, complete coagulation set, full hepatitis A panel, viral testing) and routine urine testing (culture).

   Psychosocial assessment: professional psychologist assessment – exclude forced donation and potential economic interests from donation.
3. Radiological assessment

   Abdominal B ultrasound: understand the general situation and evaluate whether there is liver steatosis or fibrosis.

   Upper abdominal CT measures the liver and graft volume: understand the anatomy of the portal vein, hepatic artery, hepatic vein, and inferior vena cava.

   Abdominal magnetic resonance cholangiopancreatography (MRCP) to assess the biliary anatomy.
4. Liver biopsy

   It is necessary to understand whether there is liver steatosis and fibrosis.
5. Endoscopic retrograde cholangiopancreatography (ERCP)

   If necessary, ERCP should be conducted to understand the detailed biliary structure.

32.5 Laparoscopically Assisted Right Hepatectomy

1. Navel channel is established. Explore abdominal cavity. Under direct vision, dissect the hepatic round ligament, position the blue dish, extend the left hand of the first assistant into the abdominal cavity to control the liver, tighten the blue dish, and reestablish the pneumoperitoneum (Fig. 32.4).
2. Use the hand-assisted ultrasonic scalpel to dissect in turn the liver sickle ligament (Fig. 32.5), the right triangular ligament (Fig. 32.6), the right coronary ligament (Fig. 32.7), and the right kidney ligament (Fig. 32.8); afterward, free the liver's bare area to protect the right adrenal gland so that the entire right liver is completely freed.

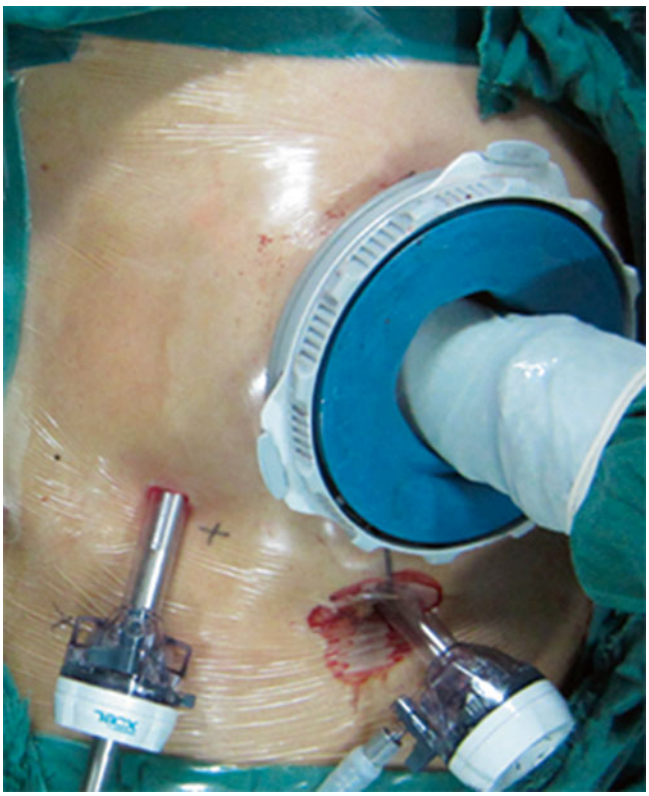

Fig. 32.4 Reestablish the pneumoperitoneum

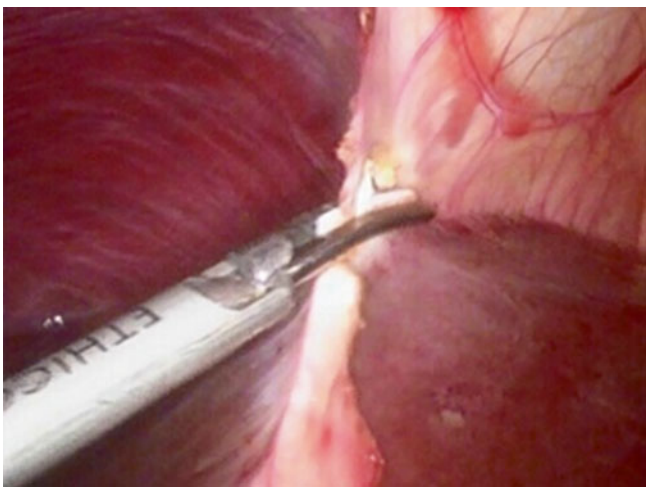

Fig. 32.5 Dissect the liver sickle ligament

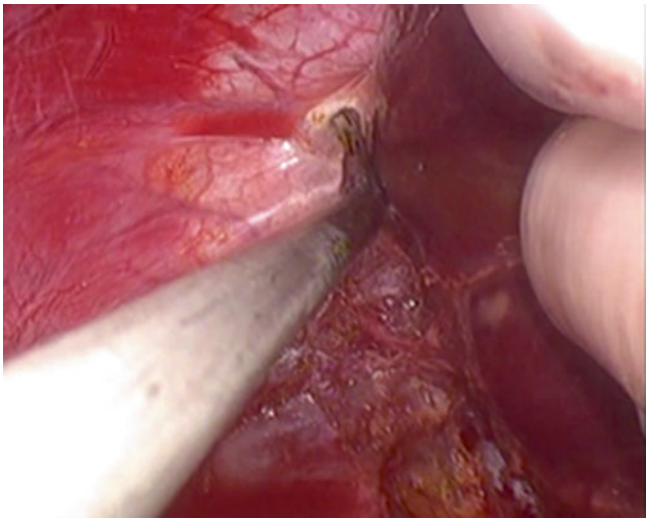

Fig. 32.6 Dissect the right triangular ligament

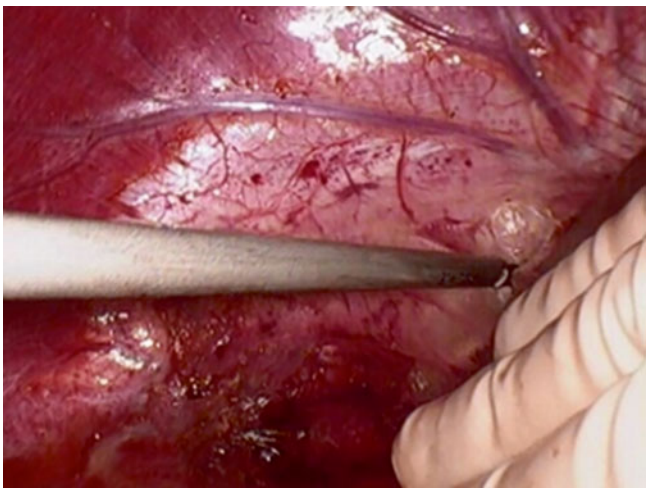

Fig. 32.7 Dissect the right coronary ligament

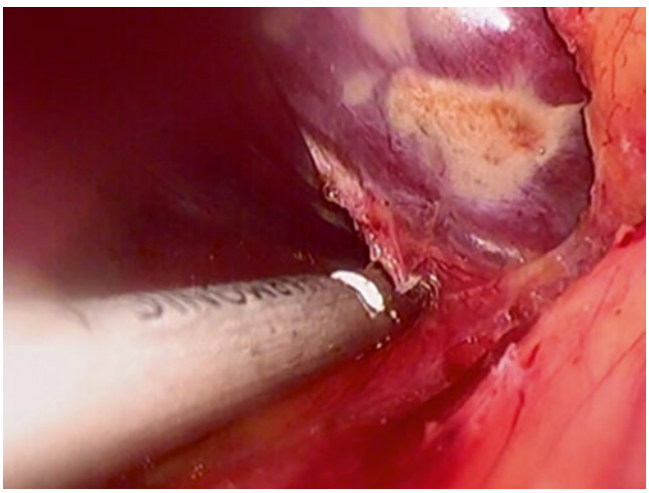

Fig. 32.8 Dissect the right kidney ligament

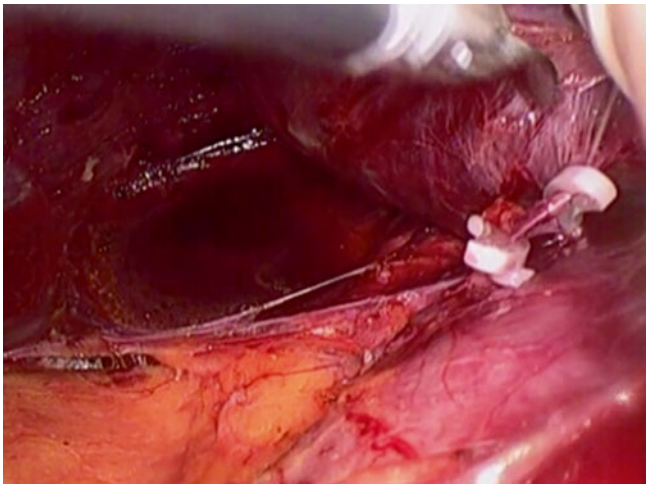

Fig. 32.9 Separated the hepatic inferior vena cava from liver

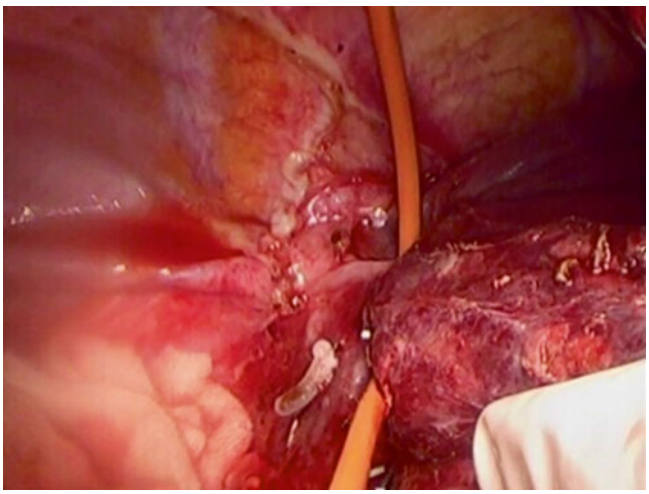

Fig. 32.10 Put an 8th catheter between the right and middle hepatic veins

3. Free from the bottom up; cut off all short hepatic veins immediately after the vein and inferior vena cava ligament so that they are completely separated from the hepatic inferior vena cava (Fig. 32.9).
4. Dissect the right hepatic vein in the boundaries between the right and middle hepatic veins, and concurrently position the 8th catheter, which is prepared as a guide for hepatectomy (Fig. 32.10).
5. Remove all of the laparoscopic and hand-assisted equipment, extend the upper abdominal incision to 12 cm, perform cholecystectomy under direct vision, and insert the catheter into the cystic duct stump to perform cholangiography (Fig. 32.11).
6. Dissect the first porta hepatis: reveal the full length of the right hepatic artery and the bifurcation of the bile ducts (Fig. 32.12).

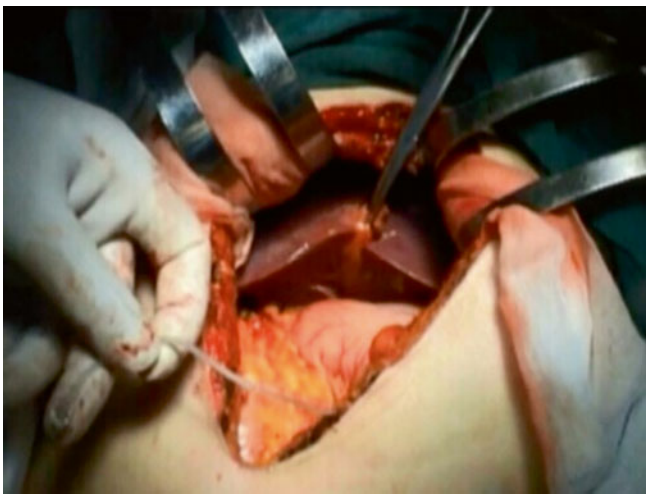

Fig. 32.11 Perform cholangiography

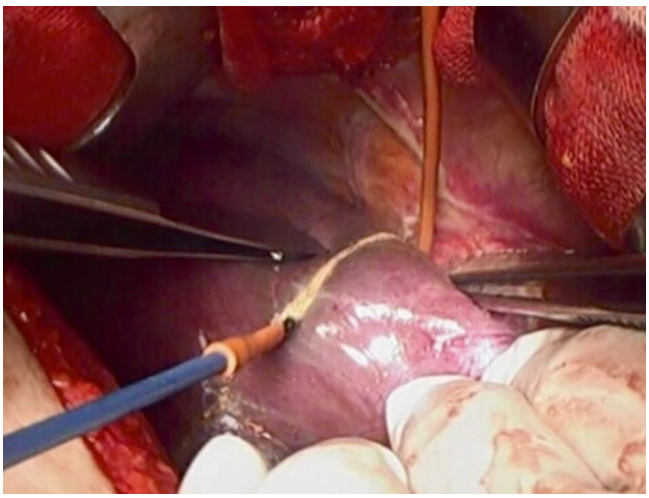

Fig. 32.13 Mark the dividing line in the left hepatic liver surface

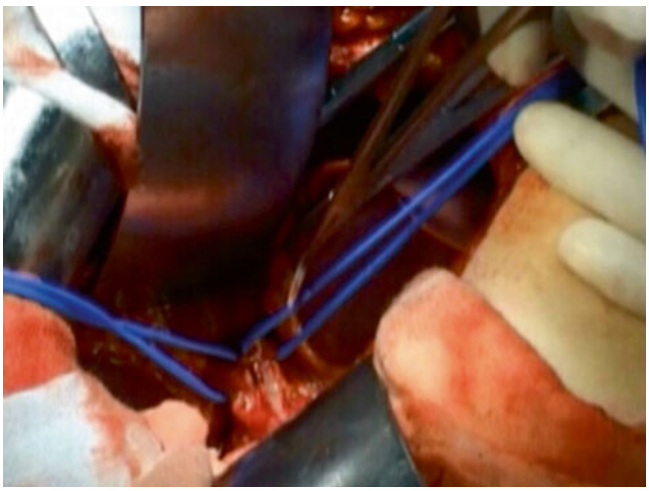

Fig. 32.12 Reveal the full length of the right hepatic artery and the bifurcation of the bile ducts

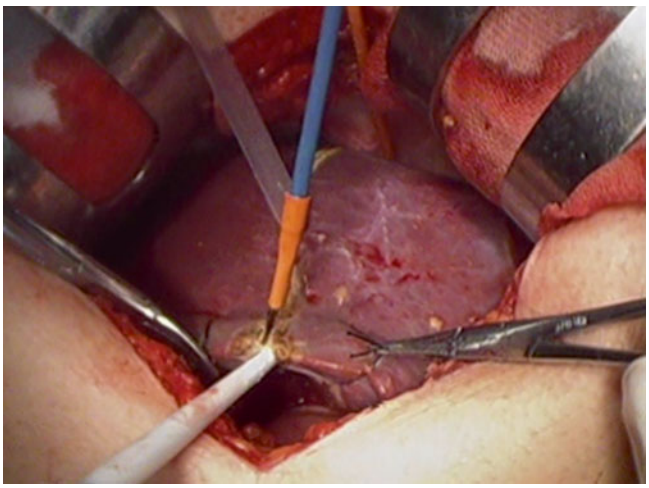

Fig. 32.14 Transect the liver parenchyma

7. Mark the dividing line in the left hepatic liver surface using the electric knife (gallbladder bed notch and right hepatic vein connection) (Fig. 32.13).
8. Transect the liver parenchyma using CUSA or a water jet; using coagulation or bleeding peptide folders to stop the bleeding in the liver section, ligate or suture the thick blood vessel branches (Fig. 32.14).
9. In the liver, using a preset catheter as a guide, perform amputation until the entire right lobe liver inferior vena cava is freed. Cut the right hepatic duct close to the left hepatic duct bifurcation, thus completely freeing the right liver graft; only the hepatic artery and portal vein and right hepatic vein remain continuous (Fig. 32.15).
10. After infusing systemic heparin for 8 min, clamp off the right hepatic artery and right portal vein (Fig. 32.16) and the right hepatic vein (Fig. 32.17); remove the implants and place them on the back table.

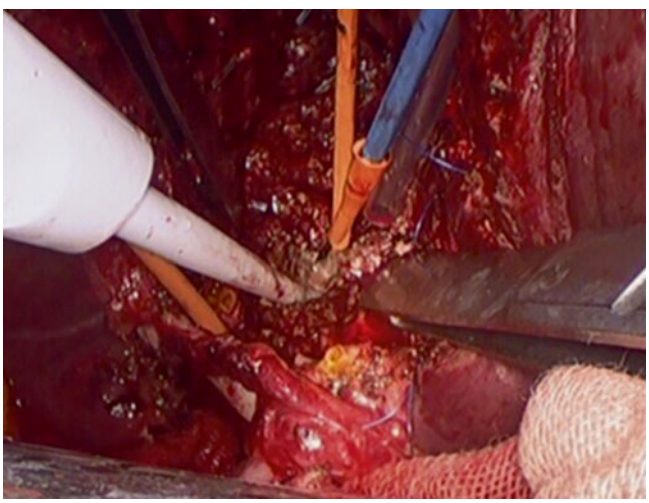

Fig. 32.15 Completely freeing the right liver graft except for the hepatic artery and portal vein and right hepatic vein

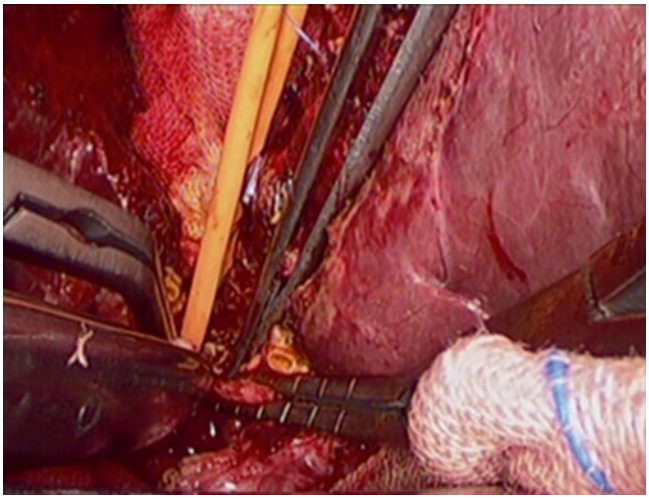

Fig. 32.16 Clamp off the right portal vein

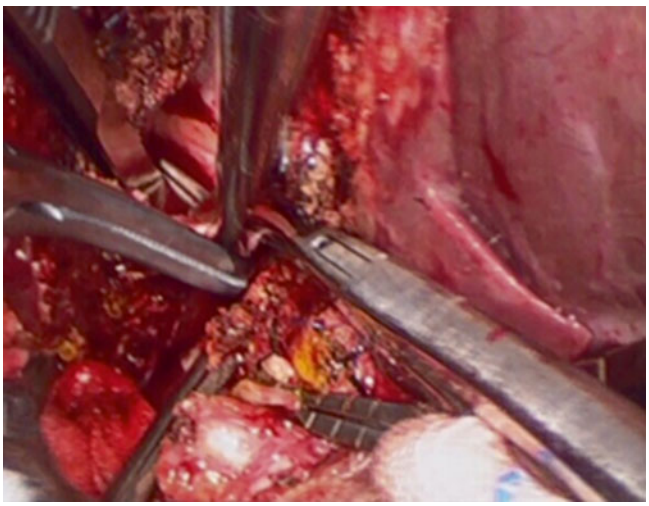

Fig. 32.17 Clamp off the right hepatic vein

11. From the back table of rows in the right portal vein catheterization, obtain the UW perfusion fluid and flush the bile duct and artery. Trim the donor, if necessary, and perform hepatic vein bypass graft or artery bypass (Fig. 32.18).

32.6 Epilogue

The choice of laparoscopic hepatectomy is different depending on the type of donor. Relatively mature laparoscopic surgery includes laparoscopic living-donor left lateral lobe resection and laparoscopically assisted living right/left hepatectomy. Although some surgeons prefer the fully laparoscopic surgical approach [26–35], the current donor-assisted laparoscopic surgery (hybrid technology) has more

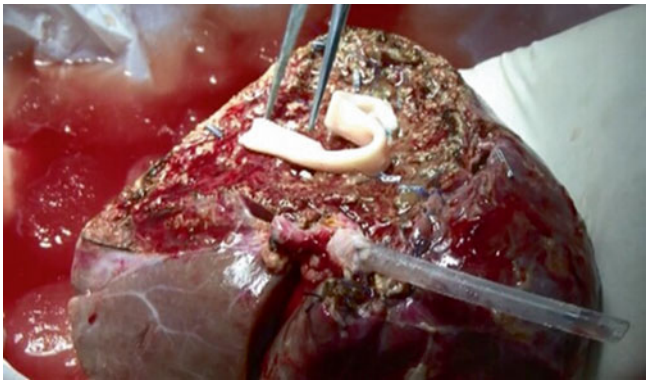

Fig. 32.18 Perform hepatic vein bypass

advantages and promotional value than complete laparoscopic surgery in living-donor liver surgery. There are several reasons for this difference. First, distinct from laparoscopic liver resection, the graft must be taken out completely and transplanted into the recipient's body. Thus, even with the successful completion of laparoscopic donor livers, a large abdominal incision still requires the graft to be completely removed. Therefore, complete laparoscopic hepatectomy no longer has the advantage of a small incision. Second, the laparoscopically assisted laparoscopic technique is relatively easy to learn and master. Third, under laparoscopic vision, the surgeon operates the hand-assisted laparoscopic instrument together with completion of part of the liver until it is free; the remainder, including cholecystectomy, first hilar dissection, and transection of the liver tissue, are associated with the same traditional open abdominal procedure that is conducted under direct vision. The surgical risk of the entire procedure is controllable and avoids harming the blood vessel, causing an air embolism or bleeding. For minimally invasive surgical resection of living-donor type selection, the most important issue is whether the surgeon masters the surgical techniques, in addition to the donors' wishes being fully respected.

