

# Liver, Gallbladder and Bile Ducts

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## 8.1 Anatomy and Physiology of the Liver

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### 8.1.1 Definitions

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- Liver, gallbladder and bile duct anatomy = variable
- Anatomy of the portal vein branches, the hepatic veins and the hepatic artery = important in liver surgery
- Liver function and liver regeneration = central concepts in understanding the techniques of liver surgery

### 8.1.2 Macroscopic and Microscopic Anatomy

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#### Macroscopic Anatomy

##### Ligaments and Ligamentous Attachments

- Lig. coronarium hepatis (Lig. triangulare dextrum + Lig. triangulare sinistrum)/coronary ligament (left and right triangle ligament)
- Lig. falciforme hepatis /falciform ligament (separates segments 4–8 from segments 2 + 3)
- Lig. teres hepatis (obliterated V. umbilicalis)/teres hepatic ligament
- Lig. venosum hepatis (obliterated Ductus venosus)/venous hepatic ligament
- Lig. hepatogastricum and Lig. hepatoduodenale (part of the omentum minus)/gastrocolic and hepatoduodenal ligament

##### Functional Subdivision

- In segments (according to Couinaud)
- Oriented to vascular supply
- Subdivision:
  - Right liver lobe (segments 5–8)
  - Left liver lobe (segments 1–4)
  - Caudate lobe (segment 1) + Lobus quadratus
  - Cava-gallbladder line = dividing line between right/left liver lobe

## Microscopic Anatomy

- Radial blood flow from portal vein and arterial blood through hepatic sinusoids to central vein
- Intercellular transport of bile into bile ducts
- Glisson's triad = interlobular branches of each portal vein, artery and bile duct

### 8.1.3 Tasks of the Liver and Functional Liver Volume

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#### Tasks of the Liver

- Liver = central metabolic organ with detoxification and synthesis functions

#### Blood Formation Site (Embryonic Period)

#### Protein Biosynthesis and Degradation

- Under hormonal control
- In particular, formation coagulation factors (under the influence of vitamin K)
- Protein degradation with formation of urea (excretion via kidney)

#### Cleavage of Carbohydrates and Glycogen Storage

- Glycogen storage
- Under the influence of: adrenaline, glucagon

#### Central Organ of Lipometabolism

- Formation and elimination of lipoproteins

#### Special Metabolic Services

- Bilirubin transport
- Biosynthesis of bile acids

#### Detoxification Function (Through Biotransformation)

- Protection of the organism from foreign substances and drugs
- In particular by means of cytochrome P450

## Central Organ of the Trace Element Metabolism

- Trace elements: iron, copper, zinc, etc.
- Numerous vitamins: especially vitamin A

## Immunological Function

- Phagocytosis of cellular elements (outdated erythrocytes), bacteria
- Elimination of immune complexes and endotoxins

## Functional Liver Volume After Resection

### Functional Liver Volume After Resection (FLR)

- Definition: Proportion (in %) of liver volume that must exist after resection in order to maintain liver function
- Crucial for predicting liver function after liver resection
- Liver disease (Nonalcoholic steatohepatitis-NASH) or pre-damage of the liver (chemotherapy associated steatohepatitis-CASH) = influence on functional liver volume after resection

### FLR Targets

- With normal liver function: FLR  $\geq 20\%$
- After chemotherapy: FLR  $\geq 30\%$
- In cirrhosis: FLR  $\geq 40\%$

### Measurement of FLR

- Mostly by 3D-CT volumetry: direct measurement of total liver volume (TLV)
- Calculation of the standardized FLR (sFLR): taking into account the portion to be resected

## 8.1.4 Location

### Position Projection

- Hepatic superior border: medioclavicular = fourth intercostal space (ICS); medioaxillary = sixth ICR; paravertebral = eighth ICS
- Liver inferior border: medioclavicular = eighth rib; medioaxillary = tenth rib; paravertebral = tenth ICS

- Topographical relationship: to the inferior pleural space + base of the lung
- Variable with inspiration/expiration

## 8.1.5 Measured Values

### Weight

- General liver = 2.5% of body weight
- Adult man = approx. 1600 g
- Adult woman = approx. 1400 g
- Volume and weight increased during digestion (blood inflow approx. 500 g)

### Linear Readings

- Cross diameter (right-left) = 28 cm (20–40 cm)
- Sagittal diameter (ventral-dorsal) = 8 cm (5–12 cm)
- Height (cranial-caudal) = 10 cm (up to 27 cm)

## 8.1.6 Blood Supply and Drainage

### Blood Supply and Drainage of the Liver

#### Arterial Inflow = Hepatic Artery

- Common hepatic artery: direct outlet from truncus coeliacus
- Hepatic artery proper: after delivery A. gastroduodenalis and A. gastrica dextra
- Division into right and left hepatic artery
- Cystic artery: usually from right hepatic artery
- Numerous position variations

Numerous variants of arterial inflow

- Aberrant outflow from superior mesenteric artery possible (complete or right hepatic artery)
- Left hepatic artery partly from left gastric artery or from coeliac trunc directly
- Variants with accessory vessels e.g. separate branch to supply segment 4 from the hepatica propria artery

#### Portal Venous Inflow = portal vein

- Liver side of the confluence of splenic vein + superior mesenteric vein, if necessary inferior mesenteric vein (position variants)

- Collaterals: V. coronarian vein + cystic vein, as well as branches to the pancreatic head
- Division pattern in liver hilum:
  - Right portal venous branch (segments 5–8); subdivision into:
    - Anterior pedicle (segments 5 + 8 + parts of 4 if necessary) +
    - Posterior pedicle (segments 6 + 7)
  - Left portal venous branch (segments 2–4)
  - Rare trifurcation

### Venous Outflow

- Hepatic veins:
  - Right hepatic vein (segments 6 + 7)
  - Middle hepatic vein (segments 4, 5 + 8)
  - Left hepatic vein (segments 2 + 3)
  - Norm variant accessory right inferior hepatic vein (segments 6 + 7)
- The hepatic veins open directly subdiaphragmally into the inferior vena cava

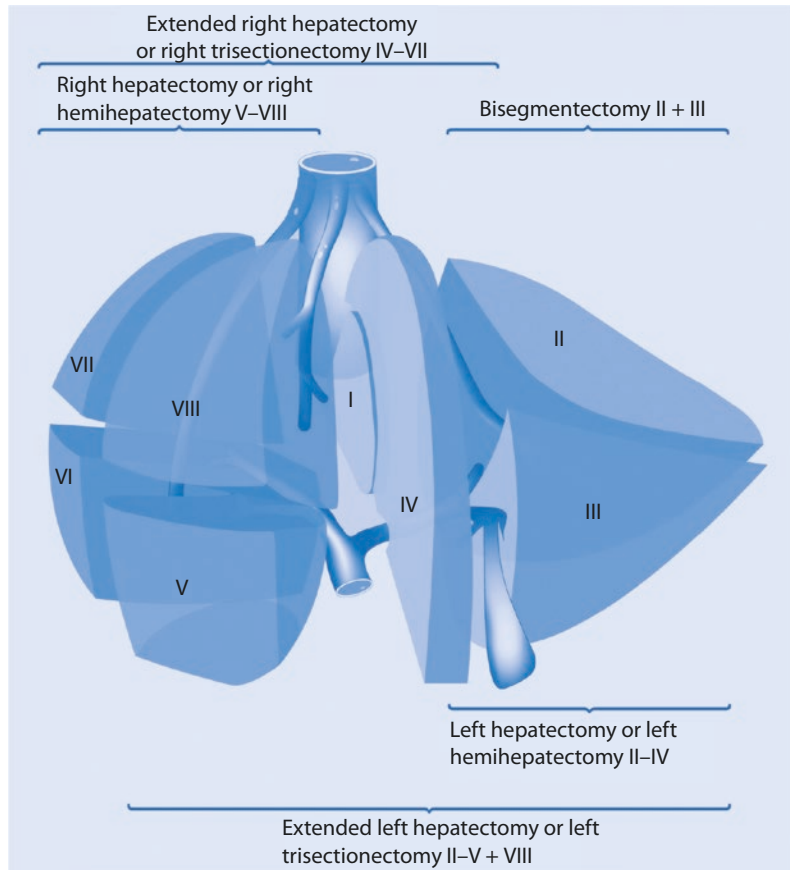
### Different variants

- Common orifice of middle + left hepatic vein
- Direct orifice of segmental veins into inferior vena cava (segment 1)
- Sonographically distinguishable from portal venous branches by the absence of a connective tissue sheath
- Blood supply to the liver: 25% hepatic artery, 75% portal vein
- Proportion of oxygenation of liver blood: 40–50% hepatic artery, 60% portal vein
- Autoregulation: low portal venous flow leads to increased arterial flow - hepatic arterial buffer response