In summary, laparoscopic live donor liver resection is safe and feasible. Compared with open surgery, minimally invasive surgery has clear advantages. With the continuous application of minimally invasive surgery, donor liver resection of this type will gradually replace traditional open surgery and become a conventional surgical procedure of living-donor liver transplantation.

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Native Liver Resection in Liver Transplantation

33

Wentao Wang, Jianyong Lei, and Zhenni Liu

Starzl performed the first successful liver transplantation in a human on March 1, 1963. In the ensuing 50 years, subsequent developments have improved the surgical procedure and its outcomes. Presently, liver transplantation is a standard method of treating end-stage liver disease in transplantation centers worldwide. Although liver transplantation is a complicated and difficult operation, its risks can be reduced if the details are handled appropriately. This chapter will describe liver resection in the recipient according to different transplantation techniques, focusing on pathological liver resection in orthotopic liver transplantation, piggyback liver transplantation, and living-related donor transplantation. As reduced-size liver transplantation and split-liver transplantation are similar to orthotopic liver transplantation, these procedures are not included in this chapter.

33.1 Pathological Liver Resection in Orthotopic Liver Transplantation

33.1.1 Position

Patients are maintained in the supine position, and the great saphenous vein is disinfected in preparation for vein bypass grafting.

33.1.2 Incision

A bilateral subcostal incision that extends to the xiphoid is known as Mercedes incision [1]. The right side of the incision reaches to the midaxillary line, the left side extends to the left lateral border of the rectus muscles, and the central aspect extends to the xiphoid, which can be removed when needed (Fig. 33.1). After incisional bleeding is completely stopped, the peritoneum and skin are sutured with interrupted stitches in order to reduce bleeding (Figs. 33.2 and 33.3).

33.1.3 Exposure

A retractor is used to expose the operating field, especially secondary porta of liver and the right liver, for ease of reconstruction and improved surgical access to the suprahepatic vena cava.

33.1.3.1 Abdominal Exploration

In recipients with liver cancer, the presence of extrahepatic metastases and portal vein tumor thrombus should be carefully evaluated. Splenectomy is preferred in patients with splenomegaly and hypersplenism in order to improve blood clotting function.

33.1.3.2 Dissection of the First Porta Hepatis

Expose the junction of the cystic duct and the common bile duct, and then cut the peritoneum on the surface of the hepatoduodenal ligament. After that, separate the cystic duct from the cystic artery and cut cystic duct and cystic artery off.

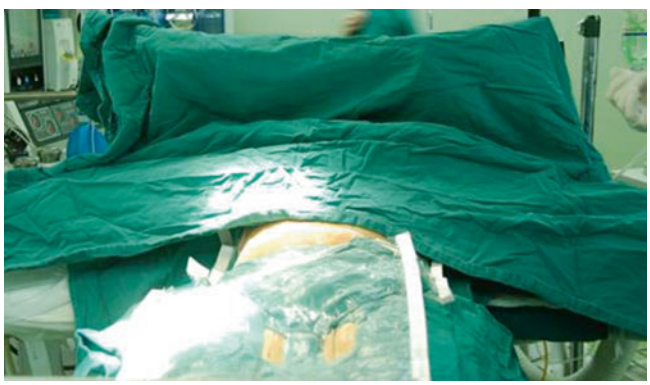

Fig. 33.1 The great saphenous vein of the recipient

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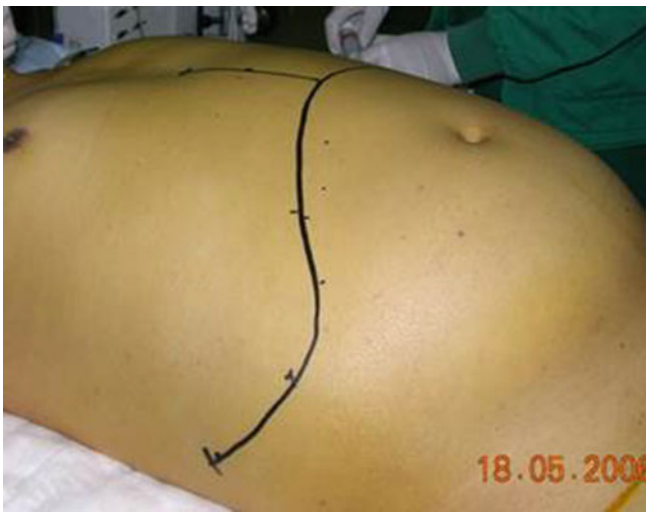

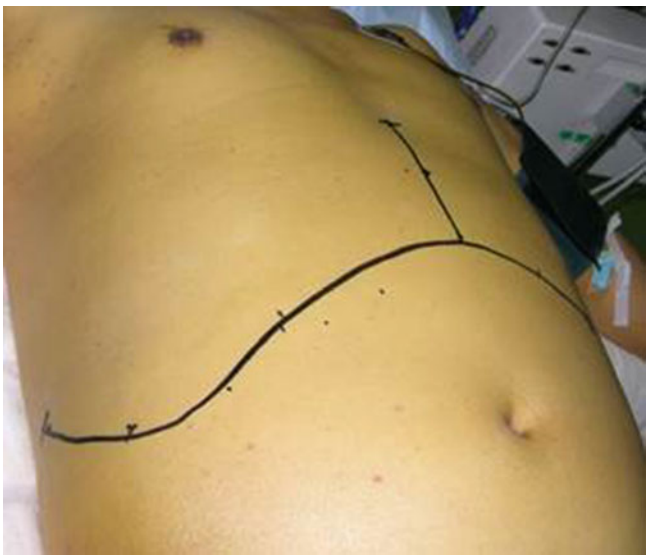

Figs. 33.2 and 33.3 Incision of receptor

Dissect the hepatic artery to the left of the hepatoduodenal ligament and dissect the right and left hepatic arteries from the bottom of the proper hepatic artery. Do not pull on the hepatic artery in order to avoid endothelial disruption.

Dissect the common bile duct up to the junction of the left and right hepatic ducts. Preserve a sufficient length of the bile duct, and then cut the common bile duct, protecting the surrounding tissue and the blood supply.

Dissect the portal vein up to the right and left portal veins and down to the head of the pancreas in order to prepare the abscission (Fig. 33.4).

In patients with HCC, lymph nodes must be removed.

33.1.3.3 Dissection of the Ligaments around the Liver

Extensive tissue adhesions and abundant collateral circulation are generally found in patients with portal hypertension.

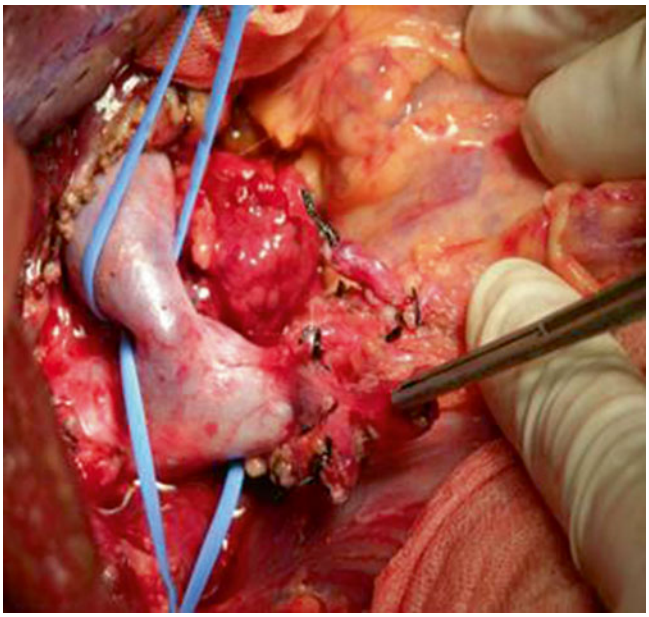

Fig. 33.4 Dissection of the first porta hepatis

To prevent bleeding, the ligaments around the liver should be dissected after dissecting the first porta hepatis. The procedure is performed as follows. An electrotome is used to remove the falciform ligament of the liver, and then the left triangular ligament must be ligated or transfixed because of collateral circulation. The left coronary ligaments are removed, the left lobe is turned outward, and the hepatogastric ligament is ligated and removed in order to reveal whether an aberrant left hepatic artery originates from the left gastric artery. Then the right triangular ligament and the coronary ligament are exposed and removed. The right lobe is pushed to the left, and the hepatocolic ligament is removed. The liver is turned to the left, the peritoneum posterior to the right lobe is opened, and the suprahepatic vena cava is dissected. The left and caudate lobes are turned to the right, and the peritoneum is cut lengthwise along the retrohepatic inferior vena cava to expose the left branch of the posterior cava; the retrohepatic inferior vena cava is then dissected. The posterior peritoneum is cut at the level of the renal veins, and the infrahepatic vena cava is dissected.

It is important to note that the dissection of the ligaments around the liver should follow the liver closely. There is no need to dissect the retrohepatic inferior vena cava completely in patients with severe portal hypertension, except in cases of retroperitoneal hemorrhage. The liver should be manipulated less extensively in recipients with cancer especially when the tumor is next to the secondary porta of liver. In such situations, the dissection of the retrohepatic inferior vena cava should be done in preparation for clipping, instead of dissecting the ligaments around the liver, which can be handled when the hepatectomy begins.

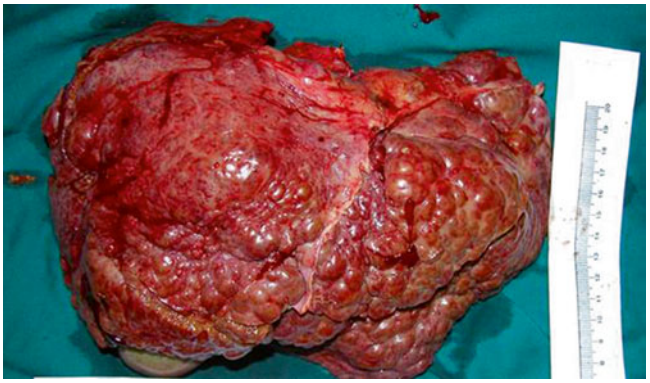

Fig. 33.5 Hepatectomy

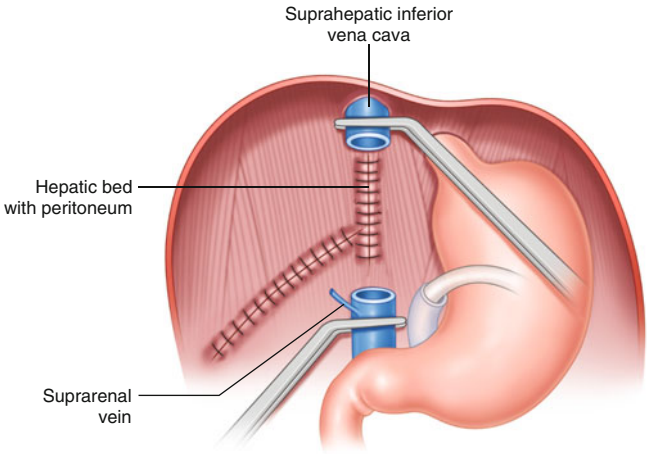

Fig. 33.6 Preserving more peritoneum to stop bleeding

33.1.4 Hepatectomy

The bile duct, hepatic artery, and portal vein are transected; then the suprahepatic vena cava is clipped with vessel forceps. The anatomical position of liver should be noted, and the vessel forceps should be kept in a horizontal position. To prevent slippage, the forceps can clamp the diaphragm and be fastened by ligation. The suprahepatic and infrahepatic vena cava is transected close to the surface of the liver. Cutting the liver near the back of the suprahepatic vena cava can reduce the surface area of the wound and decrease bleeding (Fig. 33.5).

33.1.5 Hemostasis of the Hepatic Bed

The hepatic bed should be checked carefully, and vascular ligation or transection should be performed, especially for the lumbar vein and the veins draining the diaphragm and the lesser omentum, using continuous Prolene sutures. As much peritoneum as possible should be preserved, especially at the bare area of the liver and at the surface of the wound. It is very important to stop bleeding, since liver transplantation can make it hard to identify the wound (Fig. 33.6).

33.1.6 Trim of the Vessel

Trim the portal vein and suprahepatic and infrahepatic vena cava to make sure that suprahepatic and infrahepatic vena cava have the same duct. Inferior vena cava and venule should be checked thoroughly in case of crevasse.

33.2 Hepatectomy in Piggyback Liver Transplantation

33.2.1 Position, Incision, and Exposure

These aspects are the same as in pathological liver resection in orthotopic liver transplantation.

33.2.2 Dissection of the First Porta Hepatis

This part is performed in the same fashion as orthotopic liver transplantation with respect to the dissection of the hepatic artery, common bile duct, portal vein, and the ligaments around the liver.

33.2.3 Dissection of the Ligaments around the Liver

This part is performed in the same fashion as pathological liver resection in orthotopic liver transplantation.

33.2.4 Dissection of the Third Porta Hepatis

The liver is turned bilaterally to expose and cut the short hepatic vessels. First, turn the right lobe of the liver to the left to expose and cut the inferior vena cava ligament and the short hepatic veins individually (there can be more than ten); Prolene may be required for ligature if the vessel is too thick. Turn the left lateral liver and the caudate lobe, and then cut the posterior peritoneum along with the left lateral liver. Cut the short hepatic veins from the left of the posterior vena cava, and then approach the main liver vein cranially (Fig. 33.7).

Dissecting the third porta hepatic can sometimes be difficult. In this situation, the liver can be retracted, and the short hepatic veins can be transected caudally to cranially, after completely removing the first porta hepatic.

33.2.5 Dissection of the Second Porta Hepatis

Dissect the right hepatic vein by retracting it with a rubber strap and clipping it with a vessel clamp; the vessel should then be cut and sutured together. The right and left liver veins

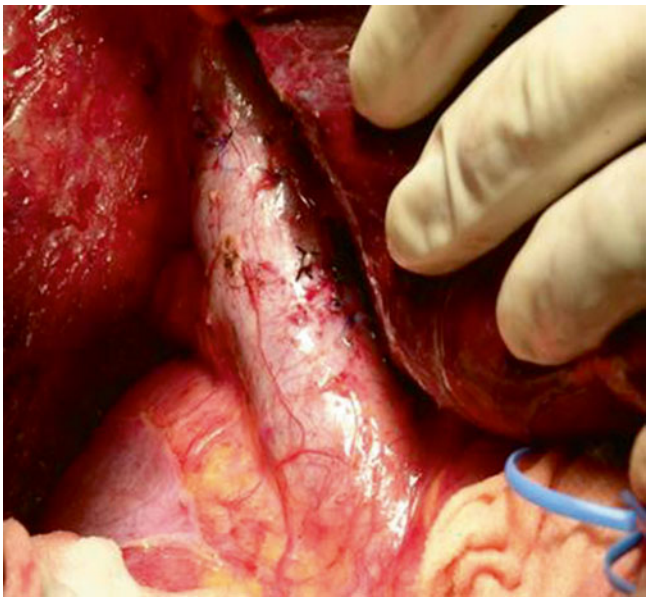

Fig. 33.7 Exposure of the third portal of the liver

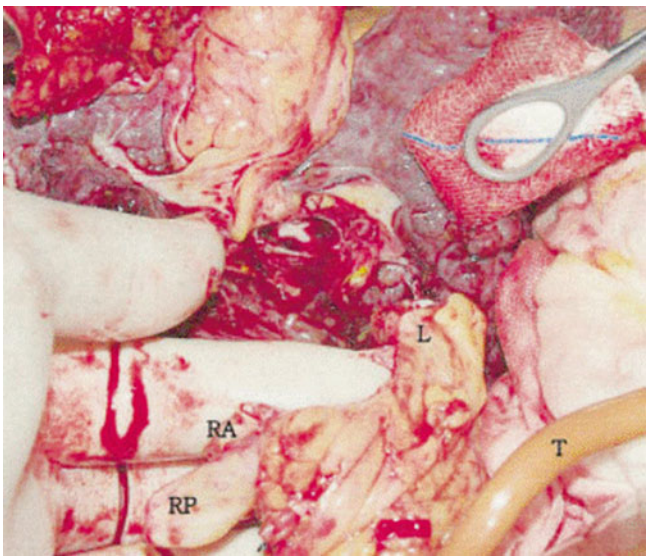

Fig. 33.8 A Korean doctor clipped the first porta hepatis from the level of the hilar plate. *RA* right anterior hepatic vein, *RP* right posterior hepatic vein, *L* left portal vein, *T* tube

should be dissected to an adequate length; then the inflow to both vessels should be clipped in order to serve as the recipient's anastomotic stoma. The anatomical position of the hepatic vein and the vena cava should be checked clearly; these structures can then be clipped and ligated in order to perform the hepatectomy [2].

33.2.6 Hepatectomy

Ligate the portal vein and the hepatic vein, and then remove the liver while maintaining hepatic blood flow and portal vein patency. Check the liver bed carefully to stop bleeding completely. Repair the recipient's hepatic vein in order to perform the transplant. This procedure is not suitable for patients whose tumors approach the vena cava, due to the possibility of incomplete removal.

33.3 Hepatectomy in Living-Related Donor Transplantation

33.3.1 Position

Positioning is the same as in orthotopic liver transplantation.

33.3.2 Incision

The incision is performed in the same way as orthotopic liver transplantation for dissection of the hepatic artery.

33.3.3 Dissection of the First Porta Hepatis

This procedure is performed in the same way as in orthotopic liver transplantation for patients with no prior surgical history. Cadaveric organs and living donor organs differ; living donors provide shorter hepatic arteries, hepatic veins, and portal veins, so it is very important to preserve as much length as possible in these vessels. Vessels from living donors may be thin, short, or vary in length, especially above the junction of the right and left bile ducts during dissection. At the same time, the blood supply in the 3 and 9 o'clock directions should be protected in order to reduce bile duct-related complications [3]. The choice of the recipient's hepatic artery depends on the length and size of this vessel. The gastroduodenal artery can be dissected at the division of the proper hepatic artery and the common hepatic artery. A Korean doctor has clipped the duct above the hilar plate after the first duct was clipped in order to maintain the length of the duct in the first porta hepatis during dissection (Fig. 33.8).

33.3.4 Dissection of Ligaments around the Liver

This is performed in the same fashion as hepatectomy in piggyback liver transplantation.

33.3.5 Dissection of the Third Porta Hepatis

This is performed in the same fashion as hepatectomy in piggyback liver transplantation.

33.3.6 Hepatectomy

Once the above steps are completed, the liver is only attached by the portal vein, the hepatic vein, and the hepatic artery. Once the liver is removed and repaired, the hepatic artery and vein can be cut after using vessel forceps to clamp these vessels. The retrohepatic inferior vena cava should be preserved completely; then, the liver can be removed. When the middle and left hepatic veins are cut, the surface of the liver must be closed in order to ensure that these vessels are long enough for repair and anastomosis.

33.3.7 Hemostasis of the Hepatic Bed

Any bleeding site must be sutured after the liver is removed. The preferred approach is to rebuild the posterior peritoneum, shrink the surface of the wound, and reduce bleeding.

Wentao Wang, Lvnan Yan

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Split-Liver Transplantation and Reduced-Size Liver Transplantation

34

Yonggang Wei and Tao Lv

34.1 History and Present

Reduced-size liver transplantation has been used to solve the donor shortage for pediatric patients waiting for a liver transplant. Due to the large number of pediatric patients waiting for liver transplantation who could not obtain a matched donor, these patients have a high mortality rate. To address this problem, Bismuth and Broelsch [1, 2] founded the RLT in the mid-1980s. Using this technique, the required organ volume could be reduced through surgical means, a partial liver resection, to fit into pediatric patients. In its early stages, reduced-size liver transplantation was limited due to technical difficulties. With continuous progress, the results for this procedure are now equivalent to or better than those for complete pediatric donor organ transplantation. However, with an increasing number of patients waiting for a liver transplant, the donor shortage in children and adults is still growing. Due to the associated wasted liver tissue and adult diversion, which inevitably affect donor resources, RLT is rarely performed.

Due to advances in RLT technology and taking donor resource waste into consideration, Pichlmay and Bismuth [3, 4] developed split-liver transplantation (SLT) on the basis of the RLT technology in 1989. The basic principle is based on Couinaud segmentation of the liver. The liver is suitable for separating into two portions for two liver transplant recipients. The initial SLT was developed in Europe with the in vivo splitting method, which uses classical complete organ acquisition technology. In this technique, the liver is separated into two halves in vitro. The advantage of this method is that it saves the time and effort spent on the donor, so the surgeon can better concentrate on the recipient. However, its drawback is that the graft's cold ischemia time is too long, and the separation process may lead to premature organ rewarming. Moreover, the process of separating the liver from the bile duct and the hepatic artery can result in accidental injury.

An initial report of SLT included four SLT donors and eight recipients and Bismuth gave one graft to two adult recipients, but other six recipients were all child/adult combination. Two recipients died within 45 days of surgery. Of the remaining three to six recipients, one survived long term and one graft failed. Three recipients (one child, two adults) survived long term (Table 34.1) [2–5]. In the early years of SLT, the rate of long-term survival of the grafts and the recipients was far less than for complete grafts. However, the surgical techniques for SLT continued to improve, and in large reports, the results for SLT meet or even exceed those of complete graft transplantation [6–9].

With respect to in vitro cleavage technology, Broelsch and Busuttil developed donor in situ separation technology. The keys to this technology were isolating the liver before the blocking and cold perfusing the aortic artery of brain-dead donors [10]. The in situ separation technique shortens the cold ischemia time, simplifies the identification of biliary and vascular structures, and reduces bleeding after reperfusion. In addition, this technique laid the technical foundation for living-donor liver transplantation. Of course, there were more difficult requirements for surgeons performing in situ separation because this procedure is longer than the isolated liver surgery; this factor also puts higher demands on the donor hospital. In addition, brain death must be recognized by the local legislative body. With respect to the recognition of brain death, liver-splitting surgery can only be performed legally on donors with heartbeat. In China, due to legislation failures related to brain death, only the traditional in vitro cleavages can be performed.

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34.2 Anatomical Basis of Split-Liver Transplantation

The Couinaud liver segmentation system is the basis for the split-liver transplantation as a surgical procedure. This system divides the liver into eight segments that are supplied by independent parts of the Glisson system. By splitting the liver along different anatomical landmarks, two different sizes of donated liver tissue can be obtained, each with independent blood supplies and drainage tubes. Splitting the liver along the falciform ligament results in a smaller left lateral lobe (II + III, left lateral lobe, LLL) and a larger right trefoil lobe (I, IV–VIII, extended right lobe, ERL) for pediatric and adult grafts, respectively. In contrast, splitting the liver along the hepatic vein results in two similar-size donor tissues. The left lobe tissue (I–IV, left lobe, LL) can be used for a smaller adult body transplant, and the larger right lobe (V–VIII, right lobe, RL) can be used as a larger-size human liver (Table 34.2).

In contrast to living-donor liver transplantation, splitting the liver can cause ischemia or preservation injury. Thus, recipients require a GRWR that is most likely higher than 0.8 % for living-donor liver transplantation.

34.3 The Choice of the Donor

Donor evaluation and carefully selected recipients are keys to successful split-liver transplants. Split-liver donors should generally meet the following conditions: age from 10 to 40 years, normal or below normal body weight, ABO blood type matched, normal liver function, hospitalized for a shorter time, normal basic hemodynamics, no significant hypotension, and matched size for a recipient [11–13]. Although the preoperative evaluation of these factors cannot absolutely guarantee the safety of the recipients, a conservative safety assessment can minimize the possibility of primary graft dysfunction and delayed function. Evaluating the organ after the operation is also very important both to assess the function of the liver parenchyma and to perform the anatomic analysis of the vasculature and bile duct.

34.4 The Choice of the Recipients

An accurate estimation of the liver volume that is required for the recipients after the transplant is a key factor for recipient selection. The primary disease of the recipients, the degree of illness severity, and portal hypertension are also factors that must be considered. Under normal circumstances, the weight of the liver is approximately 5 % of the weight of an infant, and this ratio gradually decreases and stabilized in adults to no more than 2.5 %. The liver weight of males is generally larger than for females. For normal livers, the liver can still regenerate following a right trisegmentectomy (only 20 % residual liver tissue). Chronic hepatitis, cirrhosis, and fatty liver will delay or hinder the process of liver regeneration.

There are two common means of assessing matched volume of the donor and recipient. The first is referred to as standard volume (standard liver volume), which is the ratio of liver donor volume to liver volume required by the

Table 34.1 Initial attempts at split-liver transplantation

Center/author	Time	Recipients	Result
Hanover/Pichlmayr	February 1988	Left liver: 2 years/biliary atresia Right liver: 63 years/primary sclerosing cholangitis	Re-transplant 4 months later Postoperative survival 12 years
Paris/Bismuth	May 1988	Left liver: 45 years/acute liver failure Right liver: 55 years/acute liver failure	Died 20 days after operation Died 40 days after operation
Chicago/Broelsch	July 1988	Left liver: March/acute liver failure Right liver: July/antitrypsin deficiency	Died 2 days after operation Postoperative survival 12 years
Brussels/Otte	November 1988	Left liver: 5 years/tyrosinemia Right liver: 55 years/end-stage liver disease	Postoperative survival 12 years Died 3 days after operation

Table 34.2 The graft and the approximate size obtained by splitting according to different anatomical landmarks

Liver splitting	Graft	Volume (ml)	Recipient
Along the falciform ligament	Left lateral lobe (II + III)	200	Child
	Right trefoil lobe (I, IV–VIII)	1,000	Adult
Along the hepatic vein	Left liver with caudate (I–IV)	400	Adult
	Right liver (V–VIII)	800	Adult
	Left liver (II–IV)	300	Child
	Right liver with caudate (I, V–VIII)	800	Adult

recipient. The second is GRWR, which is the weight ratio of the graft and recipient. Briefly, the volume of the graft should be 40 % of the expected liver weight or at least 1 % of the patients' weight. Donations below this standard often result in SFSS, causing delayed recovery of liver synthetic function or cholestasis syndrome. In addition, the preoperative state of the recipients has a very large impact on the postoperative outcome. Poor prognostic risk factors of split-liver transplant recipients include the following: a preoperative recipient model for end-stage liver disease (MELD) score higher than 30 points, re-transplant patient, a graft ischemia duration that is too long, and a transplant that occurs at an inexperienced center [7].

34.5 Surgical Methods

34.5.1 Donor Acquisition

In vitro liver splitting is the same as the traditional method for obtaining a donor liver. Before splitting the donor liver, conventional abdominal surgery is required. This procedure requires the following: sufficiently long enough abdominal incision, exposure of the retroperitoneal colon and duodenum structures, inferior mesenteric vein catheter placement to alternate mild cold perfusion via the portal vein, and celiac control over the abdominal aorta and the renal artery. These steps are necessary, so once the donor situation is unstable, abdominal aortic occlusion and catheter perfusion through the abdominal aorta can quickly result, allowing for rapid graft acquisition and a shortened warm ischemia time. The incisions are similar to the steps for a living donor, with the difference that the donor inferior vena cava must be cut. This step may require trimming of the hepatic vein grafts for a vascular flap. This flap is beneficial for the graft with respect to outflow tract reconstruction.

34.5.2 Splitting the Left Lateral Lobe (SII + III) and Extended Right Lobe (SI, IV–VIII)

First, identify where the inferior vena cava and hepatic vein combine; then, dissect the left hepatic vein and remove the vascular leash. This step will help confirm the final site of the splitting of the liver parenchyma. The left hepatic vein and hepatic vein often have a common trunk. These veins must be isolated in the liver parenchyma after the separation is completed. If the hepatic veins have two or three branches, both of the final two vessels and the part of inferior vena cava valve where two vessels join should be retained (Fig. 34.1).

When dissecting the hepatic hilus, the round ligament roots should be cut first, followed by separation of the left branch of the hepatic artery, the left portal vein, and the left hepatic duct. The total length of the left branch of the hepatic artery should be completely exposed, taking care to retain the four initial segments of the hepatic artery segment. If the origin of the fourth segmental arteries in the left branch of the hepatic artery is very high and relatively thick, the hepatic artery needs to be recut to fit the gastroduodenal artery stump. When the bile duct and artery are difficult to identify, injection of methylene blue can help to confirm their location. Ligate the fourth paragraph of the portal vein branch and free it, separating it along the right side of the navel. Then, the entire left portal vein can be completely separated (Fig. 34.2).

After vascular control of the left lateral lobe is achieved, transect the liver tissue. Approximately 1 cm from the right edge of the liver falciform ligament, mark a line on the liver surface via coagulation. Separate the liver parenchyma between the left lateral lobe and the fourth paragraph, reserving the liver parenchyma 1 cm above the umbilicus biliary crack.

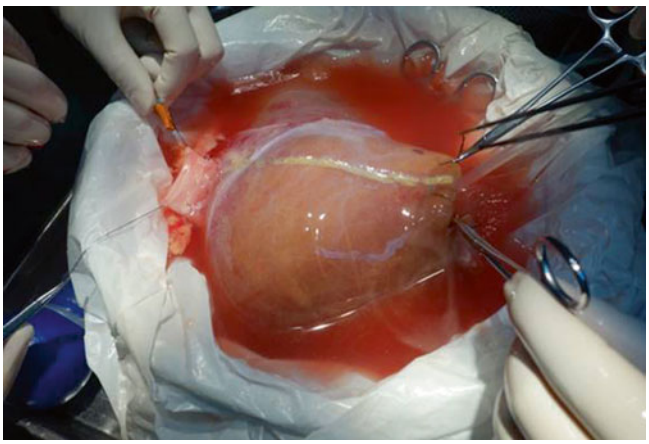

Fig. 34.1 Overhang left hepatic vein to determine the suspension and splitting line

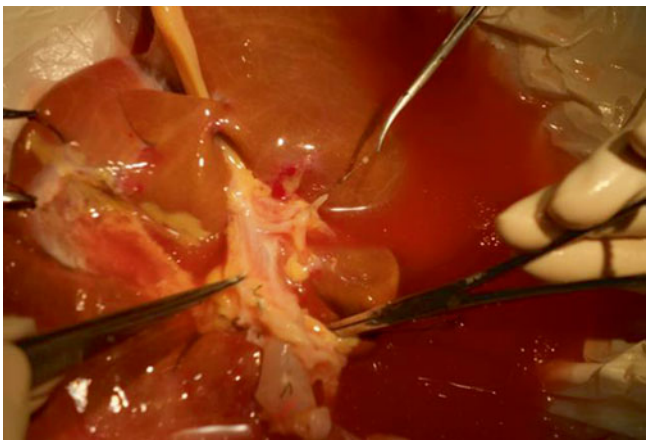

Fig. 34.2 Anatomic structures of the left hilar side

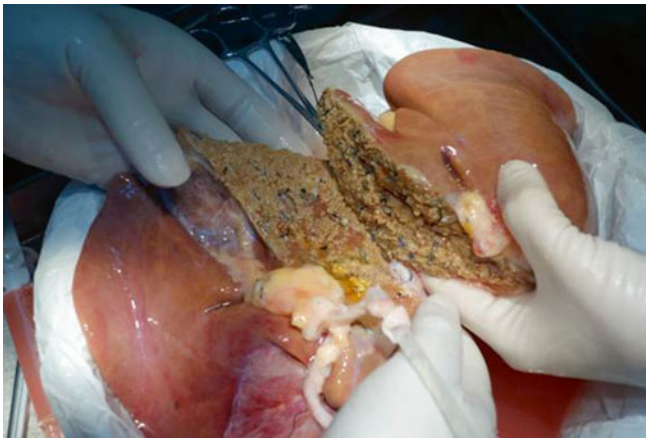

Fig. 34.3 The hilar vascular pedicle and venous drainage

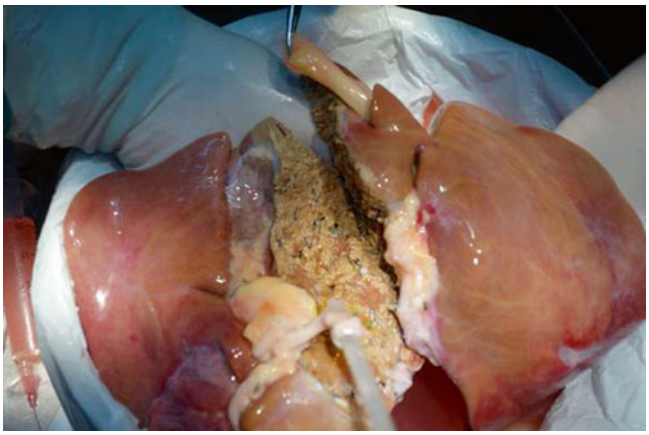

Fig. 34.4 The left lateral lobe and extended right lobe

Dissect the liver and bile duct inside the hilar structure to completely obtain the left lateral lobe of the liver parenchyma, leaving the hilar vascular pedicle and venous drainage. Block blood flow from the left hepatic artery, left portal vein, left hepatic duct, the left hepatic vein, and the vascular flap of the vena cava. Perform a conventional right clover resection and cryopreserve the liver tissue in UW solution (Fig. 34.3).

The right clover liver preparation also includes closure of the left hepatic vein, the left portal vein, and the left hepatic artery stump, while the left hepatic duct stump is sutured closed. Careful examination of the liver sections, blood vessels, and bile duct stump sutures prevents leakage (Fig. 34.4).

34.5.3 Splitting the Left Liver (SII–IV) and Right Hepatic Lobe with a Caudate (SI, V–VIII) Graft

For older children, the left liver can be used. Perform the surgical steps as mentioned above, paying attention to identify the roots of the hepatic vein and the left hepatic vein at the root of the boot straps. Dissect the left hepatic duct, left hepatic artery, and the full length of the extrahepatic left portal vein. Four hepatic arteries should be reserved. Free the full length of the left portal vein branch and side lobe (Fig. 34.5).

Use a line from the midpoint of the gallbladder fossa to the right edge of the hepatic vein to determine the parenchymal resection. Use coagulation to mark the liver resection line to the hilus, splitting the liver tissues. Ligate the vasculature that is encountered. Cut off the left hepatic duct within the liver hilar plate. The celiac artery should be kept to the left or right. Determine whether the right or left hepatic artery is more distal. Cut near the origin of the right or left hepatic artery.

After above steps are complete, the main portal vein and liver bile duct are only connected to the right side. The left hepatic vein is resected from the inferior vena cava, and the two parts make a complete dry sleeve piece. Before saving the tissue, rinse the left hepatic duct with cold UW solution. Residual tissue of right lobe is harvested according to standard procedure. If the revascularization is needed, the vessel of donor can be utilized for after graft harvested (Fig. 34.6).

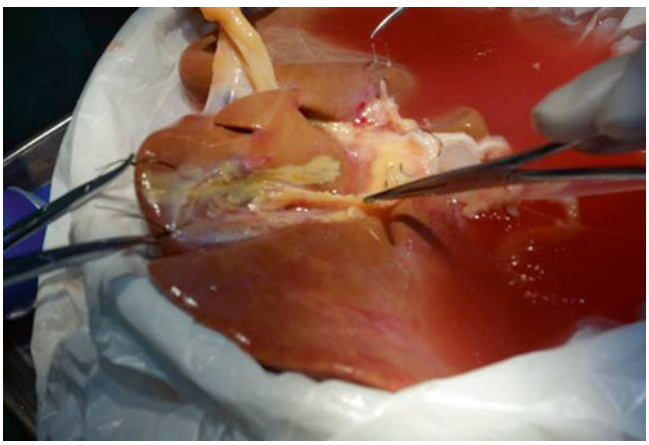

Fig. 34.5 The splitting line of left liver graft

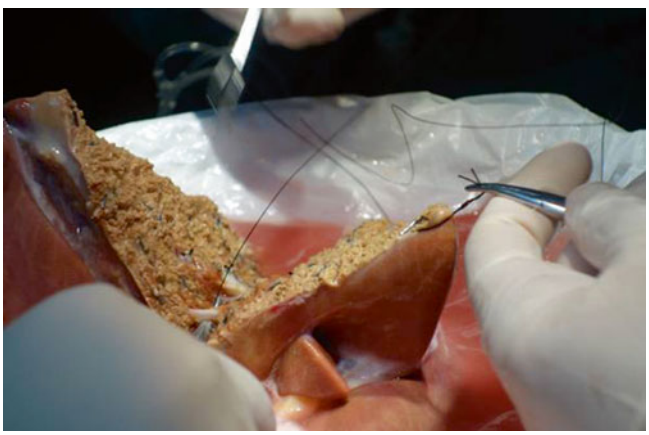

Fig. 34.6 The left liver graft and right liver graft with right lobe and caudate lobe

34.5.4 Left Liver Lobe with Caudate (SI–IV) and Right Liver Graft (SV–VIII) Splitting

Approximately half of standard liver excisions are donors with large left lobes; these grafts can be used for adults weighing less than 50 kg at the time of transplantation. Right liver donation requires a donor-recipient weight ratio matched to that of the recipient. First, dissect the hepatic vein and confirm the vena cava location. Explore and expose the right hepatic artery along the side wall of the common bile duct, avoiding skeletonized artery bifurcation to avoid damaging the supply of the fourth section of the hepatic artery. Approach the right portal vein from the outer side of the right portal vein bifurcation; free it of ligaments (Fig. 34.7).

In the liver hilum, separate the left hepatic duct and hepatic portal vein along the fissure, separating the liver parenchyma. Separate the right hepatic vein portal and right branch vessels one by one. After these steps are completed, cut the right portal vein branch at the distal bifurcation, and cut the hepatic artery at its origin. If the left superior vena cava or hepatic liver must be retained, a complete resection is required. Rinse the biliary tract and graft in cold UW solution. Then, remove the left lobe using standard resection techniques, and cryopreserve in the same manner as above. Close the hepatic vein, portal vein, and small branches of the hepatic artery before transplantation (Fig. 34.8).

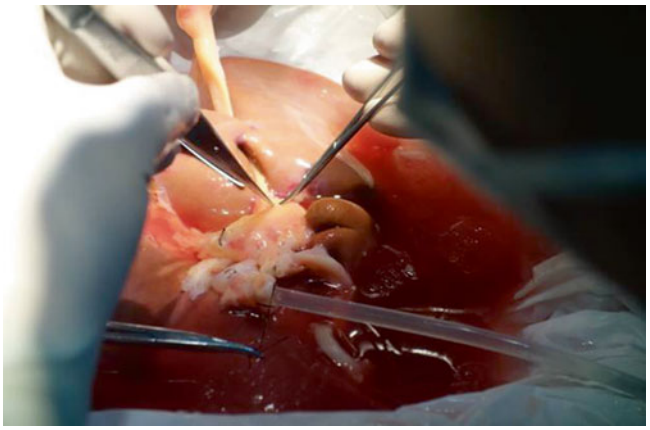

Fig. 34.7 Anatomic structures of the liver hilum

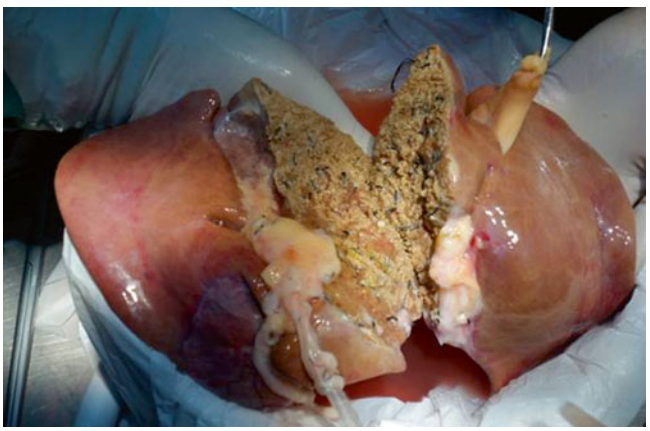

Fig. 34.8 Left liver and right liver graft

34.6 The Long-Term Effect Evaluation of Grafts

Split-liver transplantation was established as a surgical procedure to solve the donor shortage for pediatric liver transplants. In recent years, with an increasing number of patients waiting for liver transplantation, the shortage of donor livers in adults and children is becoming increasingly serious, and split-liver transplantation has an important practical value in the effective use of donor livers. However, the long-term outcome after split-liver transplantation is still the main concern. In current reports of the long-term effect of different grafts, large differences remain among transplant centers.