### 8.1.7 Terminology of Liver Resections (■ Fig. 8.1)

- Consensus Terminology: International Conference (Belghiti et al. 2000)

■ **Fig. 8.1** Functional subdivision of the liver and terminology of liver resections. (Mod. according to Scott-Conner 2002)



## Anatomical (= Typical) Liver Resections

- Right hemihepatectomy = right hepatectomy: resection of segments V–VIII
- Left hemihepatectomy = left hepatectomy: resection of segments II–IV
- Left-lateral sectorectomy = Bisegmentectomy II + III: Resection of segments II–III
- Extended right hepatectomy = right trisectorectomy: resection of segments IV–VIII
- Extended left hepatectomy = left trisectorectomy: resection of segments II–IV + V + VIII

## Atypical Liver Resections

- Resections outside the anatomical landmarks (regardless of the resected liver volume)

## 8.2 Diseases of the Liver

### 8.2.1 Benign Diseases

#### Key Points

- Adenomas are precancerous and need to be resected depending on both size and histology
- Hemangiomas and FNH (focal nodular hyperplasia) are resected if symptomatic

## Hepatocellular Adenomas

### Definition and Subtypes

#### Definition

- Clonal non-encapsulated neoplasms
- Mostly from highly differentiated hepatocellular cells

#### Subtypes

- HNF-1alpha-inactivated adenomas = 40% of all adenomas; association with MODY type 3
- Inflammatory adenomas = 50% of all adenomas, increased risk of bleeding due to ectasia of sinusoidal structures
- $\beta$ -Catenin-mutated adenomas, high risk of malignant transformation (approx. 40%)

- Unclassified adenomas = approx. 10% of all adenomas
- Adenomatosis  $\geq 10$  adenomas

## Epidemiology and Risk Factors

### Epidemiology

- Incidence = 3–4/100.000 in Europe

### Risk Factors

- Taking oral contraceptives
- Anabolic Abuse
- Glycogen storage disorders, galactosemia
- perfusion disturbances of the liver

## Symptoms and Complications

- Often diagnosed incidentally in asymptomatic patients
- Possible complications:
  - Spontaneous rupture and hemorrhage
  - Malignant transformation into HCC (hepatocellular carcinoma), risk 8–13% in  $\beta$ -Catenin-mutated adenomas

## Diagnosis

- Sonography
- MRI
- Biopsy: indicated for all adenomas

## Surgery Indication

- $\beta$ -catenin mutated adenomas
- Adenomas  $> 5$  cm
- Adenomas in men—differentiation from HCC often difficult
- Adenomas with risk of rupture (in case of acute bleeding first embolization, surgery two-sided)
- Size progression after discontinuation of oral contraceptives

## Focal Nodular Hyperplasia (FNH)

### Definition

- Tumor with hepatocellular origin, polyclonal
- Absence of central and portal veins (= absence of classical hepatic architecture)
- Macroscopic: typical picture with central scar and ochre parenchyma
- Risk factor: taking estrogen-containing preparations

## Epidemiology

- Second most common benign liver tumor

## Diagnosis

- Sonography
- MRI
- Biopsy: not indicated with clear imaging

## Complications

- Progressive growth
- Rupture
- Portal hypertension
- Bleeding: rare
- Necrosis: rare
- Malignant degeneration: not described

## Therapy

### Conservative Approach: Generally

### Surgical Therapy

- Indications:
  - Symptomatic patients
  - Large displacing-growing FNH
  - Cholestasis
  - Vascular compression

## Hemangiomas

### Definition

- haemangioma of mesenchymal origin

### Epidemiology

- Most frequent benign lesions = 0.5–7% of all patients
- Women three times more often affected than men

## Clinical Presentation and Complications

### Clinical Presentation

- Mostly incidental findings and often asymptomatic

### Complications

- No malignant transformation risk
- Kasabach-Merritt syndrome:

- Hemangioma bleeding, thrombocytopenia and consumption coagulopathy
- Rare complication of generalized giant hemangiomas
- Mortality risk in case of hemorrhage 30–40%

## Diagnosis

- Sonography (also contrast medium supported ultrasound)
- CT
- Biopsy: not indicated

## Therapy

### Conservative Therapy

- Whenever there is no indication for surgery

### Surgical Therapy

- Surgery indication:
  - Symptomatic patients
  - Lesion >5 cm
  - Significant hemorrhage, location near the capsule with risk of rupture
  - Acute bleeding without the possibility of control by interventional radiology

## Echinococcosis

### Definition

- Tapeworm zoonosis
- Human = intermediate host
- Tapeworm species:
  - Echinococcus granulosus = Echinococcus cysticus = dog tapeworm
  - Echinococcus multilocularis = Echinococcus alveolaris = fox tapeworm

### Clinical Presentation

#### E. granulosus (Cysticus, Unilocularis), Dog Tapeworm

- Displacing growth
- Infestation of lung and pericardium also possible
- Pericyst partly calcified as membrane around cystic hydatid
- Often asymptomatic
- Due to size non-specific upper abdominal complaints or infection symptoms

## E. multilocularis (alveolaris), Fox Tapeworm

- Infiltrative (tumor-like) growth with formation of small cysts
- Recognised occupational disease in hunters and foresters
- Often asymptomatic
- Due to size non-specific upper abdominal complaints or infection symptoms

### Diagnosis

- Incidental finding on imaging
- Serological: Detection of antibodies
- Puncture: Contraindicated!

### Therapy

#### Surgical Therapy

- Whenever possible
- Only under perioperative medication with mebendazole or albendazole
- Treatment only in cooperation with infectiologists

#### Surgical Procedure

##### Surgery for Echinococcosis Cyst

- Rupture of the cyst and/or extravasation of cyst fluid must be avoided at all costs, otherwise contamination of the situs with the development of disseminated intra-abdominal disease
- Endocystectomy (procedure of choice for *E. granulosus* (Kniepeiss et al. 2020)):
  - Repositioning of the liver and the cyst with cloths soaked in 20% saline solution
  - Puncture of the cyst with a disposable trocar + aspiration of the cyst fluid while filling with physiological saline solution
  - Uncapping of the cyst
  - Exclusion of connection to the bile duct system = e.g. White test (white fat emulsion approved for i.v. infusion, e.g. lipofundin®, intralipid® via ductus cysticus)

- Installation of compresses soaked in 20% saline solution for 20 min = **Caution:** If bile ducts are opened, bile duct necrosis!—rule out beforehand and over sew bile leaks if necessary
- Suturing of the caspel edge or bipolar coagulation
- Pericystectomy: Resection of the entire cyst plus surrounding liver tissue—technically more difficult, risk of rupture!
- Typical/anatomical liver resection according to oncological criteria in *E. multilocularis*

## 8.2.2 Malignant Diseases of the Liver

### Key Points

- Distinguish primary—such as CCC (cholangiocarcinoma), HCC (hepatocellular carcinoma)—and secondary malignant findings (metastases)

### Primary Tumors

#### Hepatocellular Carcinoma (HCC)

##### Epidemiology and Risk Factors

- Incidence
  - Incidence = 10/100.000 in Germany
- Risk factors
  - Cirrhosis of the liver of any etiology (alcohol, hepatitis, hemochromatosis, etc.)
  - Chronic hepatitis B/C virus infection
- Cumulative 5-year risk of developing HCC in patients with HCV (hepatitis C virus)-associated liver cirrhosis in Europe = about 17%
  - Non-alcoholic fatty liver hepatitis (NASH) as a consequence of diabetes mellitus and the metabolic syndrome—number 1 rising risk factor world wide
  - Aflatoxin exposure



### Early Detection

- Screening program for all patients with:
  - Liver cirrhosis
  - Chronic hepatitis B/C
  - Fatty liver disease,
  - Steatohepatitis
- Sonography every 6 months

### Special Forms

- Fibrolamellar HCC—young patients often better prognosis
- Mixed differentiated tumors (combined HCC/intrahepatic cholangiocarcinoma)
- Early HCC—transition from regenerated node to HCC

### Clinical presentation and Classification

- Clinical presentation
  - Mostly asymptomatic
  - Conspicuous in routine examinations of cirrhotic patients
- TNM classification (HCC)
  - T (tumor)
    - T1 Solitary tumor without vascular invasion
    - T2 Solitary tumor with vascular invasion or multiple tumors all <5 cm
    - T3a Multiple tumors >5 cm
    - T3b Multiple tumors involving a major branch of the V. portae or Vv. hepaticae
    - T4 Tumor with invasion of adjacent organs or perforation of the visceral peritoneum
  - N (lymph nodes)
    - N0 No locoregional lymph nodes
    - N1 Locoregional lymph nodes
  - M (metastases)
    - M0 No distant metastases
    - M1 Distant metastases
  - UICC stages according to the TNM classification (eighth edition, January 2018)

I	T1 N0 M0	II	T2 N0 M0
IIIA	T3 N0 M0	IIIB	T4 N0 M0
IVA	Any T N1 M0	IVB	Each T Each N M1

### Diagnosis

- Diagnostic imaging
  - CM Sonography
  - Primovist MRI
  - CT
  - Characteristic signs in imaging
  - Arterial hypervascularization with rapid washout of the contrast medium and relative contrast reversal to the surrounding liver parenchyma
- Biopsy
  - Only if unclear imaging or therapeutic consequence
- Tumor marker
  - AFP only suitable for assessment of progression, not for diagnosis

### Surgical Therapy

- Liver resection (Lin et al. 2012; de Santibañes et al. 2017)
  - Indications:
    - Patients with potentially resectable HCC without cirrhosis
    - Patients with potentially resectable HCC and Child A/B cirrhosis
    - Presence of portal hypertension (ascites, platelets <100.000, splenomegaly) = not a sole exclusion criterion for resection, but significantly increases the surgical risk
    - Atypical resections = leaving as much functional liver tissue as possible
    - 5-year survival = 30–50%, but high recurrence rates due to de novo tumors in cirrhosis or micrometastases
- Liver transplantation (Lin et al. 2012)
  - Indications depending on local/national legal regulations and/or guidelines
  - Treatment of HCC + underlying liver cirrhosis
  - Prioritization and organ distribution according to local/national legal regulations and/or guidelines (Eurotransplant region—MELD (Model for End-Stage Liver Disease) score based:
    - Patients receive extra points with increasing waiting time)
    - Transarterial chemoembolisation (TACE), local thermal ablation (up to 3 cm diameter), liver resection: allows

- bridging during waiting period = recommended to avoid progression
- Other local ablation procedures (RFA (radiofrequency ablation), PEI (percutaneous ethanol injection), SIRT (selective internal radiotherapy), IRE (irreversible electroporation), cryotherapy)
- 5-year survival rates = up to 70%; local recurrence rate < 15%

## Intrahepatic Cholangiocarcinoma: CCC

### Definition

- Originating in the liver from the bile ducts

### Epidemiology

- Incidence
  - Incidence = 1–2/100.000 in Germany
- Risk factors
  - Cholelithiasis
  - Cirrhosis on the basis of chronic hepatitis C infection, alcoholic and non-alcoholic hepatitis
  - Uptake of carcinogens (nitrosamines, aflatoxins, anabolic steroids, etc.)
  - Congenital anomalies of the bile ducts
  - Concomitant diseases (e.g. primary sclerosing cholangitis, ulcerative colitis,  $\alpha$ -antitrypsin deficiency)

### Symptoms and Classification

- Symptoms
  - Abdominal pain
  - B-symptomatics
  - Icterus
- TNM classification (CCC)
  - T (tumor)
    - Tis carcinoma in situ intraductal tumor
    - T1 Solitary tumor without vascular infiltration
    - T2a Solitary tumor with vascular infiltration
    - T2b Multiple tumors with or without vascular infiltration
    - T3 tumors with infiltration of the peritoneum or direct invasion of extrahepatic structures
    - T4 tumors with periductal invasion

- N (lymph nodes)
  - N0 No lymph node metastases
  - N1 Lymph node metastases
- M (metastases)
  - M0 No distant metastases
  - M1 Distant metastases
- UICC stages according to the TNM classification

0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
III	T3	N0	M0
IVa	T4	N0	M0
	Each T	N1	M0
IVb	Each T	Each N	M1

### Diagnosis

- Imaging
  - Sonography
  - CT
  - MRI with MRCP (with Primovist)
  - ERCP (endoscopic retrograde cholangiopancreatography)
- Tumor marker
  - CA 19-9 = progress assessment
  - **Caution:** Also elevated in cholangitis and jaundice

### Therapy

- Surgical therapy
  - Resection = only curative option
  - Anatomical resection + lymphadenectomy in the hepatoduodenal ligament recommended
  - Contraindications:
    - Satellite nodules and or bilobar manifestation
    - Remote metastases
    - Peritoneal carcinomatosis
    - 5-year survival rates = 23–42% after R0 resection without lymph node metastases
- Adjuvant therapy:
  - according to local guide lines, preferably within the context of clinical trials

## CCC of the Common Hepatic Duct Bifurcation: Klatskin Tumors

### Definition

- First described by Gerald Klatskin in 1965 (hence the synonym Klatskin tumor).
- Perihilar cholangiocellular carcinoma in the region of the common hepatic duct bifurcation

### Epidemiology

- Incidence 1/100.000 in Germany

### Symptoms and Classification

- Symptoms
  - Icterus
  - Pruritus
  - Abdominal pain
  - B-symptomatics
- Differential diagnosis
  - HCC
  - Liver metastases
  - Pancreatic cancer
  - Cholangitis
  - Cholecystitis, choledocholithiasis
  - Biliary strictures, bile duct cysts
- Classification according to Bismuth-Corlette in type I-IV
  - I Distal common hepatic duct to the confluence of the right and left bile duct
  - II Common hepatic duct bifurcation
  - IIIa Common hepatic duct bifurcation and right hepatic duct
  - IIIb Common hepatic duct bifurcation and left hepatic duct
  - IV Common hepatic duct bifurcation and both hepatic ducts or multifocal
- TNM classification (Klatskin tumours)
  - T (tumor)
    - Tis carcinoma in situ, intraductal tumor
    - T1 Tumor limited to bile duct with spread to muscularis
    - T2a Tumor infiltrates periductal fat tissue
    - T2b Tumor infiltrates surrounding liver tissue
    - T3 Tumor with infiltration of the equilateral portal vein or hepatic artery