Left lobe and right liver grafts were the earliest splitting procedures and have been widely used. Left lobe grafts for pediatric recipients and extended right lobe for adults are ideal in terms of appropriate recipients. The vast majority of split-liver transplantations are conducted in this way. Although there have been no large studies, a report from Italy examining a cohort of 154 cases showed that survival rates for adults and children 3 years after grafting were 67 % and 79 %, respectively [7]. Moreover, UNOS data show that the graft 5-year survival rates for adults and children were 66 % and 64 %, respectively [14]. In the early years of SLT, bile duct and artery complications were the major problems affecting the curative effect [15–17]. However, over time, biliary and arterial complications for SLT in centers with a great deal of experience have improved [18].

Due to the standard of splitting the liver in half (S I–IV and S V–VIII) for two adults, there is generally a shortage of donor liver volume. Although some studies have reported that the splitting method can obtain satisfactory long-term outcomes, two other cohort studies found that the effect is still lower than for whole-liver transplantation [19, 20]. Moreover, in contrast to living-donor liver transplantation, splitting the liver can cause ischemia or preservation injury. Thus, recipients require a GRWR of 0.8 % for living-donor liver transplantation. With respect to keeping the hepatic vein in the left or right liver grafts, French researchers found that keeping or not keeping the hepatic vein led to some differences in liver function recovery for right liver grafts, although there were no differences in the long-term graft survival rate [21]. The split-liver graft may require less outflow than for a living-donor liver graft because of the larger volume [22].

At present, the split-liver transplantation is an extensive operation that effectively solves the problem of the shortage of donor livers. This method and parent liver transplantation are the most important operations with respect to liver transplantation in children. Left lobe and extended right lobe in pediatric and adult recipients has become the standard operation for splitting. Splitting half of the liver for adult/adult recipients has been successfully performed in some centers, but recipients should be selected carefully, and it is important to note that the long-term curative effect needs further validation.

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Ex Vivo Liver Resection and Autotransplantation

35

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35.1 History

Ex vivo liver resection and autotransplantation (ELRA) was first introduced by Pichlmayr R (Klinik für Abdominal- und Transplantationschirurgie, Medizinischen Hochschule, Hannover, FRG) [1]. The procedure was performed in February 1988 in a 46-year-old patient to remove large metastases from a leiomyosarcoma of the stomach. Subsequently, Hannoun et al. [2] and Sauvanet et al. [3] developed a simplified technique of "ex situ" hepatic surgery, in which wide access to all parts of the liver is provided by sectioning the infrahepatic and suprahepatic vena cava, while preserving the continuity of the portal triad.

The fundamentals of ELRA can be integrated with two major technical features of modern liver transplantation and hepatectomy, namely, the use of hypothermic perfusion and venous bypass, in order to overcome the limitations of ischemic damage to the liver in unresectable liver tumors. Clinical practice has demonstrated that ELRA is a safe and effective approach to radical resection for tumors that are routinely thought to be unresectable due to a posterior location in the liver or invasion of the vena cava. Vascular repairs and reconstructions are also possible, especially in cases of vena caval invasion. It is considered to be landmark innovations in liver transplantation to break through the taboo of central intrahepatic lesions invading the main hepatic vein of inferior caval vein.

35.2 Indications

ELRA can be used for the resection of tumors that lie deep within the liver and invade or compress the main hepatic vein as it enters the inferior vena cava, especially the posthepatic inferior vena cava. This technique was initially used for hilar hepatocellular tumors, Klatskin tumors, or metastases that invade the main hepatic vein or posthepatic inferior vena cava. Recently, the use of this technique has also been reported for the treatment of benign liver lesions (such as giant hepatic hemangioma or hepatic alveolar echinococcosis) and serious liver injuries [4–6].

However, it should be noted that ELRA is a complicated and high-risk operation. Patients with benign hepatic diseases are often the best candidates for the procedure due to improved long-term results.

Contraindications: Patients with liver lesions and diffuse hepatic disease have a higher incidence of liver failure after surgery due to the complete bypass of the liver's blood supply during ex-vivo liver resection under hypothermic perfusion.

35.3 Autotransplantation

The following passage presents a case study of the use of the ELRA procedure in a female patient with hepatic alveolar echinococcosis at the author's hospital. A 43-year-old woman was transferred to our center due to a 3-year history of liver lesions. Laboratory examinations demonstrated a total bilirubin level of 269.5 μmol/L. After treatment with persistent percutaneous transhepatic cholangial drainage (PTCD) and supportive care, the patient's liver function recovered to a normal level (with a Child-Pugh score of 5), and she was prepared for surgery (Figs. 35.1, 35.2, 35.3 and 35.4).

35.3.1 Resection of the Liver

35.3.1.1 Body Position and Choice of Incision

The patient should be placed in the supine position, and the great saphenous veins should be disinfected for stripping, when necessary. The Mercedes incision was chosen for

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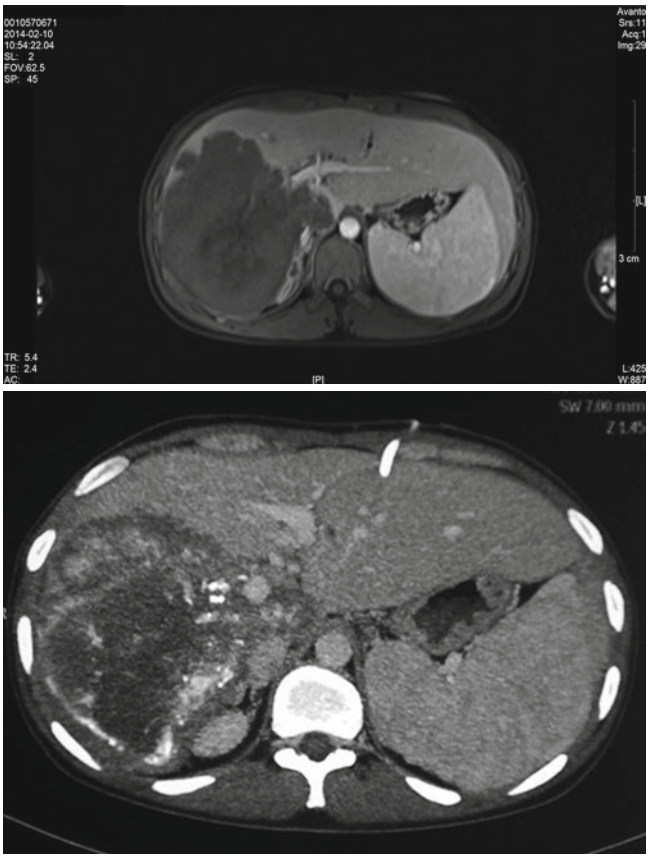
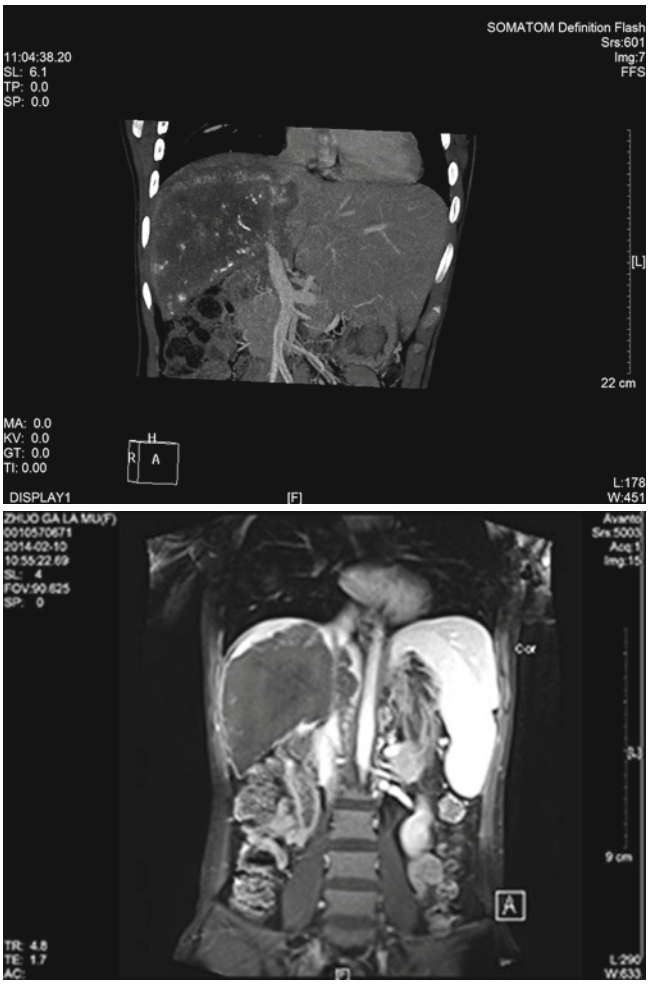


Figs. 35.1 and 35.2 Preoperative axial CT image of the proximal porta hepatis



Figs. 35.3 and 35.4 Preoperative coronal CT image of the proximal porta hepatis

abdominal exploration which range from right linea axillaris media and lateral margin of left rectus abdominis exoloma.

35.3.1.2 Abdominal Exploration

The various organs of the pelvic and abdominal cavities should be explored in the appropriate order to characterize the extrahepatic and perihepatic extent of disease.

35.3.1.3 Anatomy of the First Porta

Efforts should be made to avoid damaging the bile ducts, hepatic arteries, and portal veins, since the resected liver will ultimately be transplanted back in situ with anastomosis of the first porta (Fig. 35.5).

35.3.1.4 Lysis of the Perihepatic Ligaments

The perihepatic ligaments are usually invaded, especially the diaphragmatic muscle. Sometimes, part of the diaphragmatic muscle should also be resected (Figs. 35.6 and 35.7).

35.3.1.5 Resection of the Liver

After mobilizing the perihepatic structures, resection begins. The structures should be transected in the following order: the bile duct, hepatic arteries, and portal veins in the first porta, then the posthepatic inferior vena cava, and finally, the suprahepatic vena cava and the liver.

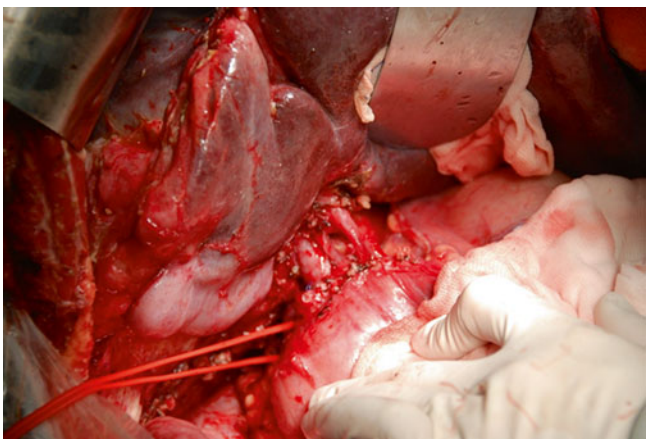


Fig. 35.5 Invasion of the first hilar structure

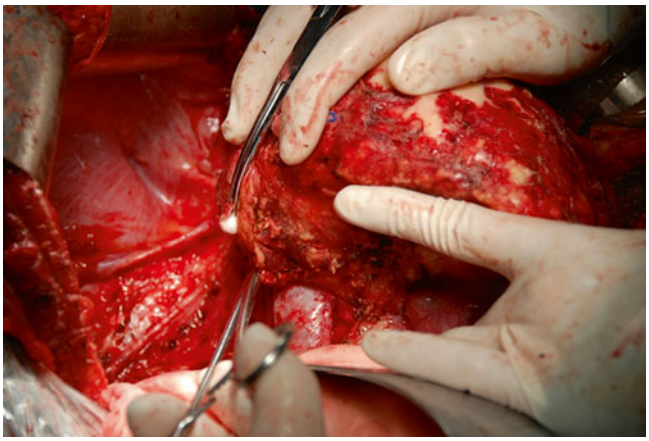


Fig. 35.6 Invasion of the diaphragmatic muscle and mobilization of the liver

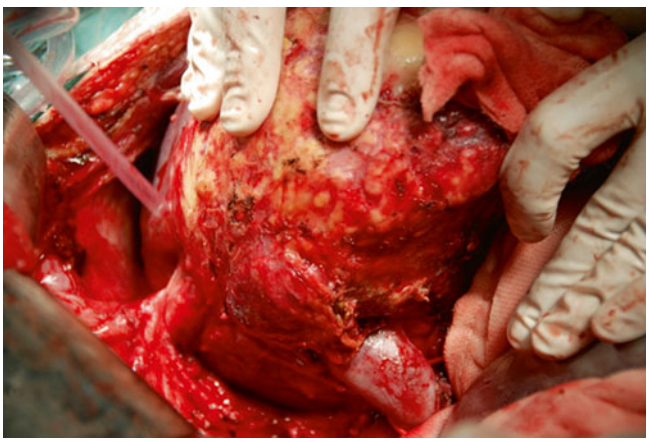


Fig. 35.7 Invasion of the posthepatic inferior vena cava

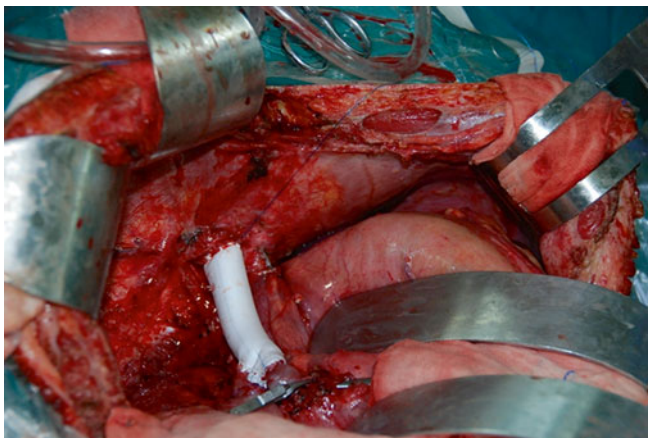


Fig. 35.8 Reconstruction of the inferior vena cava and portal vein with an artificial blood vessel

35.3.2 Reconstruction with an Artificial Blood Vessel

The resected part of the IVC was reconstructed with an artificial blood vessel. Then, an end-to-side anastomosis was created between the portal vein and the artificial blood vessel for the portacaval shunt. This can restore circulation in the portal venous system and stabilize the underlying circulation and the internal environment (Fig. 35.8).

35.3.3 Parenchymal Transection and Repair

As soon as the liver was completely resected, the liver graft was perfused with University of Wisconsin solution (0–4 °C) via the portal vein. Parenchymal transection should be based on the segmental anatomy of the liver, and the reserved hilar structures should be repaired for the reconstruction (Figs. 35.9, 35.10, 35.11, 35.12 and 35.13).

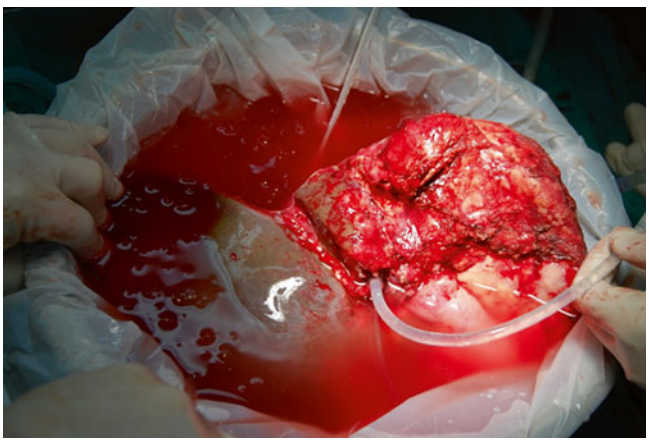


Fig. 35.9 Perfusion with University of Wisconsin solution on the back table

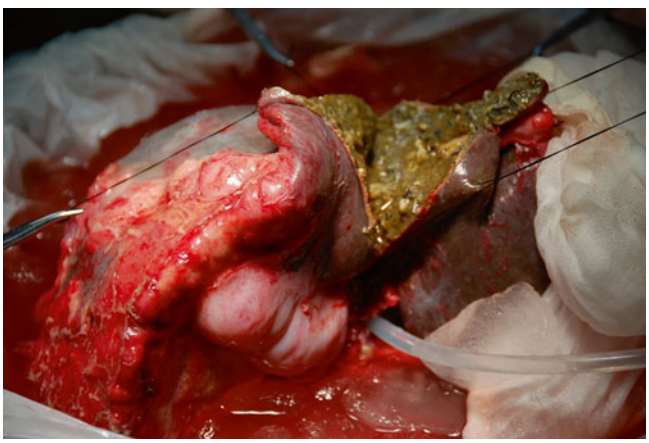


Fig. 35.10 Parenchymal transection on the back table

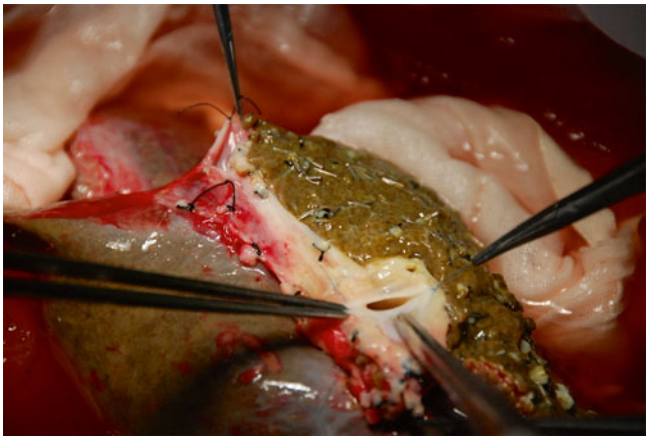


Fig. 35.11 Segments 2 and 3, which were prepared for transplant, and repair of hilar structures

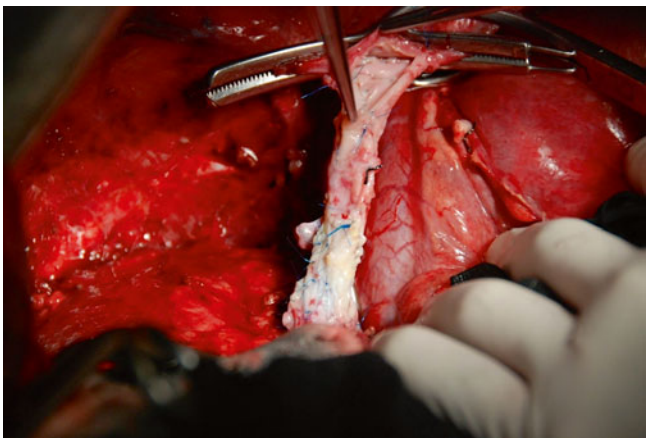
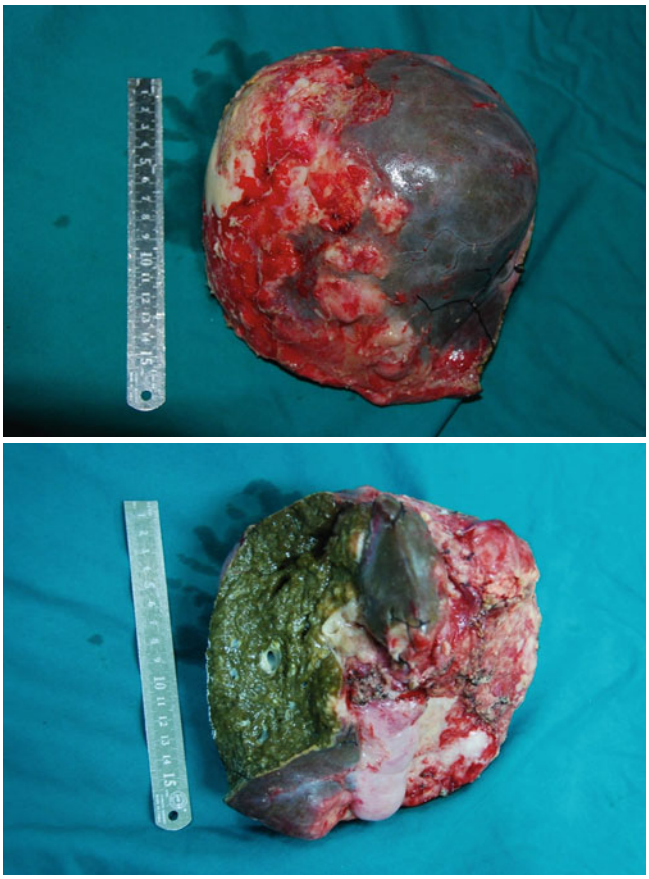


Fig. 35.14 Reconstruction of the posthepatic inferior vena cava with an autologous venous graft after removal of the temporary artificial blood vessel and before transplantation



Figs. 35.12 and 35.13 Segments 1, 4, 5, 6, 7, and 8, which were resected

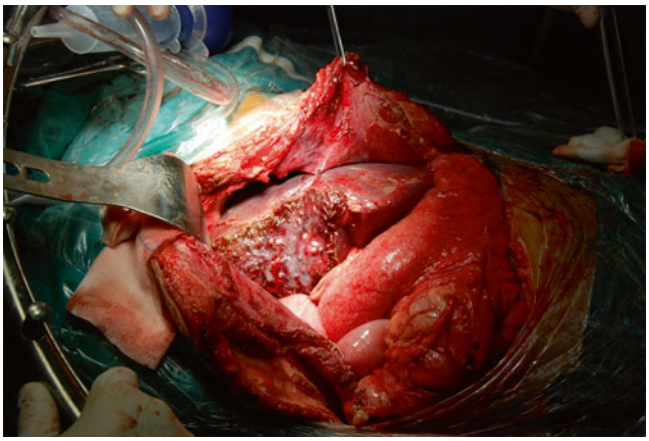


Fig. 35.15 The operative field after autotransplantation

35.3.4 Transplantation of the New Liver

Reconstructions were performed using a standard method that was described previously for living-donor liver transplantation: First, the hepatic vein was reconstructed, followed by the portal vein, the hepatic artery, and the bile duct. The hepatic biliary duct was drained by a Roux-en-Y hepaticojejunostomy, as it is often being invaded by the primary disease (Figs. 35.14 and 35.15).

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Vessel Exposure and Reconstruction in Liver Transplantation

36

Jichun Zhao and Peixian Chen

Vessel exposure and vascular reconstruction play pivotal roles in liver transplantation (LT) and in other surgical techniques performed during transplantation. Either poor vessel exposure or vascular reconstruction results in unsuccessful liver transplantation. Satisfactory vessel exposure is a prerequisite for successful vascular reconstruction during liver transplantation. Dissection and protection of the to-be-reconstructed vessels and determining proper strategy for reconstructing vessels under nonideal conditions are crucial to successful vascular reconstruction. Vascular remodeling, including reconstruction of the suprahepatic inferior vena cava (IVC), hepatic veins, portal vein, and hepatic arteries, is of paramount importance in liver transplantation. Any type of vascular complication can lead to the failure of liver transplantation, especially arterial complications which can result in graft failure [1–3]. Herein, we introduce some common techniques in vessel exposure and reconstruction in the context of liver transplantation.

Indications (1) End-stage liver disease, (2) fulminant liver failure, (3) hereditary metabolic liver disease, and (4) unresectable hepatic malignancy without metastasis

Contraindications (1) Patients with severe infection, sepsis, AIDS, extrahepatic malignancy, and drug addiction; (2) patients with severe heart, lung, brain, hypertensive, or diabetic comorbidities and hypertension; (3) patients with severe renal insufficiency; (4) patients with intrahepatic biliary infection; (5) patients with past psychological problems; and (6) patients with portal thromboembolism or embolism

Preoperative Preparation Patients with end-stage liver disease are predisposed to systemic multi-organ disorder, which will be exacerbated by liver transplantation. Therefore, patients' organ function should be assessed thoroughly to help predict what will occur during the operation and make relevant preparation. These steps are also very important for planning anesthetic usage and for ensuring patient safety and a successful operation.

Liver transplantation candidates should receive assessments with respect to organ function, blood biochemistry, and coagulation function. The preoperative assessment includes an extrahepatic organ function evaluation, determination of the patients' willingness, surgical risk magnitude, and preoperative preparation and treatment for wait-listed patients. The surgeon and gastroenterologist should cooperate during preoperative preparation and design of the treatment plan for wait-listed patients to improve the condition of the patients, reduce the risks of anesthesia and operation, and ensure smooth operation. The waiting time can be as long as several weeks to several months due to organ shortage. Some liver transplant candidates can experience deterioration during this time. Further assessment is therefore necessary when the operation date is confirmed. Examinations such as hematologic analysis, biochemistry, and ECG should be repeated to reappraise patient condition and to make specific and necessary preparations for potential problems. Patients with sepsis, severe respiratory infection, or severe heart disease should be excluded from operation [1, 2].

Anesthesia and Position Intratracheal intubation, general anesthesia, and supine position

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36.1 Liver Removal and Vessel Exposure in Classic Orthotopic Liver Transplantation (OLT)

Steps

1. Position: The patient is supine, with both upper extremities abducted. The left axillary vein and left great saphenous vein are exposed and prepared for venous bypass.
2. Incision: A bilateral subcostal incision is performed and extended to the xiphoid process on the midline, to the midaxillary line on the right, and to the external border of the left rectus abdominis. The left incision is generally 4–6 cm below the rib or more than 6 cm in patients with massive ascites, because the incision would rebound above the rib when the ascetic fluid recedes. The xiphoid process can be cut off if necessary (Fig. 36.1). Hemostasis should be carefully managed on each layer along the incision. Interrupted sutures combining the peritoneum and the skin can shrink the wound and reduce oozing.
3. Exposure: Satisfactory exposure is achieved using retractors (Fig. 36.2). Attention should be given to exposing the second hepatic hilum and right hepatic area so that the suprahepatic IVC can be easily exposed and reconstructed and the retro-hepatic IVC area can be easily dissected.
4. Intra-abdominal exploration: Extrahepatic metastases and cancerous emboli in the portal vein and IVC should be carefully inspected in recipients undergoing LT for hepatic malignancy. A splenectomy that is indicated in patients with splenomegaly and hypersplenism should be performed prior to liver removal, which improves coagulation function and facilitates liver resection.
5. Exposure of hepatic artery and portal vein: The hepatic artery proper can be located on the left border of hepatoduodenal ligament and freed up a short distance beyond the area of arterial bifurcation from its point of origin. Hepatic arteries should not be clamped or tracted by suture (Fig. 36.3). Periarterial tissue instead of the arterial sheath tissue is dissected to expose the hepatic artery and preserve its adventitia intact. The left and right hepatic

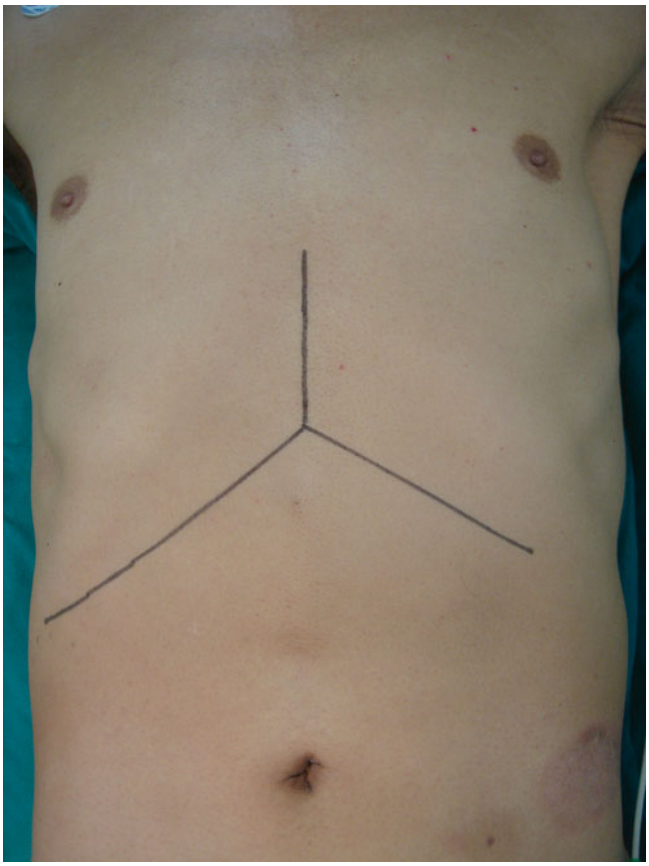

Fig. 36.1 Recipient's incision

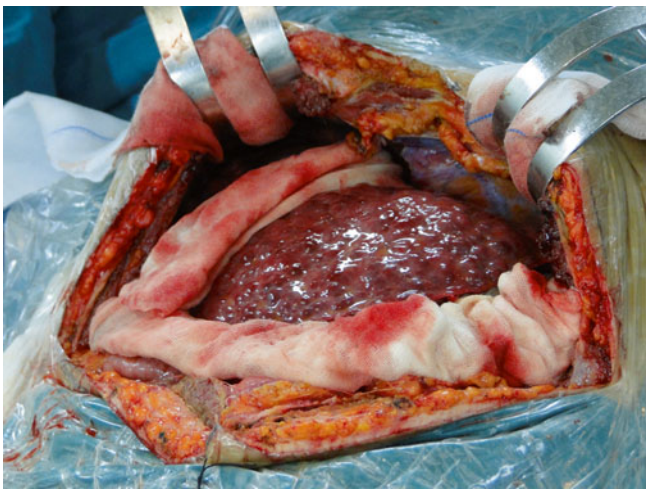

Fig. 36.2 Exposure using retractors

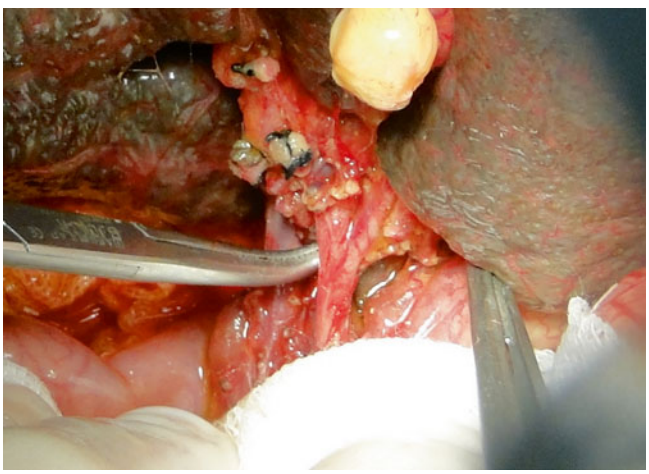

Fig. 36.3 Dissection of bifurcation of the hepatic artery

arteries can be ligated and cut close to the liver to facilitate later procedures (Fig. 36.4). The portal vein can be perfectly exposed when the surrounding tissue and lymph nodes are removed after both the hepatic artery and common bile duct are freed. The portal vein should be exposed from its bifurcation to the superior surface of the pancreas. Sutures are placed at the root of the left and right branches of the portal vein, respectively, for later ligature and division (Figs. 36.5 and 36.6).

6. Suprahepatic IVC exposure: Extensive adhesions and abundant collaterals can be found around the liver in patients with portal hypertension. As a result, the periodontal ligaments of the liver should be cut off after dissection of the first liver hilum to prevent severe bleeding. The left triangular ligament is cut off subsequent to hepatic falciform ligament division using an electrotome. Both ends of the left triangular ligament should be ligated or sutured because collaterals commonly form in this ligament. The hepatogastric ligament can be exposed and cut off when the left lateral segment is turned over to the right after the left coronary ligament is cut off. The accessory left hepatic artery originating from the left gastric artery can be found in the hepatogastric ligament and hence requires double ligation before division. The right triangular ligament and right coronary ligament are cauterized. The ligamenta hepatocolicum and hepatorenal ligament can be cauterized after the right lobe is lifted gently to the left. The right venas suprarrenales should be ligated and detached close to the retro-hepatic IVC after exposure. The right posterior border of the retro-hepatic IVC should also be exposed. The left posterior border of the IVC can be exposed by longitudinal opening peritoneal reflection on the left side of the retro-hepatic IVC after lifting the left lobe and caudate lobe to the right. The suprahepatic IVC can be freed using an index finger and a right-angle clamp. The infrahepatic IVC can be reached by opening the lateral peritoneum along the duodenum. The pleural short hepatic veins joining the IVC should be carefully handled and ligated. A blood vessel loop should be placed around the infrahepatic IVC at the converging point of the right renal vein. Delicacy and patience is required in blunt dissection of the suprahepatic IVC so as to avert injury. Dissection of the ligaments around the liver should be performed under direct vision as close to the liver surface as possible. To avoid retroperitoneal hemorrhage, complete mobilization of the retro-hepatic IVC can be neglected in patients with severe portal hypertension or those with difficulties in exposing the IVC. At

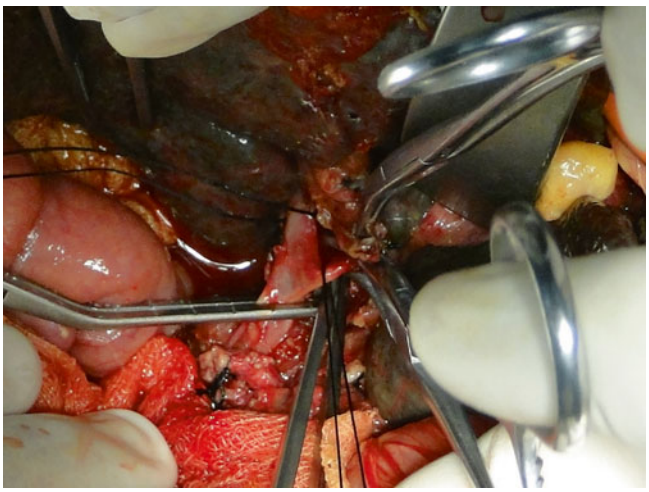

Fig. 36.6 Exposure of portal vein and its branches

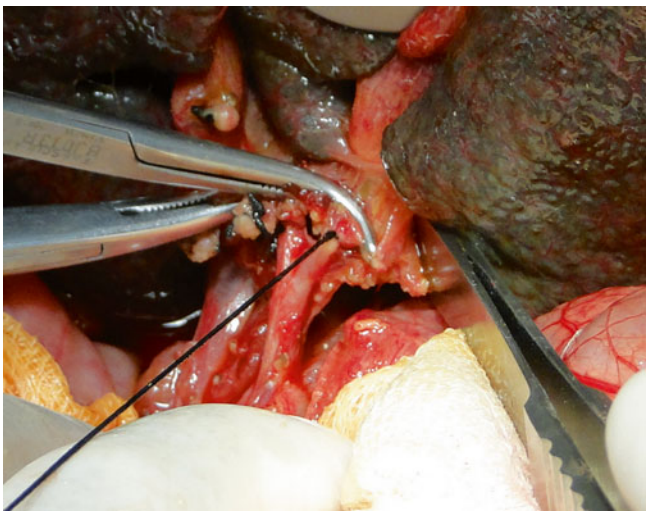

Fig. 36.4 Ligature of the left and right hepatic arteries

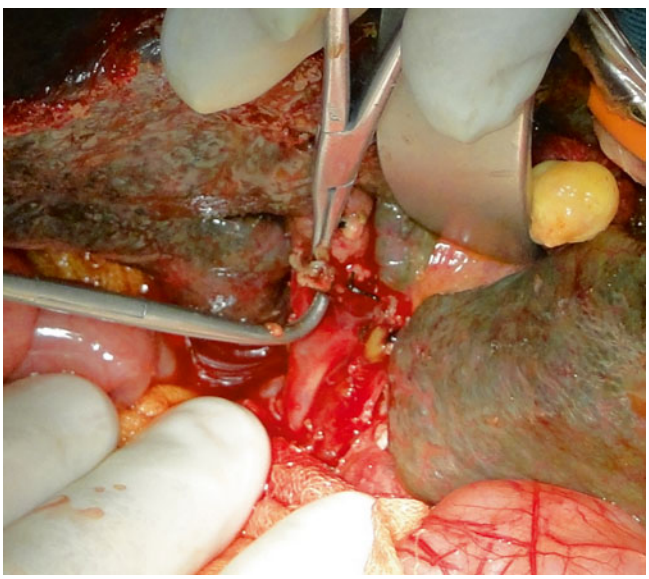

Fig. 36.5 Portal vein mobilization

this time, the supra- and infrahepatic IVC can be exposed, and the area behind the vena cava can be handled when the liver is removed (Figs. 36.7 and 36.8).

7. Management of the portal vein and infrahepatic IVC at liver removal: Blockage of supra- and infrahepatic IVC is achieved using harmless vascular clamps (Satinsky's vascular clamps). The liver should be maintained at its anatomical position, and the clamps should be placed in a horizontal manner. The left and right renal veins should not be clamped. Partial diaphragmatic tissue can be included when the suprahepatic IVC is clamped to prevent accidental slip; however, the phrenic nerve should be protected. The opening of the clamp can be further coalesced using coarse thread. The posterior hepatic plane can be detached from the IVC by lifting the liver after cutting off the portal vein and infrahepatic IVC. At this time, diaphragmatic tissue posterior to the liver and retroperitoneal collaterals can be clamped. A long posterior wall of suprahepatic IVC should be spared for reconstruction when it is cut apart from the point close to the liver surface. Injury to the liver bed and the volume of bleeding can be minimized by removing the liver as close to the back of the retro-hepatic IVC as possible.
8. Repair of the portal vein and suprahepatic IVC: The cut end of the portal vein, the supra- and the infrahepatic IVC should be trimmed. The suprahepatic IVC should be kept unobstructed. The openings of the joining veins and damage from the wall of IVC should be carefully checked [4–7].

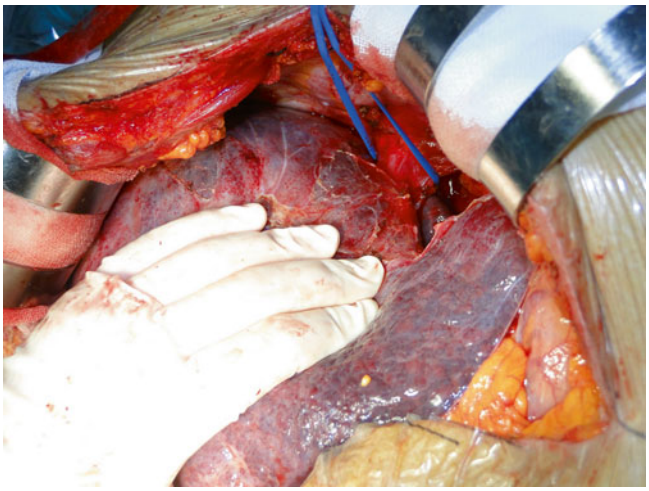

Fig. 36.7 Exposure of the suprahepatic IVC

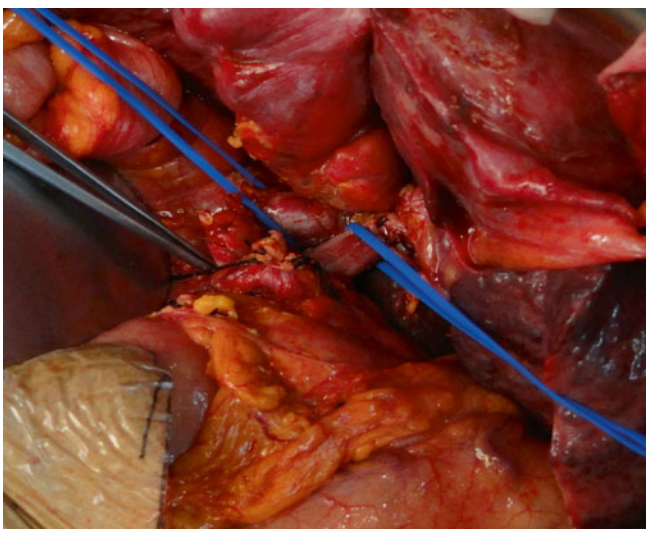

Fig. 36.8 Exposure of the infrahepatic IVC

36.2 Liver Removal and Vessel Exposure in Living-Donor Liver Transplantation (LDLT)

Steps

1. Position, incision, and exposure: See Sect. 36.1.
2. Exposure of the hepatic artery and portal vein: See Sect. 36.1. To shorten the hepatic duration, the portal vein should not be occluded until the dissection of the second and third liver hilar is finished because venous bypass is absent in LDLT.
3. Exposure of supra- and infrahepatic IVC: Abundant collaterals can be found in the perihepatic ligaments in cirrhotic patients. Therefore, the perihepatic ligaments need to be severed using an electrotome and sutured when there is bleeding. The perihepatic ligaments are generally severed in the following order: left triangular ligament, coronary ligament, right triangular ligament, hepatocolic ligament, hepatorenal ligament, right suprarenal vein, left hepatogastric ligament, and the peritoneal reflection beneath the IVC. Then, blood vessel loops are placed around the supra- and infrahepatic IVC after mobilization (Fig. 36.9).
4. Exposure of the second liver hilum and hepatic veins: The tissue about the right hepatic vein (RHV) is carefully divided to provide sufficient exposure of the RHV for a right-angle clamp to be inserted under the vein to permit the placement of a blood vessel loop for traction. The RHV is doubly clamped with harmless vascular clamps. Both ends of the RHV are oversewn with 5-0 Prolene sutures. The left and middle hepatic veins are freed of liver substance until a sufficient distance is gained to permit the application of a pair of long curved Cooley vascular clamps. The confluence of the left and middle hepatic veins should be expanded and spared for anastomosis. In cases with difficulty in exposing the RHV, the RHV can

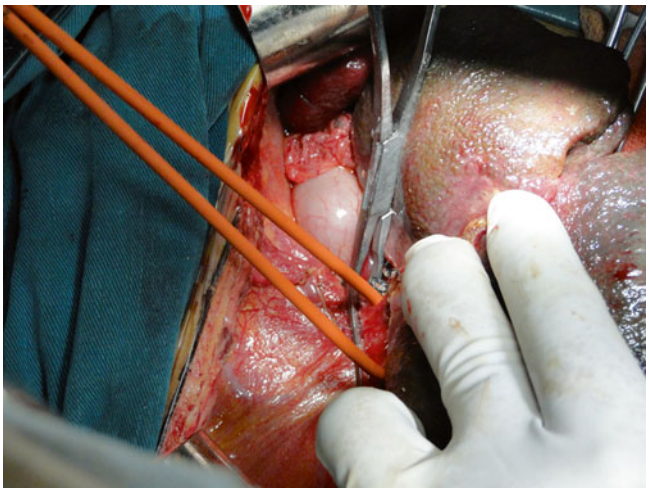

Fig. 36.9 Traction and occlusion of the suprahepatic IVC

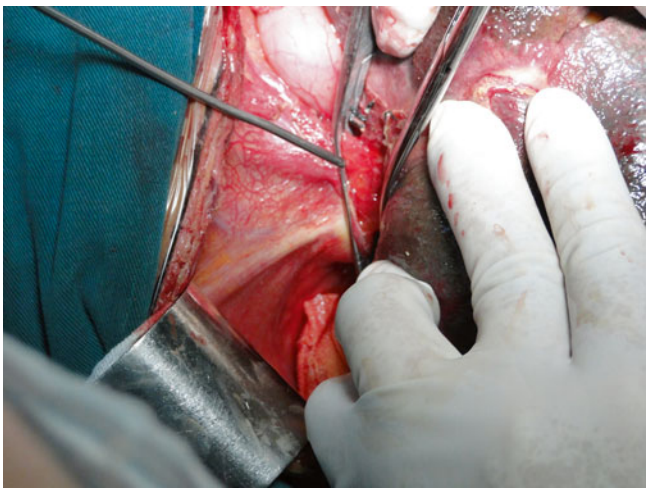

Fig. 36.10 Exposure of the hepatic veins

be attained subsequently to division of the left hepatic vein or to understanding the relationship between hepatic veins and retro-hepatic IVC by dividing the portal vein and lifting of the liver (Figs. 36.10, 36.11, and 36.12).