- T4 Tumor infiltrates main trunk of portal vein or bilateral portal vein branches or common hepatic artery or secondary bile ducts bilaterally or secondary bile ducts unilaterally with invasion of contralateral portal vein or hepatic artery
- N (lymph nodes)
  - N0 No lymph node metastases
  - N1 Regional lymph node metastases (incl. metastases along the cystic duct, choledochal duct, portal vein and hepatic artery)
  - N2 Lymph node metastases periaortic, pericaval, along the superior mesenteric artery and or truncus coeliacus
- M (metastases)
  - M0 No distant metastases
  - M1 Distant metastases
- UICC stages according to the TNM classification

0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
III	T3	N0	M0
IVa	T4	N0	M0
	Each T	N1	M0
IVb	Each T	Each N	M1

### Prognosis

- Prognostic factors:
  - Lymphnode metastases
  - Tumor differentiation
  - Perineural invasion
  - R1 resection status

### Therapy

- Surgical therapy
  - Resection = only curative option
  - Indications:
    - Type 1 Extrahepatic bile duct resection possibly with duodenopancreatotomy
    - Type 2–4 Extrahepatic bile duct resection + liver resection

### Surgical Procedure

#### Klatskin Tumors

- Depending on the type (extended) hemihepatectomy right or left + creation of biliodigestive anastomosis + lymphadenectomy in the hepatoduodenal ligament
- if necessary in combination with resection of the equilateral portal vein and hepatic artery in case of infiltration
- General portal vein resection without oncological advantage
- Intraoperative frozen sections from the proximal and distal resectional margins; **caution:** discontinuous growth
- If bilirubin is highly elevated = preoperative PTCO (cholangiodrainage) or ERCP + stent = relief of cholestasis = better liver function and less morbidity postoperatively
- In preparation for augmentation procedures to increase functional liver reserve prior to resection (portal vein embolization)

- Contraindication:
  - Secondary bile ducts infiltrated on both sides
  - Invasion of the portal vein or hepatic artery of the opposite side
  - Bilateral vascular infiltration
  - Remote metastases
  - Liver cirrhosis or pronounced fibrosis (functional liver reserve)
- Chemotherapy/radiochemotherapy:
  - according to local guide lines, preferably within the context of clinical trials

### Liver Metastases

#### Indications

- Resection of metastases of colorectal cancers = standard therapy
- Resection of metastases from non-colorectal cancers:
  - Increasing frequency
  - Individual tumor biology and the possibility of R0 resection are decisive here
  - Recurrent resections as well as two-stage resections possible

### Therapy

- All resection techniques and circumferences possible
- Decisive = possibility of extrahepatic tumor freedom
- Prognosis-limiting factor = R0 resection
- If necessary, combination with multimodal concepts—neoadjuvant chemotherapy and/or interventional radiological procedures such as RFA
- **Caution:** Chemotherapy-pretreated liver = reduced regenerative capacity, at least 45% residual volume required

### 8.2.3 Technique of Liver Resection

#### Planning of the Resection

##### Technical Conditions

- Review of vascular anatomy—inflow (hepatic artery and portal vein), outflow (hepatic veins) and bile ducts; normative variants (aberrant or accessory vessels)
- Exclusion infiltration of structures

##### Parenchyma Conditions

- Normal tissue, steatosis, steatohepatitis (after chemotherapy), fibrosis, cirrhosis
- Liver function
- Planned extent of resection vs. volume of future liver remnant = functional liver reserve

##### Caution

- Normal tissue 25% residual volume sufficient
- After chemotherapy at least 45% residual volume
- In cirrhosis only if hyper-Child-Pugh A or A and bilirubin <2—otherwise high mortality after conventional (open) resection; laparoscopic parenchymal-sparing minor resection also acceptable in Child C patients, the minimal invasive robotic approach has similar complication rates as open or laparoscopic procedures (Murtha-Lemekhova et al. 2022)

## Strategy of Resection

- Limited resections only
- Anatomical resections along the segment boundaries
- Always choose the most parenchyma-sparing procedure if possible
- if necessary, two-stage resections or multimodal combination with ablation

## Resection Type

### Minor Resection (<3 Segments)

- Monosegmentectomy
- Bisegmentectomy
- Anterior (segments V + VIII) or posterior (segments VI + VII) sectorectomy
- Wedge resection = for superficial findings
- Atypical resection = incision after marking and sonography of vascular structures which must be spared

### Major Resection

- Right hemihepatectomy (segments V, VI, VII, VIII)
- Left hemihepatectomy (segments II, III, IVa, IVb)
- Extended right hemihepatectomy (segments IVa, IVb, V, VI, VII, VIII)
- Extended left hemihepatectomy (segments II, III, IVa, IVb, V, VIII)
- Mesohepatectomy (segment IVa, IVb, V, VIII)

### Surgical Procedure

#### Liver Resection (Conventional/Open)

- Supine position
- Reversed L shape incision for right/left or extended right/left resections; median laparotomy for left lateral resections
- Inspection and palpation of the liver, the hepatoduodenal ligament and the entire abdomen
- Complete mobilization of the liver: use of the falciform ligament to pull on the liver, transection of the triangular ligaments and the teres hepatis ligament to obtain enough mobility for sonography and resection
- Dissection along the vena cava:

- **Caution:** Makuuchi ligament between segment 8 dorsal to v. cava often includes veins draining into v. caval vein (to be divided for right hemihepatectomy)
- **Caution:** Mobilize the whole liver and not only the liver lobe that will be resected!
- Intraoperative ultrasound to check vascular anatomy, extent of findings and positional relationship of lesions to vascular structures obligatory
- Complete lymphadenectomy in the hepatoduodenal ligament only indicated for cholangiocarcinoma and gallbladder cancer; for liver metastases of CRC in studies
- Cholecystectomy with long-left ductus cysticus—temporary closure with Bulldog clamp for later white test (Lipofundin®, Intralipid®, or similar) for visualization of the bile ducts at the resection area
- For all major resections:
  - Intravascular control: exposure and tightening of the artery and portal vein of the half of the liver to be resected (right pedicle in the area of the Gans fissure)
  - Outflow control: visualization and tightening of the hepatic vein to be resected
- Before parenchymal transection a CVP <5 is obligatory = less bleeding! (Anti-Trendelenburg positioning, low volume supply, if necessary vasodilators i.v.)
  - Control of the arterial inflow by dividing the feeding artery by means of clips or hemostatic suturing
  - Dividing the portal vein and hepatic vein by means of a vascular stapler or hemostatic suturing after clamping
- Parenchymal transection:
  - Ultrasonic dissection (CUSA = Cavitron Ultrasonic Surgical Aspirator) in combination with bipolar coagulation, clipping and ligation = advantage: precise transection; disadvantage: time-consuming

- Endovascular staplers (= stapler hepatectomy (Schemmer et al. 2006)) = crush clamp of the liver parenchyma with a straight clamp with subsequent stapling = advantage: time-saving; disadvantage: not applicable for all anatomical resections (e.g. isolated segment VIII)
- Water jet dissection = similar to ultrasonic method
- Ultrasonic scissors = especially for atypical resections, less precise than ultrasonic dissector
- Advanced coagulation technology = e.g. LigaSure<sup>®</sup>, Ultracision<sup>®</sup>/Sonicision<sup>™</sup>, bipolar scissors, Habib-Sealer (thermoablative)
- Finger fracture = crushing of liver tissue between fingers, supply of vessels by means of clips or stitches

8

## Technology

- It is essential to ensure that the vascular and bile duct structures of the remaining liver areas are protected, irrespective of the resection procedure used
- Pringle maneuver:
  - Targeted short-term clamping of the portal vein + hepatic artery during the transection phase using silicone reins in order to reduce the tendency to bleed
  - Rarely used with modern open resection techniques as ischemia-reperfusion damage in the remaining liver tissue as well as a higher tumor recurrence rate can be detected
  - No differences between intermittent and continuous Pringle manoeuvre
  - If necessary, maximum 20 min recommended
- Post-resection phase:
  - Achieving haemostasis with argon beamer, bipolar electrocoagulation, etc.; if necessary over sawing of vessels
  - Retrograde control for bile leakage with White-Test (alternatively diluted blue staining = lower detection rate) via cystic duct under manual compression of

the Ductus choledochus (**Caution:** Dislodging of the Ductus choledochus with clamp or bulldog may lead to necrosis) = if necessary re-positioning of bile ducts at the resection area

- Optional application of haemostyptics or sealants
- If necessary, reconstruction of the bile duct by means of biliodigestive anastomosis according to Y-Roux

## Possible Complications

- Postoperative (posthepatectomy) liver failure PHLF—insufficient residual volume—definition according ISGLS (Rahbari et al. 2011)
- Protein deficiency—edema, ascites
- Hepatorenal syndrome
- Postoperative bleeding
- Biliary leakage and bilioma formation—definition according ISGLS (Koch et al. 2011):
- Low “sweating out” of bilirubin = usually suspended
- High volume leakage: indicates bile leakage = revise early + oversaw
- Superinfected fluid collection/abscess = interventional CT-guided drainage
- Biliopleural fistula = rare, especially after simultaneous diaphragmatic resection
- Atelectasis + pleural effusion on the right = respiratory training and drainage if necessary

## 8.3 Liver Transplantation

### 8.3.1 General and Legal Basis

#### (National) Legal Basis

##### Definition

- Regulated by:
  - Local official regulations and guidelines

##### Indication and Listing

##### Indication for Liver Transplantation

- Based on the local official regulations and guidelines
- Set in the interdisciplinary transplant conference in consensus between the departments involved and legal guidelines

## Listing

- Potentially all patients with rapidly progressing or already far advanced irreversible chronic liver diseases, for which no conservative-internistic or surgical treatment alternative with equal chances of success exists
- Listing for transplantation (waiting list), if probability of survival appears to be greater with a liver transplant
- Listing based on assessment of liver function and tumor stage (HCC and others (Talakic et al. 2021) as well as disease-specific complications (dominant stenosis PSC)

## Organ Allocation

### Eurotransplant

- Organization for organ allocation based on national guidelines
- Coordinates the allocation of organs subject to transfer such as heart, kidney, liver, lung, pancreas and intestine (§ 8 TPG)
- In Austria, Belgium, Croatia, Hungary, Luxembourg, the Netherlands, Slovenia and Germany

### Principles of Organ Allocation

- Allocation of organs to individual patients or centres by Eurotransplant on the basis of national regulations
- Patients' listing on the Eurotransplant wait list for transplantation as soon as the treating transplant centre has made the indication and all necessary examinations are available

## 8.3.2 Evaluation and Follow-Up of Liver Function

### Clinical Follow-Up

- Basic parameters:
  - Progressive physical weakness, fatigue, muscular deficits
  - Hepatic encephalopathy
  - Therapy refractory ascites
  - Spontaneous bacterial peritonitis
  - Hepatorenal syndrome

- Gastrointestinal bleeding/variceal bleeding
- Hepatopulmonary syndrome
- Progressive osteopathy
- Recurrent biliary sepsis
- Occurrence of hepatocellular carcinoma

### Laboratory Parameters of Liver Synthesis and Excretion

- Only limited suitability for risk assessment

### Hepatocellular Integrity

- GOT
- GPT
- LDH

### Biliary Integrity

- alkaline phosphatase
- $\gamma$ -GT

### Synthesis Performance of the Liver

- Albumin
- Cholinesterase (CHE)
- PT
- INR
- Fibrinogen

### Excretory Capacity of the Liver

- Bilirubin (direct, indirect)
- Bile acids

### Scoring Systems for Liver Function and Prognosis

- For the assessment of patient survival and mortality risk (limited possible)

### Child-Pugh Score (▣ Table 8.1)

- Disadvantages:
  - Subjective assessment of the therapeutic response of ascites and encephalopathy
  - Continuous deterioration of the patient's condition is often not reflected in a change in child classification

### MELD Score

- MELD Criteria:
  - Bilirubin
  - Creatinine

**Table 8.1** Child-Pugh score<sup>a</sup>

	1 point	2 points	3 points
Encephalopathy	None		
Ascites, therapy	No ascites	Moderate, controlled by therapy	Pronounced despite therapy
Bilirubin	<35 μmol/L	–35 to 50 μmol/L	>50 μmol/L
Albumin	>3.5 g/dL	–2.8 to 3.5 g/dL	<2.8 g/dL
INR	<1.7	–1.7 to 2.3	>2.3

INR International Normalized Ratio

<sup>a</sup>Child A = 5–6 points; Child B = 7–9 points; Child C = >10 points

- Coagulation: INR (International Normalized Ratio; Prothrombin Ratio)
- Formula:
  - MELD score =  $10 \times (0.957 \times \log(\text{creatinine}) + 0.378 \log(\text{bilirubin}) + 1.12 \log(\text{INR}) + 0.643)$

### 8.3.3 Indications for Liver Transplantation: Relevant Underlying Diseases in Adults

#### Chronic Liver Disease

##### Underlying Disease for Liver Cirrhosis

- Hepatitis B, C, D
- Autoimmune hepatitis
- Alcoholic liver disease
- Cryptogenic

##### Cholestatic Liver Disease

- Primary sclerosing cholangitis (PSC)
- Primary biliary cirrhosis (PBC)
- Secondary sclerosing cholangitis
- Familial cholestasis syndromes
- Biliary atresia

#### Chronic Drug Toxicity

##### Metabolic Diseases/Genetic Diseases

- $\alpha_1$ -antitrypsin deficiency
- Wilson's disease
- Hemochromatosis
- Glycogen storage diseases
- Galactosemia
- Tyrosinemia

- $\beta$ -Thalassemia
- TTR (transthyretin) amyloidosis
- Cystic Fibrosis
- Hypercholesterolemia (LDL receptor deficiency, Crigler-Najjar syndrome type 1)
- Erythropoietic protoporphyria
- Primary amyloidosis
- Urea Cycle Defects

##### Other Diseases

- Congenital cystic liver
- Echinococcosis of the liver
- Chronic Budd-Chiari syndrome

##### Acute Liver Disease

- Fulminant liver failure
  - Etiologies:
    - Poisoning
    - Hepatitis
    - Budd-Chiari Syndrome
    - Drug toxicity, etc.
  - Definition: Acute liver failure based on Kings College score, Clichy criteria, or BiLE score
- Pregnancy-associated liver diseases
- Extensive liver trauma
- Postoperative liver failure after liver resection or transplantation

#### Malignant Diseases of the Liver

##### Hepatocellular Carcinoma (HCC)

- Based on national German guidelines indication only if within MILAN criteria for the entire period prior to liver transplantation = singular HCC <5 cm or up to 3 foci



<3 cm (international scientific based guidelines i.e. MILAN criteria (with possible downstaging), UCSF criteria, Up-to-5 criteria, Kyoto criteria, AASLD, EASL) (Bento de Sousa et al. 2021; Cusi et al. 2022; European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; European Association for the Study of the Liver 2018)