5. Third hepatic hilum and retro-hepatic IVC exposure: This is the most challenging part of liver removal in LDLT and hence requires patience, meticulousness, and accuracy in handling. The caval ligament can be exposed and then severed after lifting the right lobe to the left. The caval ligament is a fibrous tissue that bridges each side of the caudate lobe behind the IVC. The number of short hepatic veins varies among patients and can be as many as ten. Hepatic veins, which are short fragile, tend to be torn, resulting in IVC wall bleeding and air embolism. Short hepatic veins can be cut off when each end is closed using metal clips to avoid slippage. The ends of short hepatic veins joining the IVC can be closed using harmless suture after liver removal. Caution must be executed as an inferior RHV can be encountered in many cases. The right lobe is placed back and the left lateral and caudate lobe are rotated medially. The caudate lobe and posterior peritoneal transferring portion are cut open using an electrotome. Short hepatic veins can be handled from the left side of the IVC toward the major hepatic veins cranially after the caudate lobe is freed from the IVC (Fig. 36.13).
6. Management of the portal vein and hepatic veins: At this time, the liver is connected to the body only by the portal vein, hepatic artery, and hepatic veins. The liver is removed by cutting off the portal vein, hepatic artery, and hepatic veins when there is 15–30 mins left to finish repairing the donated liver. The left, middle, and right hepatic veins are clamped individually using curved Cooley vascular clamps and then divided. Compared to cadaveric livers, living-donor livers provide shorter stumps of hepatic arteries, portal vein, and hepatic veins.

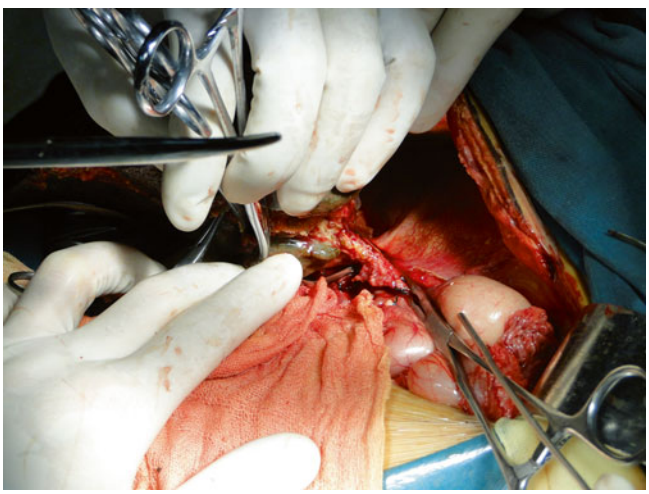

Fig. 36.11 Dissection and division of the hepatic veins

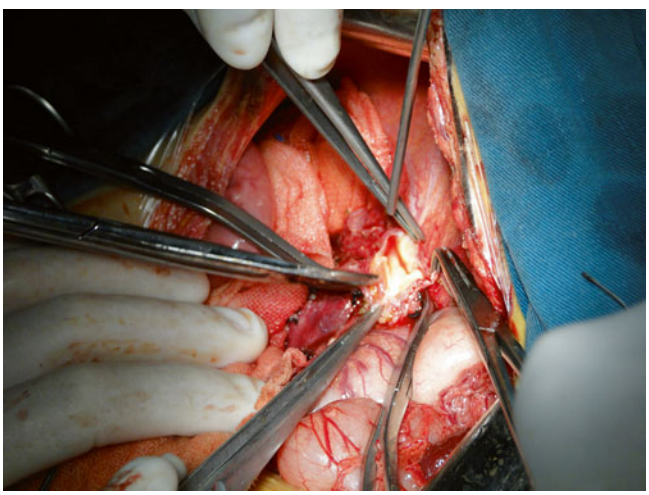

Fig. 36.12 Hepatic vein trimming

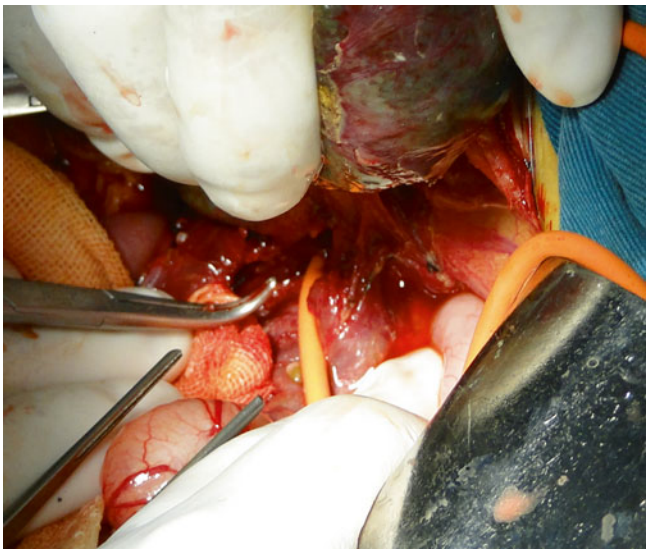

Fig. 36.13 Exposure of the third hepatic hilum and retro-hepatic IVC

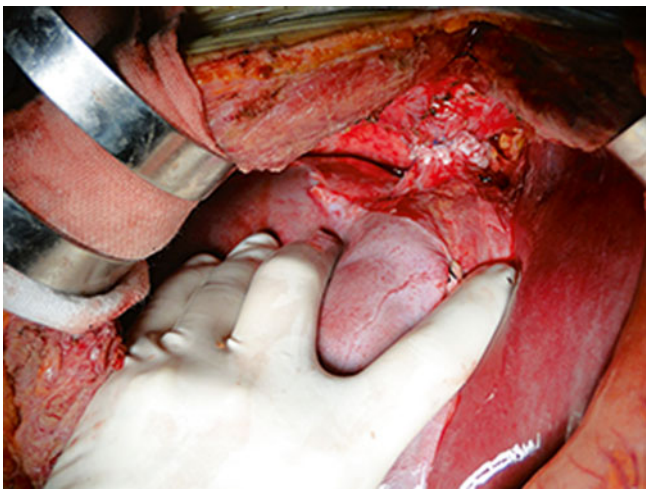

Fig. 36.14 Completed reconstruction of the suprahepatic IVC

As a result, it is critically important to preserve the stumps of hepatic arteries, portal vein, and hepatic veins of the recipient as long as possible. Recipient's hepatic arteries and portal veins should be dissected as close to the first hepatic hilum as possible. The portal vein should be freed up a short distance beyond the area of arterial bifurcation. The point of division of the recipient's hepatic artery depends on its own size and length, which can be as far as the bifurcation of the hepatic artery proper, or the point of gastroduodenal artery leaving the common hepatic artery. The middle and left hepatic veins should be severed as close to the liver as possible to spare a long enough venous remnant for repair and anastomosis. When the liver is removed, the liver bed should be checked carefully for bleeding, and the openings of the recipient's hepatic veins need to be trimmed to match those of the donated liver. LDLT is not suitable in patients with hepatic malignancy adjacent to hepatic veins and retro-hepatic IVC because it is hard to achieve complete liver removal [8–11].

36.3 Vascular Reconstruction in OLT

Steps

1. Reconstruction of the suprahepatic IVC: The suprahepatic IVC reconstruction begins in the midline anteriorly and posteriorly with 3-0 Prolene sutures, and knots are tied when the donated liver is implanted. Two corner stitches are placed using 4-0 Prolene sutures for suture traction when the IVC is anastomosed. A back row anastomosis is completed first. Over-and-over suturing is then carried from the endothelial surface outward, ensuring the endothelium is tacked down as well as avoiding the involvement of the contralateral wall. At the end, it is tied in the midline anteriorly. Key points: (1) The suprahepatic IVC from either the donated liver or the recipient should be trimmed to an appropriate length before anastomosis. Otherwise, when it is too long, the suprahepatic IVC can overlap or obstruct following the anastomosis. (2) The anastomosis can twist if involution of the suprahepatic IVCs from the donor and the recipient is not satisfactory. (3) Anastomotic stenosis or thrombosis can be avoided when sutures are carried from the endothelial surface outward. (4) The large-sized end of IVC can be readjusted in a parallel mattress suture fashion. (5) The final knot should be made 1 cm far from the IVC wall in order to avert anastomotic stenosis when blood fills the IVC (Fig. 36.14).
2. Reconstruction of the infrahepatic IVC: The infrahepatic IVC is reconstructed using 3-0 Prolene suture in a similar fashion as for the suprahepatic IVC. A number 8 urinary catheter is passed from the anastomosis into the retro-hepatic IVC, facilitating blood flush out when the portal vein is patent (Fig. 36.15).
3. Reconstruction of the portal vein: The portal vein of the recipient is clamped proximally, while that of the donor is cut off close to the hilum. Reconstruction begins in the midline anteriorly and posteriorly with 5-0 Prolene sutures. Continuous suturing running bilaterally is then carried from the endothelial surface outward, ensuring the endothelium is tacked down. The contralateral wall of the portal vein should not be involved when the other side is being anastomosed. A continuous flush of heparinized saline is used to decontaminate the anastomosis. The vein is irrigated with heparinized saline to flush out any clot and air once anastomosis is nearly completed. A knot is made on the anterior wall of the portal vein when blood fills the

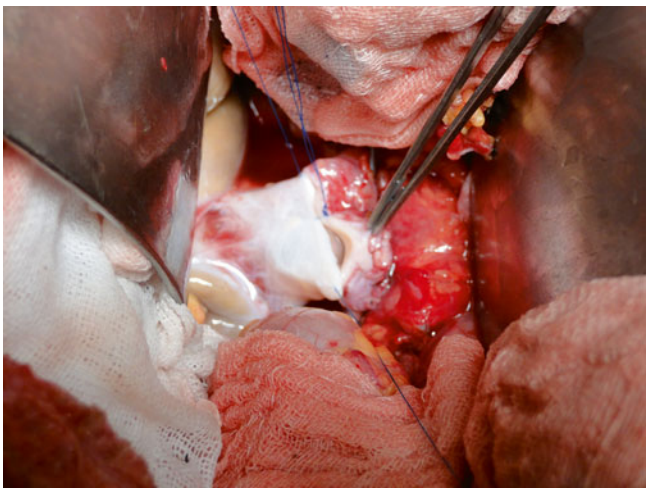

Fig. 36.15 Reconstruction of the infrahepatic IVC

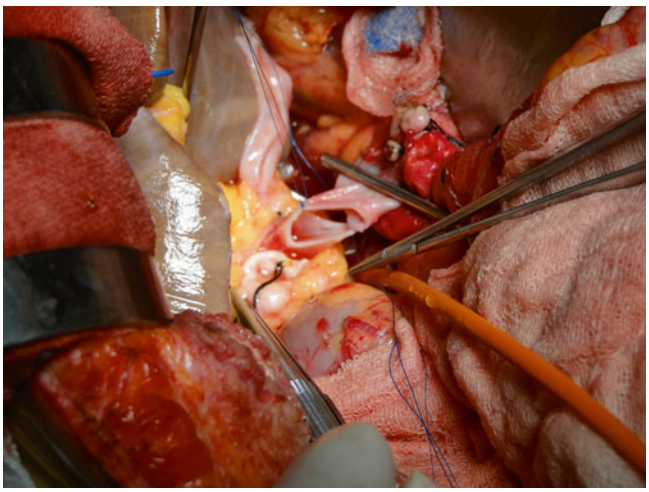

Fig. 36.17 Placement of one stitch on the anterior wall of the portal vein

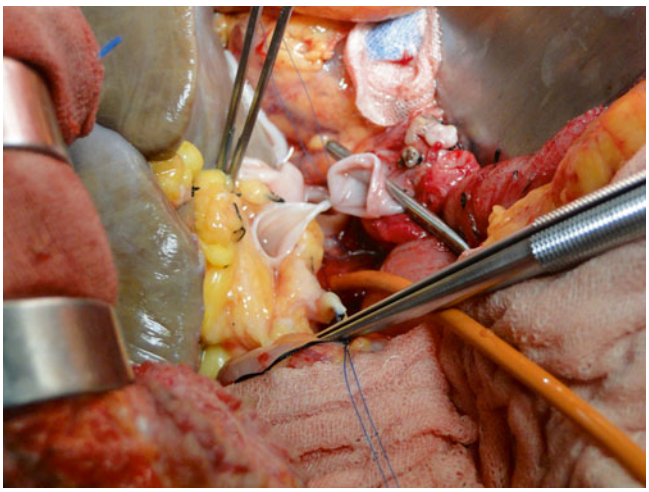

Fig. 36.16 Placement of one stitch on the posterior wall of the portal vein

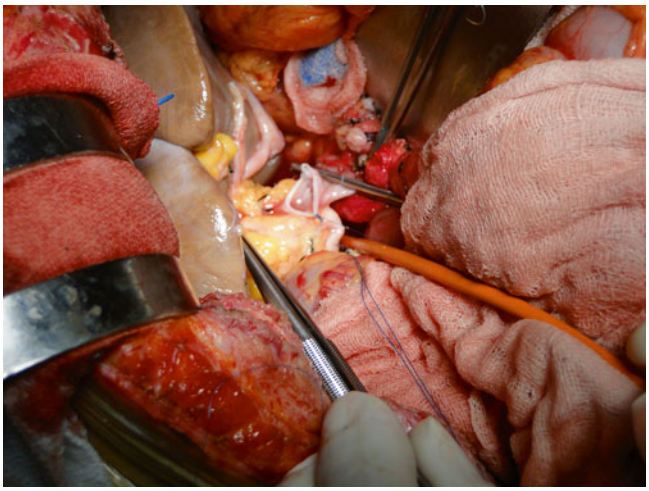

Fig. 36.18 Anastomosis of the bilateral walls of the portal vein

lumen. The clamp at the donor's side of the portal vein is released prior to that at the recipient's end, so potassium-rich and acidic metabolite can flow out along with 100–200 ml of blood from the infrahepatic IVC. The suture is tightened and knotted when the urinary catheter is withdrawn, with portal vein re-clamping. When the anesthetist is informed that hepatic reperfusion is occurring, the suprahepatic IVC, portal vein, and infrahepatic IVC regain patency in that order (Figs. 36.16, 36.17, 36.18, and 36.19). In patients with portal thrombosis or cavernous transformation, an interpositional vascular graft can be used for reconstruction because the length of the normal portal vein might not be sufficient. The donor's iliac vein, which is an optimal substitution graft source, is anastomosed to the donor's portal vein at the back table. When the portal thromboses extend to the origin of the superior mesenteric vein, the sub-

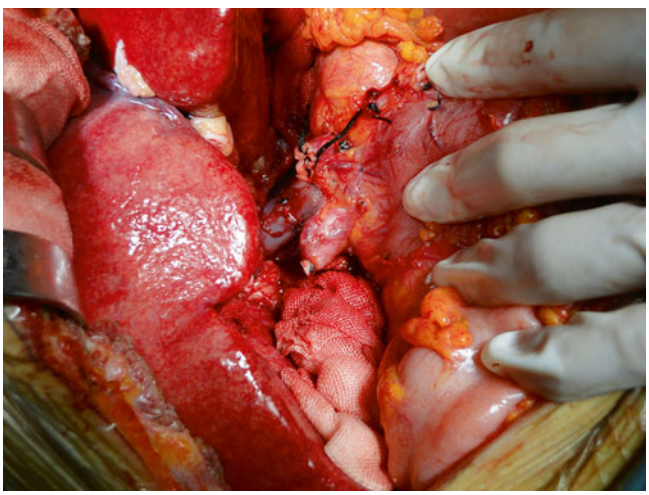

Fig. 36.19 Completed reconstruction of the portal vein

stituted vessel can be anastomosed to the anterior wall of the vessel at the root of the mesocolon transversum running behind the stomach and in front of the pancreas [5–7].

4. Reconstruction of the hepatic artery: Hepatic arterial reconstruction is an important determinant of successful liver transplantation. Arterial stenosis, flow insufficiency, and thrombosis can result in primary non-function, severe infection, and biliary complications, leading to a mortality rate of 75 %. These complications commonly require re-transplantation. Hepatic arteries from the donor and the recipient require careful appraisal and cautious management. Autologous vessels can be used for interposition when the recipient's hepatic artery is unsuitable for reconstruction [12–16].
   (i) End-to-end anastomosis: This method should be tailored to cases where the hepatic arteries from the donor and the recipients are similarly sized. The hepatic artery proper, the bifurcation where the gastroduodenal artery leaves the hepatic artery proper, the common hepatic artery, and the splenic artery from the recipient can be used for reconstruction. End-to-end arterial reconstruction can be performed in a continuous or interrupted fashion using 8-0 or 7-0 Prolene suture (Figs. 36.20, 36.21, and 36.22).
   (ii) Interposition: The recipient's hepatic artery is unsuitable for reconstruction when the common hepatic artery is obliterated, sandwiched, or aberrant. Under such circumstances, the donor's hepatic artery is bridged to the anterior wall of the recipient's aorta below the origin of the renal artery. This step is accomplished using interpositional vascular grafts harvested from the autologous great saphenous vein or cryopreserved vessels.

   The intraluminal blood flow of the hepatic artery, portal vein, and IVC is examined by Doppler ultrasound after the arterial reconstruction is completed [17, 18] (Figs. 36.23 and 36.24).