- 5 year survival up to 85%

### Cholangiocarcinoma (CCC)

- Should be performed within prospective randomized clinical trials only

### Epithelioid Hemangioendothelioma

#### ! Caution

- Indication for liver transplantation in the case of malignant primary disease
- Transplantation only in patients who have a significantly better chance for recovery and long-term survival with transplantation than without transplantation or with the use of alternative therapies
- Liver metastases in other primary tumors (e.g. colorectal tumors) = currently (at least outside of studies) no indication for liver transplantation

### 8.3.4 Contraindications for Liver Transplantation

#### Lack of Patient Adherence/ Psychosocial Problems

- Adherence = beyond consent to transplantation, willingness and ability to cooperate in the treatments and examinations required before and after transplantation
- Reliable intake of immunosuppressants + regular outpatient follow-up examinations = absolute prerequisites for successful transplantation
- Psychological consultation before transplantation = obligatory
- Continued alcohol or drug abuse = clear contraindication until completion of consistent withdrawal and addiction treatment

### High Age

- Probability of presence of concomitant diseases that speak against transplantation (such as cardiovascular problems) increases with age
- Above 65 years of age Clarify indication individually
- The decisive factor is the biological age of the patient

### Cardiovascular and Pulmonary Concomitant Diseases

- To be excluded:
  - Severe valvular heart disease
  - Severe pulmonary hypertension
  - (Alcohol Toxic) Cardiomyopathy
  - Coronary vascular disease and myocardial infarction

#### ! Caution

Cardiovascular and pulmonary concomitant diseases = risk during transplantation or longer-term transplant success.

- General fitness for anaesthesia must always be checked

### Infections

- Chronic suppurative infections (e.g. osteomyelitis, sinusitis, abscesses):
  - Need to be treated before transplantation
  - So is spontaneous bacterial peritonitis
- In active tuberculosis:
  - No liver transplant
  - Tuberculostatic therapy required for at least 3 months (if possible for 1 year)
- HIV infection = no contraindication
- AIDS = contraindication

### Extrahepatic Metastases

- Extrahepatic tumor manifestation = absolute contraindication

### 8.3.5 Surgical Principles

#### Patient Positioning

- Supine position
- Both arms alongside the body

## Laparotomy

- “Reversed L-shape incision” in the right upper quadrant of the abdominal wall (reversed angle incision to the right)
- Alternatively, transverse upper abdominal laparotomy (costal margin incision) without or with median extension to the xyphoid (bilateral rooftop incision with vertical extension)

## Recipient Hepatectomy

- Severing of the falciform ligament between ligatures
- Mobilization of the diseased liver from the hepatoligamentous structures
- Ductus hepatocholedochus, hepatic artery and portal vein separated after close-to-life preparation—corresponds to the beginning of the anhepatic phase of the recipient
- Completely mobilized liver is dissected from the recipient vena cava while supplying (clipping/LigaSure) numerous small hepatic veins (Houben et al. 2014; Kniepeiss et al. 2020)
- 3 large hepatic veins are transected with the help of two endo-vascular stackers
- Stop bleeding
- Inferior vena cava is partially clamped tangentially with a Satinski clamp

## Machine Perfusion of the liver

- Novel method for organ preservation + reconditioning (van Rijn et al. 2021; Karangwa et al. 2020; Martins et al. 2020; Ceresa et al. 2022; Sousa Da Silva et al. 2022)
- Considering shortage of donor livers suitable for transplantation, this technique may help avoid needless wastage of organs
- Goals: (1) improvement of quality of marginal livers, (2) extension of time for which liver can be preserved, (3) enabling an objective assessment of liver quality/viability
- Hypothermic vs. normothermic machine perfusion

## Implantation

- Donor organ placed in the right upper abdomen of the recipient

## Vena Cava Anastomosis

- In modified piggy-back technique side-to-side cavocaval anastomosis between donor and recipient
- Front and back wall each separately continuous with Prolene threads of strength 4-0

## Portal Vein Anastomosis

- if necessary, shortening of the portal vein to avoid kinking
- End-to-end portal vein anastomosis
- Separately for the front and back wall in continuous technique with Prolene threads of strength 5-0

## Reperfusion

- With the reperfusion of the liver the anhepatic phase is finished

## Portal vein

- Portal venous reperfusion is widely considered as standard in adults
- Subsequently, completion of the portal venous anastomosis and closure of the caudal opening of the donor’s vena cava; the cranial portion of the donor’s vena cava was already closed during backtable surgery

## Hepatic artery

- Artery is usually anastomosed with Prolene sutures of different thicknesses (5-0 to 7-0) in continuous or single button suture technique.
- Here, the back wall can be sewn continuously; front wall in single button technique
- To avoid anastomotic stenosis, the branch-patch technique is used so that the anastomosis is located between the bifurcation of the gastroduodenal artery (which is usually blocked) and the hepatic artery on the recipient side and the bifurcation between the gastroduodenal artery and the hepatic propriocoele artery on the donor side.

After reperfusion, arterial and portal venous blood flow is determined in mL/min.

## Bile Duct

- Bile duct anastomosis:
  - Usually as end-to-end anastomosis with 5-0 PDS (polydioxanon)
  - Either single knots or running suture
  - In selected cases (e.g. PSC of the recipient), a biliodigestive anastomosis with Roux-Y reconstruction is indicated
- 2 percutaneously inserted easy-flow drains, one subphrenic, the other subhepatic

## Postoperative Phase

- Interdisciplinary intensive care unit
- Interdisciplinary treatment (e.g. gastroenterologists/hepatologists, nephrologists, infectiologists, etc.)

## 8.4 Anatomy and Physiology of the Gallbladder and Bile Ducts

### 8.4.1 Gallbladder (Vesica Biliaris)

- Lateral under lobus quadratus of liver segments IVb/V
- Positional relationship to right colonic flexure, duodenum and V. portae
- Consisting of:
  - Fundus
  - Corpus
  - Infundibulum
  - Collum (= transition to the cystic duct)

### 8.4.2 Bile Ducts

- Outflow into left (segments I–IV) and right hepatic duct (segments V–VIII)
- Ductus hepaticus communis = union of right + left ductus hepaticus
- Ductus choledochus = Ductus hepaticus after inflow of the Ductus cysticus
- Common orifice of the ductus choledochus with ductus pancreaticus Orifice in papilla Vateri of the duodenum, pars inferior
- Calot's triangle = bounded by cystic duct, hepatic duct and hepatic subsurface

Variants:

- Course of the right posterior bile duct
- Crossing over/under the common bile duct, accessory bile duct of seg. IV
- Ostium of choledochal duct: common excretory duct with confluence, common ostium without confluence, separate ostia of both ducts

## 8.4.3 Blood Supply and Drainage of the Gallbladder and Bile Ducts

### Blood Supply of the Extrahepatic Bile Ducts + Gallbladder

- Right hepatic artery, gastroduodenal and retroduodenal arteries
- Cystic artery from right hepatic artery (numerous variants, rarely cystic artery directly from main hepatic artery)

### Blood Supply of the Intrahepatic Bile Ducts

- Common hepatic artery from Coeliac trunc
- After delivery of the gastroduodenal and right gastric arteries as the proper hepatic artery
- Branching into the right and left hepatic artery (variable anatomy)
- Venous outflow via the hepatic veins

## 8.5 Diseases of the Gallbladder and Bile Ducts

### 8.5.1 Benign Diseases of the Gallbladder

#### Key Points

- Gallstones in 10–15% of population (m:f = 1:1.8)
- 75% are asymptomatic at diagnosis
- 20% Of those turn symptomatic within 15–20 years
- Indication for surgery in symptomatic cholecystolithiasis with and without complications, porcelain gallbladder and stones >3 cm