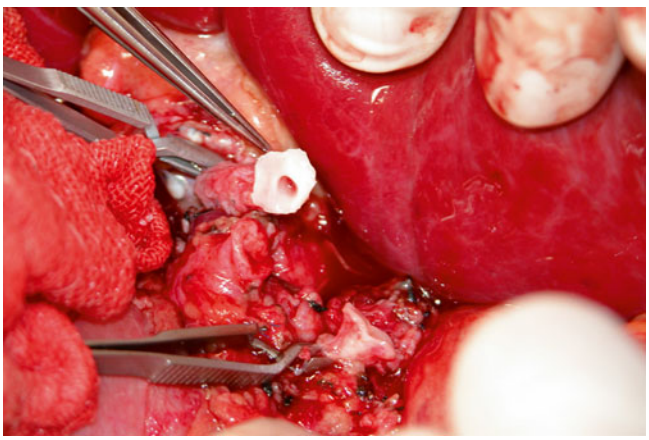

Fig. 36.20 Hepatic arteries in patch shape

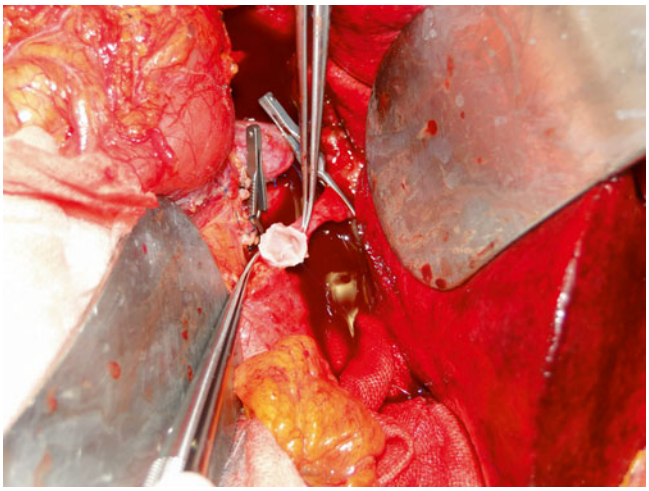

Fig. 36.21 Anastomosis of the posterior wall of the hepatic artery

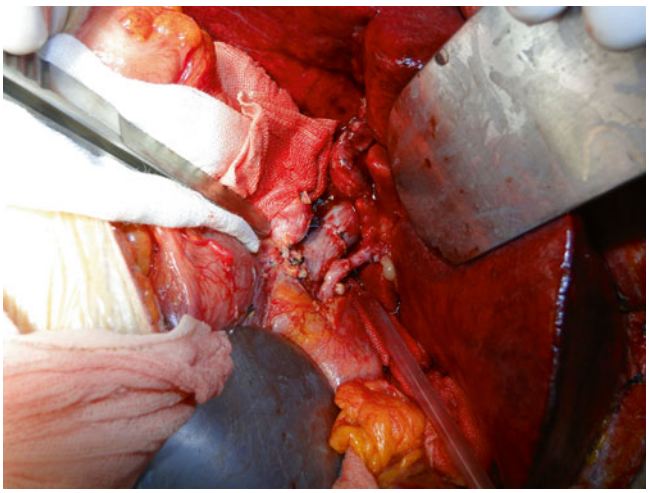

Fig. 36.22 Completed arterial reconstruction

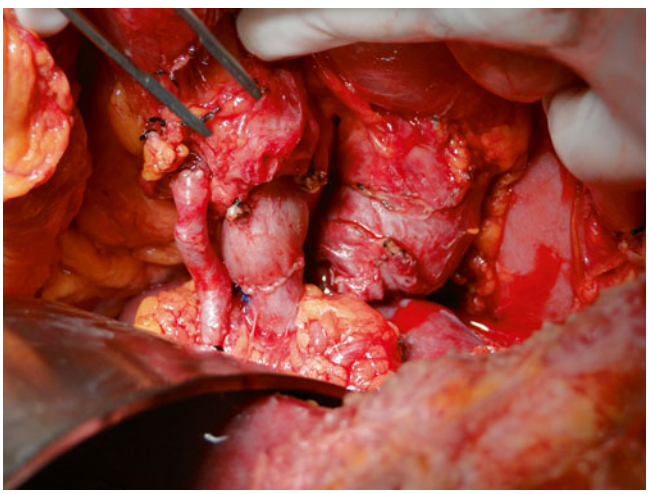

Fig. 36.23 Completed reconstruction of the hepatic artery, portal vein, and infrahepatic IVC

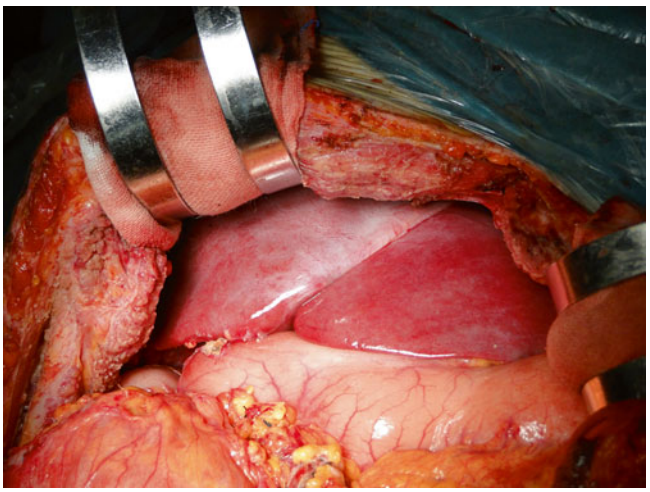

Fig. 36.24 OLT completed

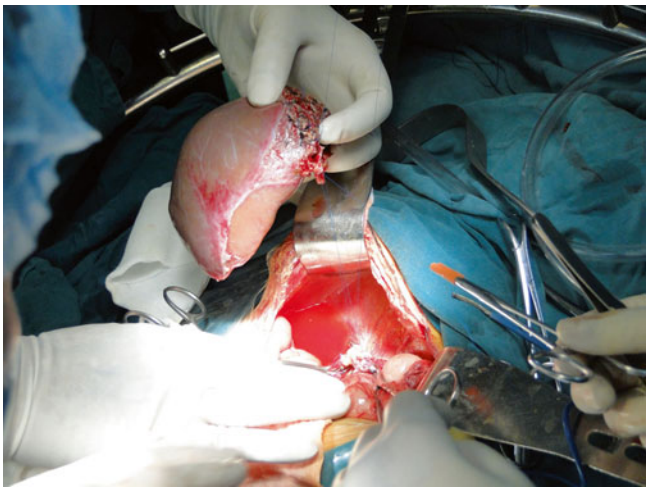

Fig. 36.25 Anastomosis of the posterior walls of donor's left hepatic vein and recipient's hepatic vein

36.4 Vascular Reconstruction in LDLT

Steps Organ shortages and high waitlist mortality remain challenging in liver transplantation. In 1969, Smith proposed LDLT, reduced-size liver transplantation (RLT), and split-liver transplantation (SLT). However, only LDLT and SLT technically mitigate organ shortage.

LDLT has been widely adopted worldwide since Strong et al. successfully performed the first LDLT in 1989. All types of LDLT have been attempted since an adult-to-adult left-lobe LDLT was successfully performed in 1994 and an adult-to-adult right-lobe LDLT was successfully performed by Fan ST et al. in Queen Mary Hospital of Hong Kong University.

1. Hepatic vein reconstruction:
   (i) Trimming of the ends of the recipient's hepatic veins: The manner in which the ends of the recipient's hepatic veins are trimmed can be determined by preoperative assessment of the donor's hepatic veins and intraoperative assessment of both the donor's and recipient's hepatic veins. When the left lateral segment or left hemiliver is used, the ends of the left hepatic vein and the middle hepatic vein are combined into a single opening for reconstruction. In a small proportion of patients, the end of the left hepatic vein or the RHV alone is used for anastomosis. End-to-side anastomosis is suitable in patients with small or short hepatic veins. More than two anastomoses of donor's hepatic veins to recipient's hepatic veins are performed in very few patients. Either the RHV or both the RHV and the middle hepatic vein are used for reconstruction in right hemiliver LDLT or extended right-lobe LDLT.
   (ii) Anastomosis of the hepatic veins: The graft is cooled in a collection of bags of ice and infused with 5 % albumin fluid through the portal vein catheter when it is placed in the liver bed. The hepatic veins of the donor and the recipient should be maintained on one axis to avert angulation and kinking. Reconstruction begins in the midline anteriorly and posteriorly with double-arm 4-0 Prolene sutures. Continuous suturing running bilaterally is then carried from the endothelial surface outward, ensuring the endothelium is tacked down. The contralateral wall of the hepatic vein should not be involved when the other side is being anastomosed. The vein is irrigated with heparinized saline to flush out any clot and air once the anastomosis is nearly completed. The suture is then tied. In right-lobe LDLT, if the inferior RHV diameter is ≥ 0.5 cm, it should be anastomosed to the opening of the right anterior wall of the retro-hepatic IVC (Figs. 36.25, 36.26, and 36.27).
2. Portal vein reconstruction:
   (i) The recipient's portal vein must be trimmed. An anastomosis can be performed after subtle modification when the size of the left branch or trunk of the recipient's portal vein at an appropriate length is comparable to that of the donor's portal vein. A major modification or interpositional graft would be required if vessels of comparable size or appropriate length are not present.
   (ii) The bifurcation of the recipient's portal vein can be modified into an oblique shape or bell-like shape for reconstruction when the recipient's portal vein has a normal wall, a proper length, branched ends, and a small caliber. The oblique angle should not be greater than 30° when the bifurcation is in an oblique shape.

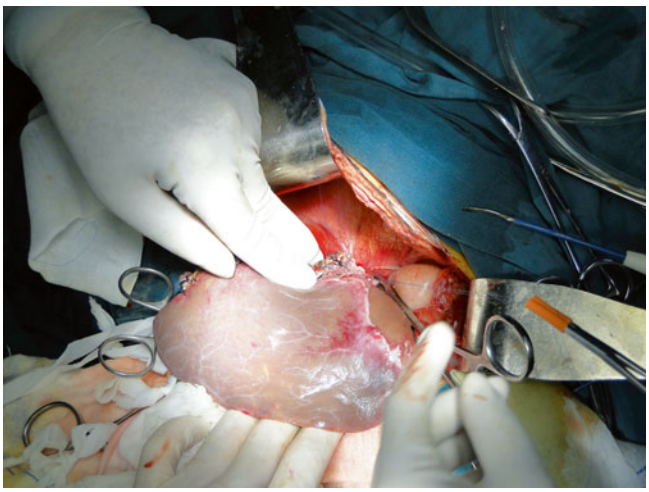

Fig. 36.26 Anastomosis of the anterior walls of donor's left hepatic vein and recipient's hepatic vein

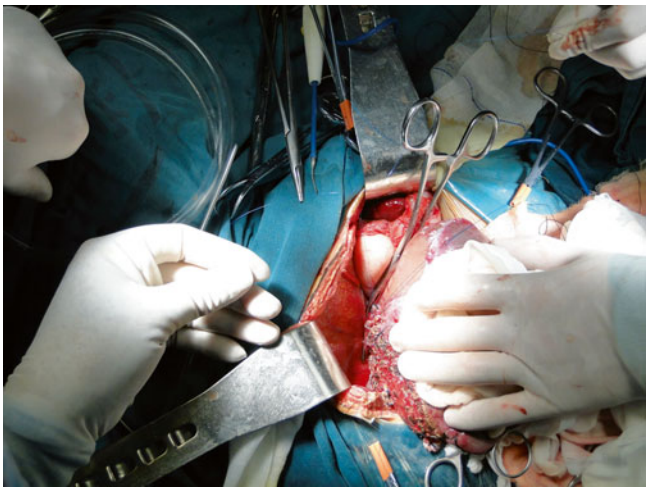

Fig. 36.27 Anastomosis of donor's left hepatic vein and recipient's hepatic vein completed

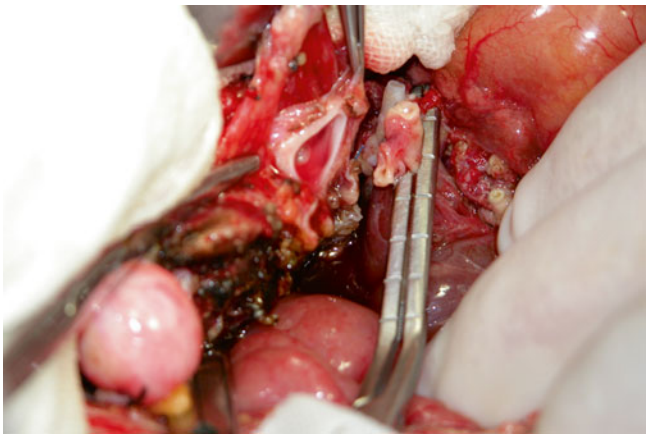

Fig. 36.28 Portal vein modification with matched size

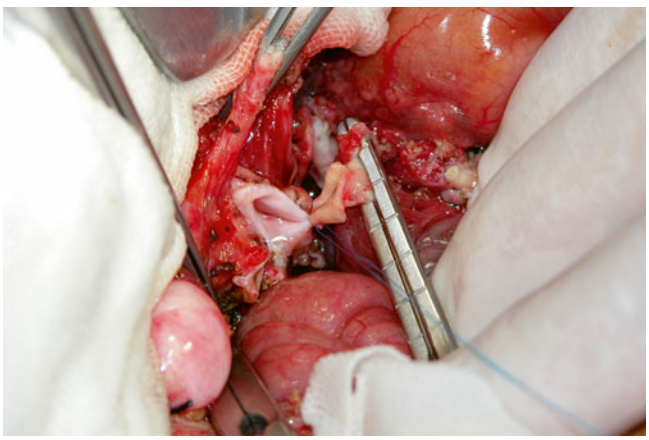

Fig. 36.29 Anastomosis of the anterior and posterior walls of the portal vein

(iii) If the recipient's portal vein is scarred, thickened, or narrow, the venous trunk is removed as far as possible to its origin. The reconstruction is carried out directly or using an interpositional graft sourced from the donor's ovarian vein or inferior mesenteric vein.

(iv) In infant recipients with normal portal veins whose size is small, the anterior walls of each branch are cut open longitudinally to form a large opening for reconstruction.

(v) For anastomosis of the portal vein, reconstruction starts when the portal vein is placed naturally. Reconstruction begins in the midline anteriorly and posteriorly with 6-0 Prolene sutures. Continuous suturing running bilaterally is then carried from the endothelial surface outward, ensuring the endothelium is tacked down. The contralateral wall of the portal vein should not be involved when the other side is being anastomosed. The vein is irrigated with heparinized saline to flush out any clot and air once the anastomosis is nearly completed. The suture is then tied. Anastomotic leaks, kinking, or stenosis should be noticed.

Hepatic veins and portal vein are unrestrained after the reconstruction of the portal vein is completed. Doppler ultrasound is used to examine the blood flow [19, 20] (Figs. 36.28, 36.29, 36.30, and 36.31).

3. Reconstruction of hepatic artery:

(i) The recipient's hepatic artery is trimmed. In LDLT, satisfactory reconstruction of the hepatic arteries requires a microsurgical technique because the donor's hepatic arteries are small and numerous. Modification before reconstruction is necessary, and the procedure is similar to that of hepatic veins or the

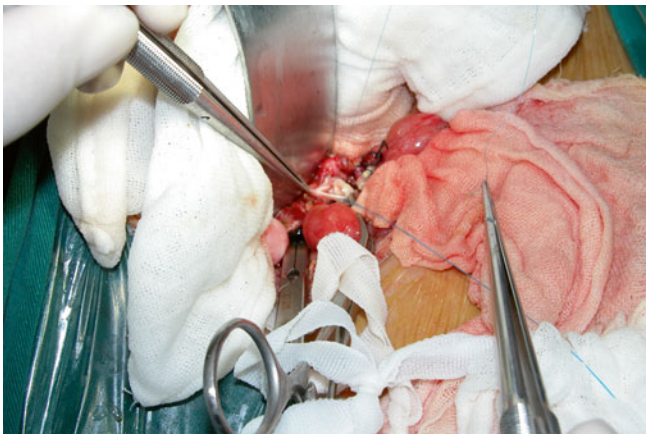

Fig. 36.30 Anastomosis of the lateral walls of the portal vein

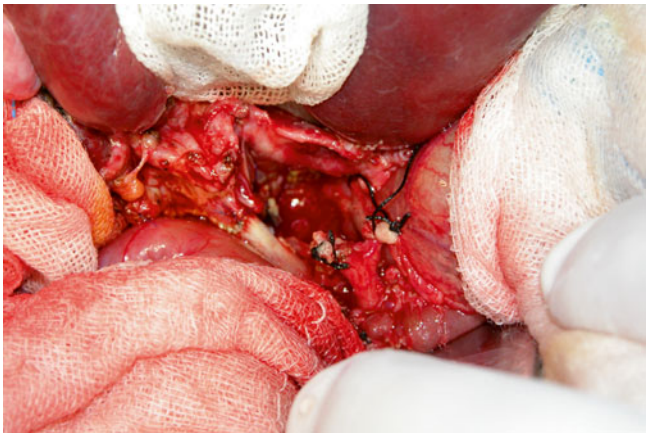

Fig. 36.31 Completed reconstruction of the portal vein

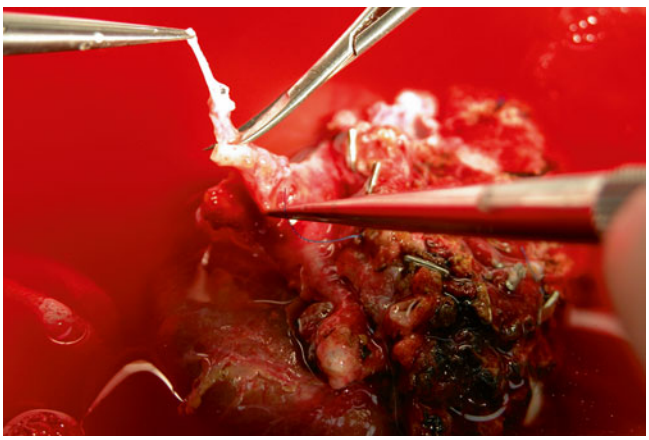

Fig. 36.32 Repair of the donor's hepatic artery

portal vein, such that the bifurcation is trimmed to be bell-like or have a 45° oblique shape for a larger opening (Figs. 36.32, 36.33, 36.36, and 36.35).

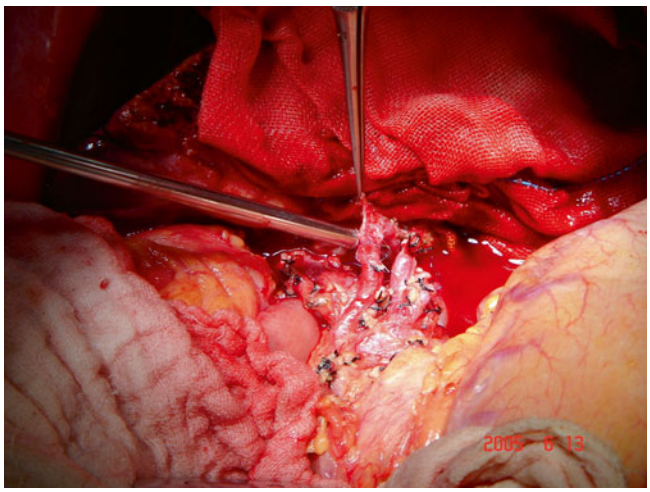

Fig. 36.33 Arterial end-to-end reconstruction

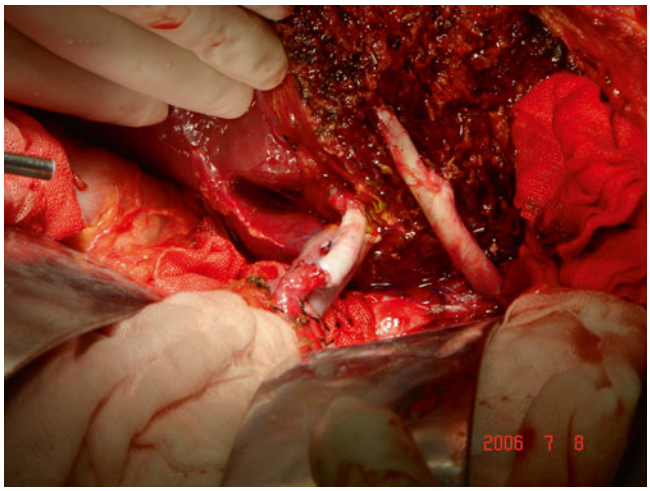

Fig. 36.34 Interposition using autologous great saphenous vein

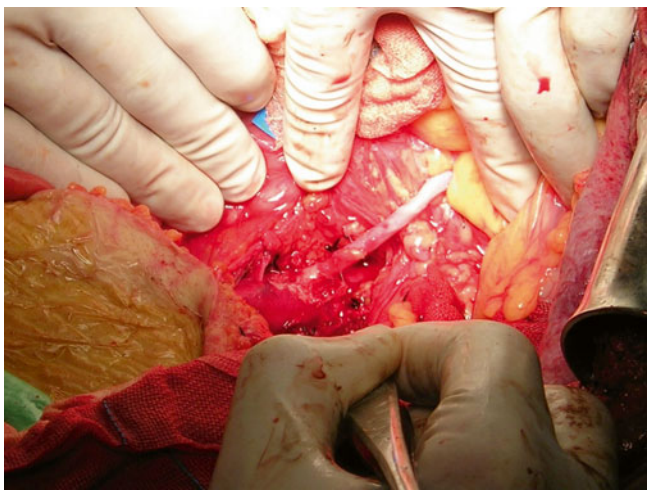

Fig. 36.35 The hepatic artery communicating with the aorta below the renal artery using autologous great saphenous vein

(ii) Hepatic arterial anastomosis: The right branch of the recipient's hepatic artery is commonly used for end-to-end reconstruction. The use of microsurgical techniques reduces the incidence of vascular complications. In adult-to-adult right-lobe LDLT, the donor's right hepatic artery is usually anastomosed to the recipient's right hepatic artery, left hepatic artery, or bifurcation or the hepatic artery proper. An anastomotic flush of heparinized saline can prevent thrombosis. Continuous suturing is employed in hepatic arterial reconstruction. Suturing is performed with 3.5-fold amplification for vascular diameters of 2–2.5 mm using 8-0 Prolene and five- to tenfold amplification for vascular diameters of ≤ 2 mm using 9-0 Prolene. Conventional vascular reconstruction involves a vessel flip to reconstruct the posterior wall, where the intima tends to be injured. In LDLT, the hepatic artery is small, and the procedure should be performed deep in the abdomen. This procedure is made more difficult by the movement of respiration. The first step begins at the deepest point on the posterior wall using a microscope. A continuous suture runs from the posterior wall to the anterior wall with knots made externally. The suture is tracted outward to guarantee intimal involution. Anastomotic tension or kinking should be avoided. Additional suturing is required if an anastomotic leak occurs when the clamp on the recipient's hepatic artery is released. The clamp on the donor's hepatic artery is subsequently released when there is no anastomotic leak. Successful arterial reconstruction is indicated by redness of the liver, good beating pulse of the vessel, and Doppler ultrasound results [19–21] (Figs. 36.36, 36.37, and 36.38).