- Laparoscopic cholecystectomy is the standard procedure
- Acute cholecystitis = most frequent complication of cholecystolithiasis; if detected = immediate indication for surgery
- Gallbladder polyps rare overall, but if gallbladder polyps  $\geq 1$  cm or symptomatic = indication for surgery

## Cholecystolithiasis

### Definition

- Inability to ensure the solubility of the bile component (cholesterol, calcium, pigments)
- Precipitation and formation of concretions (gallstones)

### Epidemiology

- Gallstone carriers = 15–20% of the population
- Risk factors:
  - Overweight
  - Rapid weight loss
  - Pregnancy
  - Multiparity
  - Female gender
  - First degree family history
  - Medications: Ceftriaxone, postmenopausal estrogens, parenteral nutrition.
  - Geographical origin (Scandinavia, American Indians)
  - Ileal diseases, secondary to resection or bypass of the small intestine
  - Age (risk increased from 40 years)
- Symptomatic cholecystolithiasis: approx. 30% of carriers
- Hereditary component in the development of gallbladder stones about 25%
- More than 190,000 cholecystectomies/year in Germany

### Classification

- Asymptomatic cholecystolithiasis
- Symptomatic uncomplicated cholecystolithiasis

- Symptomatic complicated cholecystolithiasis with complications
  - Due to trapped concrement
  - Acute cholecystitis = most frequent complication

### Symptoms

- Colicky attacks of pain
  - Of more than 15 min duration in the epigastrium/right upper abdomen
  - Radiation into the back and right shoulder
- Nausea, occasionally bilious vomiting
- Possibly intolerance for fat, alcohol
- Dyspepsia and flatulence
- Additionally in case of complicated form:
  - Fever
  - Chills
  - Painful jaundice (due to stone entrapment in the choledochal duct)
  - Defensive tension in the upper abdomen (in acute cholecystitis, gallbladder empyema or perforation)
  - Possibly signs of purulent cholangitis or biliary pancreatitis, liver abscesses

### Complications

- Stone impaction in the choledochal duct
- Acute cholecystitis
- Gall bladder empyema/perforation
- Purulent cholangitis
- Liver abscesses
- Biliary pancreatitis
- Mirizzi's syndrome: larger trapped stone in the cystic duct compresses the common hepatic duct or the choledochal duct:
  - Penetration into the duodenum—gallstone ileus
  - Development of biliodigestive fistulas possible
- Shrinking gallbladder: after recurrent inflammation and scarring
- Porcelain Bubble:
  - Chronic calcifying cholecystitis
  - Increased risk of carcinoma

#### Annual complication rate

- After first colic = 1–3%
- In asymptomatic stone carriers = 0.1–0.3%

## Diagnosis

### Clinical Presentation

- Pressure pain right upper abdomen
- possibly palpable tumor
- Murphy's sign (focal pain under direct pressure) on inspiration
- possibly sclerenicterus

### Lab Chemistry

- Bilirubin, AP,  $\gamma$ -GT, if necessary GOT, GPT, lipase, amylase, blood count, CRP

### Imaging Non-Invasive Procedures

- Sonography:
  - Sensitivity >95
  - Standardized transcutaneous B-mode sonography
  - Complete visualization of the gallbladder in variable sectional planes (in at least 2 patient positioning variants, offset by 90° to each other)
  - Assessment of: Gallbladder stones, sludge, wall composition, caliber ductus hepaticocholedochus (up to 7 mm normal), free fluid, cholestasis intrahepatic, liver abscesses, pancreatic head, multi-layered wall (cholecystitis)
- CT:
  - For poor sound conditions
  - In the case of complicated courses in individual cases
  - In case of suspected tumor for differential diagnosis
- MRI/MRCP:
  - In case of suspected tumor for differential diagnosis
- Oral/i.v. cholangiography:
  - Almost no longer used for the diagnosis of gallstones

### Imaging Invasive Procedures

- ERCP (endoscopic retrograde cholangiopancreatography):
  - For choledocholithiasis
  - If necessary in combination with papillectomy
  - In biliary pancreatitis with cholestasis/icterus and/or signs of cholangitis: as soon as possible
  - For cholangitis within 2 h after admission

- Therapeutic splitting: Bile duct repair by ERCP before cholecystectomy (CCE)
- PCT (percutaneous transhepatic cholangiography):
  - Only rarely, if ERCP is not possible

### Further Etiological Clarification

- In case of unusual clinical constellation (e.g. family history, occurrence in childhood and adolescence, intrahepatic microstones, association with diarrhoea)
- Possible etiologies: e.g., hemolytic anemias, bile acidosis syndrome, drug history, infections

## Therapy

### Conservative Therapy

- Serious complications: only 2% of gallstone carriers
- If asymptomatic cholelithiasis = monitoring, no indication for therapy

### Surgical Therapy

- Surgery indications
  - Symptomatic uncomplicated or complicated cholelithiasis
  - Asymptomatic patients with porcelain gallbladder: due to increased risk of carcinoma
  - Asymptomatic patients with gallbladder stones >3 cm in diameter: Because of increased risk of carcinoma (in men nine- to ten-fold)
  - In major abdominal surgery: simultaneous cholecystectomy even for asymptomatic stones
  - Surgery may be considered in
    - patients with *chronic hemolytic diseases* due to increased risk of biliary symptoms
    - *undergoing solid organ Tx* due to increase risk of developing symptoms post-Tx
    - *bariatric surgery patients*

**! Caution**

- No indication in asymptomatic cholecystolithiasis with gallbladder stones <3 cm in diameter
- In the first and second trimester of pregnancy only in case of urgent indication (laparoscopic, intra-abdominal pressure below 12 mmHg, intraoperative fetal monitoring), otherwise post partum
- OP procedure
- Laparoscopic/robotic cholecystectomy:
  - Worldwide standard procedure (more than 93% of all cholecystectomies started laparoscopically)
  - Conversion rate to open cholecystectomy = 4–7%
  - Identical complication rates with shorter hospital stay and shorter convalescence (fewer wound infections)
  - Contraindication laparoscopic: Manifest portal hypertension (relative), liver cirrhosis MELD score >8, gallbladder carcinoma, severe pulmonary obstruction, gravidity third trimester
- Open cholecystectomy:
  - Well suited for unclear conditions
  - In case of suspected tumor or strong bleeding tendency
- Mini-laparotomy cholecystectomy:
  - Laparotomy <8 cm
  - No differences to laparoscopic cholecystectomy with regard to complication rates, length of hospital stay and convalescence times
- NOTES cholecystectomy (“natural orifice transluminal endoscopic surgery”):
  - Transvaginal or transgastric
  - Elective surgery only
  - Complication rate = 3.1%, conversion rate = 4.9% (German NOTES registry)

**Surgical Procedure****Laparoscopic Cholecystectomy**

- Supine position with legs apart or flat supine position
- Surgeon between legs or left
- Access pneumoperitoneum at 12 mmHg, (Veress needle) or mini-laparotomy via subumbilical skin incision approx. 1.5 cm

- Insertion camera trocar + 10 mm working trocar + 1–2 × 5 mm working trocars
- Elevating the gallbladder and pulling the infundibulum to the right
- Representing the Calot Triangle
- Dissection of the cystic duct and cystic artery, including visualization of the opening into the choledochal duct.
- Clip supply—2 each to central, 1 to peripheral
- Subserosal release of the gall bladder and transfer to salvage bag
- Hemostasis
- Moving the camera in 10 mm trocar
- Removal of the gallbladder via a subumbilical skin incision, if necessary with a spreading instrument (using a salvage bag)

Inspection of the surgical area, removal of the trocars under visual control, fascial closure, skin suture.