Key Points

1. Hepatic veins: An end-to-end anastomosis using hepatic veins with appropriate sizes and lengths is preferred. Anterior and posterior walls are everted upon reconstruction to maintain the smoothness of the intima. Venous clamping should be avoided during repair and anastomosis. The topical use of heparin on the venous ends is required to prevent thrombosis.
2. Portal vein: End-to-end anastomosis using a portal vein with an appropriate size and length is preferred. The anterior and posterior walls are everted upon reconstruction to maintain the smoothness of the intima. Venous clamping should be avoided during repair and anastomosis. The topical use of heparin on the venous ends is required to prevent thrombosis. Attention is required to prevent a hematoma around the anastomosis.
3. Hepatic artery: Direct clamping and overstretch of the hepatic artery can cause intimal injury and should be avoided. An appropriate length, size, and wall thickness

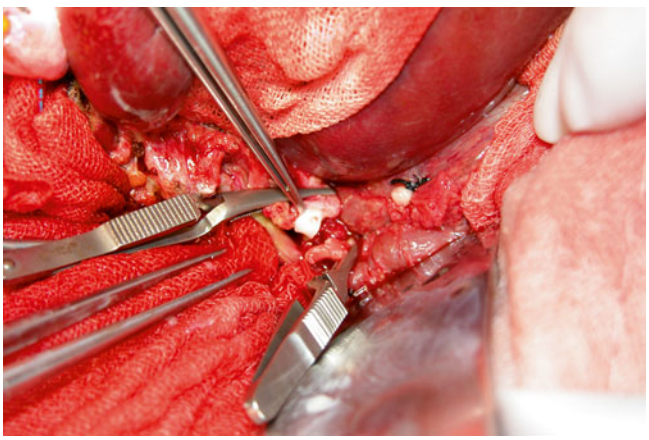

Fig. 36.37 Modification of arterial openings

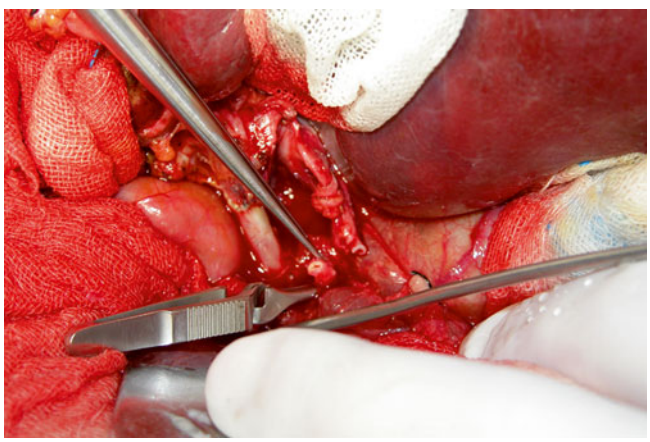

Fig. 36.36 Modification of the donor's and recipient's hepatic arteries

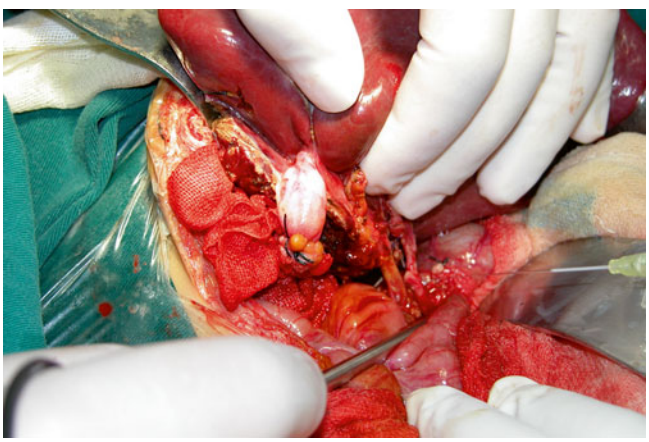

Fig. 36.38 Completed arterial reconstruction

of hepatic arteries can avert over-stripping of arterial wall. Perfect involution and microscopic technique are important to prevent arterial wall inversion and anastomotic torsion. Intra-abdominal hematomas can be prevented by thorough hemostasis. The recipient's hepatic artery should be cut off as close to the liver as possible, and arterial compress or stretch should be avoided. The arterial ends should be clamped using bulldog clamps to avoid sandwich formation or thrombosis when the liver is removed. The recipient's hepatic artery should be anastomosed to a comparable donor's hepatic artery. Blood ejection, thrombosis, or stenosis should be checked for in the recipient's hepatic arteries before anastomosis; if absent, the ends of hepatic arteries are clamped and rinsed with heparinized saline. The vascular ends can be modified to form comparable caliber openings. The bifurcation of the recipient's hepatic artery can be trimmed into a patch shape, underwear shape, or an oblique surface. Modification of the aberrant donor's hepatic arteries and choosing the anastomotic position are priorities during the arterial reconstruction. The anastomotic position should be decided using the arterial size to prevent angulation or an overly long artery. The accessory hepatic artery of the donor, if present, should be reconstructed at the back table.

Postoperative Management The difficulty and technical requirements of vascular reconstruction in LDLT are much greater than for OLT. Portal thrombosis can deteriorate graft function. Recipients with portal thrombosis commonly present with ascites, indicating a reduced blood supply in the portal system and portal hypertension. Increasing temperature, elevated white blood cell count, and discomfort are signs of hepatic arterial thrombosis, which can cause abrupt graft function deterioration or ischemic biliary leak. Subacute or chronic hepatic insufficiency can be secondary to hepatic venous stenosis or right heart failure, which can be diagnosed by Doppler ultrasound. Invasive angiography and thrombolysis should be considered when a thrombosis is suspected but the diagnosis cannot be confirmed by Doppler. The vascular reconstruction is more challenging in LDLT than for OLT; as a result, postoperative anticoagulation appears to be paramount. Posttransplant anticoagulation commonly involves heparin, low molecular weight heparin, dextran, and PGE1, which induce a low coagulation status (PT or APTT, 1–1.5-fold longer; INR, 1.5–2) and an HCT below 35 %. Low blood viscosity helps prevent vascular thrombosis, especially arterial anastomotic thrombosis, subsequently avoiding disastrous outcomes. The incidence of hepatic arterial thrombosis is as high as 5–21 % in LDLT. The hepatic graft can become necrotic soon after hepatic arterial thrombosis occurs, and re-transplantation is the only curative treatment. The duration of anticoagulation treatment after transplantation should be at least 2 weeks, at which point coagulation and the blood supply to the graft should be closely monitored. Warfarin is suggested in patients undergoing LT for Budd-Chiari syndrome because these patients are susceptible to recurrent thrombosis after transplantation [17, 22].

Major Surgical Complications

1. Hepatic artery thrombosis (HAT): HAT is one of the most severe complications after liver transplantation and can lead abruptly to graft necrosis. The incidence of HAT after deceased-donor liver transplantation (DDLT) is 1.6 %. Olthoff et al. reported that the posttransplant 3-month incidence of HAT was 6 % ($n=22$) among 385 cases of adult-to-adult LDLT at nine transplantation centers in the USA. The reasons for HAT are multifactorial and include hemodynamic changes in the graft, ABO incompatibility, preoperative coagulation status, and postoperative coagulation treatment. However, surgical technique remains the most important factor. The manifestation of HAT varies, including reduced bile outflow, an abrupt elevation of serum aminotransferase, changes in bile characteristics, continuously prolonged PT, or elevated bilirubin level. When HAT occurs early after liver transplantation, patients can manifest abrupt abdominal pain focused on the hepatic region, a high temperature, ascites, abnormal liver function, bile leaking, liver abscess, and sepsis. The clinical manifestations are usually atypical when HAT occurs late after liver transplant because arterial collaterals form. Patients with HAT commonly show one of the following symptoms. (1) Chronic graft necrosis and sepsis. Decompensated liver function can occur soon after sepsis, fever, hypotension, and coagulation disorder. The laboratory test results suggest that liver enzyme levels and blood cell counts increase, PT prolongs, and blood culture is positive. The radiographic result indicates hepatic gas gangrene. (2) Recurrent liver abscess and bacteremia. Liver necrosis and sepsis can occur quickly in patients with liver abscess and can be observed on ultrasound or CT scan. (3) Biliary complications. Cholangitis, bile duct stenosis, and bile leakage may occur. Ischemic bile duct injury and bile leak are usually observed once HAT occurs because the hepatic artery is the only blood supply to the graft biliary tree. (4) Few asymptomatic patients are diagnosed as HAT because liver function is usually normal or the enzyme level increases slightly. Although hepatic angiography is accepted as the gold standard in diagnosing HAT, Doppler ultrasound has been employed to monitor hepatic artery in many transplantation centers in recent years. Furthermore, a helix CT scan is helpful in the diagnosis. The hepatic artery can be evaluated using 3-D remodeling

of hepatic vessels. In symptomatic or asymptomatic recipients with HAT early after liver transplantation, emergent rebuilding of the hepatic artery is recommended. Successful revascularization depends on early detection. Thrombectomy is considered in patients with acute HAT. If this procedure is not successful, re-transplantation is required. In patients with HAT whose graft necrosis is not severe, HAT can be treated by intraluminal injection of thrombolytics using an interventional procedure [14, 15, 17, 18, 20, 22, 23].

2. Portal venous thrombosis and stenosis: Portal venous thrombosis is not as common as hepatic arterial thrombosis after liver transplantation. The incidence of portal venous stenosis is generally higher in patients undergoing LDLT than in those receiving OLT because the length of the portal vein harvested in LDLT is limited. Olthoff et al. indicated that the incidence of the portal venous thrombosis is 2 % within 3 months after liver transplantation among 385 adult-to-adult LDLT cases in nine transplantation centers in the USA. Surgical technique plays a key role in portal venous thrombosis, which can be secondary to acute rejection, especially in pediatric recipients. The clinical manifestation in patients with portal venous thrombosis is time dependent. Severely damaged liver function, prolonged PT, portal hypertension, variceal bleeding, severe ascites, and intestinal edema may be present in patients with portal venous thrombosis early after liver transplantation. The symptoms are minor in patients with sufficient collateral circulation. Variceal bleeding, ascites, or hypersplenism is present in patients with portal venous thrombosis later after liver transplantation, when the liver function is normal. Portal venous thrombosis can be rapidly diagnosed by Doppler ultrasound, which can reveal diminished or dramatically reduced blood flow in the portal vein, massive hepatic necrosis, and hepatic abscess formation. In suspected cases, the diagnosis can be confirmed by MRI or angiography, which shows portal venous blockage or stenosis.

   The hepatic graft can be salvaged by thrombectomy and anastomotic repair when portal venous thrombosis is diagnosed early after liver transplantation. In recipients with acute portal venous thrombosis who present with hepatic failure and portal hypertension, a timely thrombectomy can recover the hepatic blood supply. Balloon dilatation or thrombolysis through a portal catheter is used to treat patients with chronic portal thrombosis or portal venous stenosis, respectively. Re-transplantation is required when chronic portal thrombosis or portal venous stenosis is irreversible or continuously aggravating. In patients with portal venous thrombosis occurring late after liver transplantation, only portal hypertension needs to be treated, and shunting or devascularization is used to palliate esophageal-gastric varicose. Generalized collaterals establish in patients with portal venous thrombosis late after liver transplantation. Treatment is commonly not required, and the long-term survival rate is satisfactory [17, 24, 25].

3. Hepatic venous stenosis: The incidence of hepatic venous complication is less than 1 % after liver transplantation. If present, the outcomes are disastrous, and most patients rapidly develop hepatic necrosis and liver failure. Hepatic venous complications include hepatic venous thrombosis and stenosis. Hepatic venous stenosis is rare in patients undergoing OLT, while it is occasionally reported in those undergoing SLT and LDLT. Hepatic venous stenosis after LDLT can lead to outflow blockage, ascites, abnormal liver function, or even liver failure. If the blockage persists, cirrhosis and symptoms associated with portal hypertension become evident. In cases of RLT using the left lateral lobe, acute hepatic venous thrombosis or stenosis can lead to severe graft disorder because the left hepatic vein is the only outflow for the graft. Doppler ultrasound is helpful in making the diagnosis, and hepatic venous stenosis is indicated by a flattened waveform and slow velocity (<6 cm/s) of the hepatic vein and reduced blood flow in the portal vein. Arterial flow imaging indicates high blood flow in the hepatic artery. Percutaneous hepatic venography is used to diagnose hepatic venous stenosis, although it is invasive. Necrosis of a hepatic central lobule can be found on biopsy. Measures to prevent hepatic venous stenosis are as follows: The falciform ligament and coronary ligament should be suspended from the diaphragm to avoid liver shifting when the transplantation is complete; patients should maintain a supine position and avoid turning over and ambulation within 1 week after operation; kinking, angulation, and inversion should be averted on anastomosis; and hematomas around the anastomosis can be avoided by careful hemostasis. Prompt operation is needed as soon as hepatic venous blockage is confirmed. Re-transplantation should be considered in patients with irreversible liver damage. Balloon dilatation is preferred in patients with hepatic venous stenosis. If this intervention fails, an operation should be considered. Re-transplantation is required in patients with severe hepatic disorder [25, 26].

Expert Comments

1. Reconstruction technique is strongly associated with portal venous thrombosis and stenosis. Unskilled hands are the leading cause of portal vein complication, followed by portal vein malformation and small-sized portal veins. These factors result in anastomotic angulation, torsion, stenosis, and vascular inversion. The risk of postoperative portal vein thrombosis can increase when preoperative portal vein thrombosis or portal phlebitis is present.

2. Arterial reconstruction in LDLT: End-to-end anastomosis under a microscope is helpful in reducing postoperative arterial complications. The right hepatic artery of the donor is usually anastomosed to the right hepatic artery, left hepatic artery, or bifurcation or the hepatic artery proper of the recipient in adult-to-adult right-lobe LDLT. 3-D helix CTA, MRA, or selective celiac angiography is used to evaluate blood distribution, vascular anatomy, and variation in both the donor's and recipient's hepatic arteries before liver transplantation. Branches from the hepatic artery require protection during liver harvest. The donor's right hepatic artery should be harvested at its origin. The end of the cystic artery should be preserved to protect the arterial intima, and the graft blood supply should be assessed after anastomosis. A continuous suture is employed in hepatic arterial reconstruction, with suturing performed with 3.5-fold amplification using 8-0 Prolene for vascular diameters of 2–2.5 mm and five- to tenfold amplification using 9-0 Prolene for vascular diameters of ≤ 2 mm. Conventional vascular reconstruction involves a vessel flip to reconstruct the posterior wall, where the intima tends to be injured. In LDLT, the hepatic artery is small, and the procedure should be performed deep in the abdomen. This procedure is made more difficult by the movement of respiration. The first step begins at the deepest point on the posterior wall, using a microscope. A continuous suture runs from the posterior wall to the anterior wall, with knots made outside the vessel. The suture is distracted outward to guarantee intimal involution. Vascular tension or kinking should be avoided upon anastomosis. Additional suturing is required when an anastomotic leak occurs when the clamp on the recipient's hepatic artery is released. The clamp on the donor's hepatic artery is released when there is no anastomotic leak. Successful arterial reconstruction is indicated by redness of the liver, a good beating pulse of the vessel, and the results of Doppler ultrasound. Left arterial reconstruction in adult-to-adult left-lobe LDLT is similar to that in right-lobe LDLT; however, accessory left arterial reconstruction is commonly required in left-lobe LDLT. In either right- or left-lobe adult LDLT, an interpositional graft using an autologous great saphenous vein is required in cases when the donor's hepatic artery is as short as <1 cm. In cases where arterial sandwich, adventitial hematoma, or vascular obliteration is present in the recipient's hepatic arteries, an interpositional graft using an autologous great saphenous vein or cryopreserved iliac artery is anastomosed to the aorta below the renal artery. In adult dual-donor liver transplantation, the left and right hepatic arteries of the donor are connected to the corresponding hepatic arteries of the recipient. If hepatic arteries are not sufficiently long, interpositional reconstruction using autologous great saphenous vein is used for end-to-end anastomosis, or the donor's hepatic arteries are connected to the aorta below the renal artery using the autologous great saphenous vein or a cryopreserved iliac artery as the bridging graft.

   The common factors for hepatic arterial thrombosis after liver transplantation that are relevant to surgical technique include the following: (1) hepatic arterial spasm, (2) injury of the vascular intima, (3) anastomotic inversion, (4) pressure from peri-anastomotic hematoma, (5) arterial kinking, and (6) small-sized arteries. The use of microsurgical technique in arterial anastomosis is helpful in reducing the risk of hepatic arterial thrombosis and improving recipient's survival.
3. Surgical technique-related factors, such as graft shifting or torsion due to unstable fixation, are the main causes of hepatic venous stenosis after LDLT. In severe cases, anastomotic stenosis due to poor anastomosis or pressure from peri-anastomotic hematoma can lead to hepatic ischemia or even necrosis. When anastomotic stenosis persists, Budd-Chiari syndrome can develop after liver transplantation.

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Looking Forward to the Future

37

Lunan Yan

Over the years, I have always believed that surgical techniques are procedures that emphasize tradition but also show great novelty. The vast majority of surgical procedures for abdominal surgery were established over a hundred years ago in the 1880s. Examples include the Whipple procedure for pancreaticoduodenectomy, the Billroth I and II procedures for gastrectomy, the Lembert (Cushing, Halsted) and Connell suture for intestinal anastomosis, and the Miles and Dexin operations for colorectal cancer. These surgical procedures are still in use today without any changes, and no improvements have achieved better results than the original design. Hence, I believe that tradition is the core of surgical procedures. However, surgeons have an excellent ability to accept innovative techniques and new methods. Endoscopy, laparoscopy, and even robotics are all surgical concepts that have been rapidly accepted and used by surgeons who have promoted the development of the surgeries. Therefore, surgeons are the most innovative physicians.

The goals of the development of surgical techniques are to decrease the complication rates and reduce trauma, ultimately allowing the use of drugs and various measures to replace and eliminate surgery. The prospects for future development of liver surgical techniques may include the following aspects:

1. Liver cross-section bleeding. Bleeding during hepatectomy was a serious issue two to three decades ago. In recent years, this problem has been basically addressed by the development of techniques such as hepatic blood flow occlusion and hepatectomy. The blood transfusion rate in liver surgery has fallen below 20 %. This problem will be completely addressed by medical device innovation and drug development in the future.
2. Remnant liver failure. In this case, the priority lies in hepatectomies in patients with concomitant cirrhosis. Evaluation of liver resection volume and remnant liver volume by CT has greatly reduced the incidence of postoperative liver failure. B-mode ultrasound, CT, MRI, and other noninvasive methods have been employed in recent years, and these methods can accurately evaluate the degree of liver cirrhosis and thereby properly estimate the reasonable remnant liver volume, further reducing the incidence of liver failure.
3. Use of associating liver partition and portal vein ligation for staged hepatectomy (ALPPS). Currently, ALPPS is often used for cirrhosis-free metastatic cancer as well as gallbladder and bile duct cancers. Its use for liver cancer with concomitant cirrhosis is gradually becoming more common in mainland China. Further use will help to determine whether cirrhotic liver cancer can regrow and to evaluate the speed and degree of its regrowth. Based on such work, new guidelines can be developed to benefit more patients with large liver cancer through ALPPS.
4. 3D CT imaging. 3D imaging has gradually matured, allowing for more accurate assessment of the extent of liver resection and revascularization. Moreover, 3D printing has begun to show clinical value. The further development of 3D CT imaging will provide more beneficial effects for hepatectomy performance.
5. Development of minimally invasive techniques. Technical difficulties remain when performing a laparoscopic hepatectomy for liver resection of certain segments (e.g., segments VII, VIII, and I) that require further improvement of the devices and instruments. Meanwhile, the robotic-assisted hepatectomy technique is in need of further accumulated experience. Undoubtedly, the development of minimally invasive

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techniques will advance hepatectomy surgery so that it will benefit more patients.

6. Xenotransplantation and cloning of the liver are expected research outcomes that will completely address the worldwide problem of donor liver shortages.

While the world is advancing and surgical techniques are being developed, the young, developing field of liver surgery will serve as a bellwether of abdominal surgery and lead to continuous surgical innovation and development. We look forward to the future!