**Surgical Procedure****Open Cholecystectomy**

- Rib-arch margin incision or transrectal incision
- Antegrade subserosal extirpation of the gallbladder
- Settling of the cystic duct + cystic artery in Calot's triangle near the gallbladder
- Clip supply of these structures—2 each to central, 1 to peripheral

**— Complications**

- Recurrent cholelithiasis = 2% of cases
- Bile leak (mostly liver bed) = 0.4–1.5%
- Wound infection = 1.3–1.8%
- Pancreatitis = 0.3
- Bleeding = 0.2–1.4
- Bile duct injury rate = 0.2–0.4%
- Subhepatic abscess
- Infected bilioma/hematoma
- Occlusive icterus due to remaining concretions

- Post surgical care
  - Clinical control first post-op day
  - Blood count, CRP and bilirubin on post-op day 2
  - Discharge when symptom-free + laboratory inconspicuous
  - In case of bilirubin elevation: sonography to exclude cholestasis

## Gallbladder Polyps

### Definition

- Benign tumors of the gallbladder wall
- Subdivision into 2 groups:
  - Benign pseudotumors (e.g. cholesterol polyps or adenomatosis)
  - Adenomas

### Epidemiology

- Prevalence of gallbladder polyps = between 1 and 7%
- Polyps  $\geq 1$  cm in diameter = significantly increased probability of neoplastic genesis (adenomas) = risk of carcinoma in up to 50%
- Risk factors for adenoma development:
  - Age  $> 50$  years
  - Solitary polyps
  - Gallstones
- Presence of more than one polyp = speaks against an adenoma and for the presence of cholesterol polyps
- Risk factors for malignancy:
  - Age  $> 60$  years
  - Coexistence gallstones
  - Size increase
  - Size  $> 10$  mm

### Clinical Presentation

- Mostly asymptomatic
- Otherwise see Cholecystolithiasis

### Diagnosis

- Sonography
  - No change in position when repositioning the patient
- If necessary endosonography and CT

## Therapy

### Surgical Therapy

- Surgery indication
  - Gallbladder polyps  $\geq 1$  cm: Independent of symptoms
  - For polyps  $> 18$ – $20$  mm: Because of the significant risk of malignancy, primarily consider open cholecystectomy
- Laparoscopic vs. open cholecystectomy

### Conservative Therapy

- For polyps  $< 1$  cm
- Sonographic control:
  - Initially every 6 months
  - Later annually, if no increase in size

## Acute Cholecystitis

### Definition

- The most frequent complication of cholecystolithiasis
- Acute inflammation of the gallbladder wall

### Pathophysiology

#### Course

- Stone entrapment with passive or permanent occlusion of the cystic duct
- Gallbladder hydrops with abacterial infection
- Secondary colonization by ascension from duodenum or hematogenous/lymphogenous dissemination
- possibly gallbladder empyema and ulcerophlegmonous course

### Other Risk Factors

- Diabetes mellitus
- Atrial fibrillation
- Terminal renal failure
- Severe liver dysfunction

## Symptoms

### Symptoms

- Colicky upper abdominal pain
- Fever + possibly chills
- Nausea + vomiting

### Complications of Acute Cholecystitis

- Gallbladder gangrene
- Gall bladder empyema or perforation
- Rare formation of biliodigestive fistula (60% to the duodenum)
- Gallstone ileus

## Diagnosis

### Clinical Presentation

- Positive Murphy sign
- Defensive tension right upper quadrant in peritonitis

### Lab

- AP,  $\gamma$ -GT, transaminases, bilirubin, lipase, coagulation parameters (INR, PTT), CRP and blood count
- Clear signs of infection: leukocytes plus CRP elevated
- Cholangitis: AP,  $\gamma$ -GT elevated

### Sonography

- Sensitivity = 94%; Specificity = 78%
- Wall thickening (>4 mm) with possibly triple stratification of the gallbladder
- Pericholecystitis with free fluid
- Dense internal pattern: with empyema
- Evidence of covered or open perforation, if applicable

## Therapy

- Always operative

### Indication

- If acute cholecystitis is detected, surgery is indicated immediately
- In patients on anticoagulants:
  - If necessary, adjustment of coagulation or start of fluid substitution
  - Antibiotic administration and electrolyte balance
  - Subsequent early selective surgery within 1–3 days

- If patient cannot be operated early (diagnosis too late, other medical reasons (= too high risk of surgery): Cholecystectomy in interval only after 6 weeks
- ACDC (“acute cholecystitis: early versus delayed cholecystectomy”) study (Gutt et al. 2013): early selective laparoscopic cholecystectomy vs. interval cholecystectomy after primary conservative antibiotic therapy:
  - Reduction of morbidity and mortality
  - Total in hospital time significantly lower
  - Significantly reduced hospital costs
  - Comparable numbers of bile duct injuries and bile leakages

### OP Procedure

- Laparoscopic cholecystectomy:
  - Standard procedure
  - Conversion rate 2–7% (some series up to 20%)
- Primary open surgery:
  - In case of expected complications
  - In case of multiple previous operations
  - For “intensive gallbladder”

Acute cholecystitis in patients requiring intensive care (acute acalculous cholecystitis):

- Incidence = 0.2–0.4% in patients who were in an intensive care unit for more than 2 days
- Often associated with high morbidity and mortality
- Surgical rehabilitation obligatory as long as no clinical contraindications are present
- Open procedure justified with similar peri- and postoperative complication rates
- No operability given:
  - Interventional percutaneous cholecystostomy or endoscopic transpapillary bile duct drainage
  - Secondary cholecystectomy after re-evaluation and stabilization of the patient (early or late elective = no clear recommendations)

## 8.5.2 Benign Diseases of the Bile Ducts

### Key Points

- Choledocholithiasis in up to 15% of patients with cholecystolithiasis
- Hyperbilirubinemia + sonographically dilated bile duct suspicious



- Therapeutic splitting ERC (endoscopic retrograde cholangiography) and CCE (cholecystectomy) recommended
- Choledochal cysts very rare overall

## Choledocholithiasis

### Definition

- Concrement in the common bile duct (Ductus choledochus)
- Most frequently: formation of the calculus in the gallbladder and migration into the choledochal duct; rarely formation directly in the choledochus

### Epidemiology

- Prevalence of gallstones in patients with cholelithiasis = age-dependent: 5–15%
- High probability of simultaneous choledocholithiasis in:
  - Sonographically dilated bile duct (>7–10 mm) + hyperbilirubinemia + elevated  $\gamma$ -GT/GPT
  - Bile duct >10 mm + gallbladder stones + colic
  - Direct sonographic detection of stones in the bile duct

### Clinical Presentation

- Strong evidence of choledocholithiasis
  - Cholangitis
  - Stone visible in ultrasound
  - Icterus
  - Hyperbilirubinemia + sonographically dilated bile duct

### Therapy

#### Indication

- Patients with gallbladder + bile duct stones = therapeutic splitting recommended
- Preoperative ERC = primary procedure in combination with papillotomy
- In case of cholangitis or severe biliary pancreatitis within 24 h
  - Cholecystectomy only after pancreatitis has subsided

- In case of cholelithiasis under risk assessment = cholecystectomy within 6 weeks if possible
- Symptomatic bile duct stones in gravidity: primary endoscopic papillotomy + stone extraction
- If ERCP is not possible:
  - Laparoscopic cholecystectomy + simultaneous surgical bile duct revision (transcystic bile duct exploration or laparoscopic choledochotomy, cholangiography and extraction via grasping forceps, basket, Fogarty catheter if necessary with bougienage of the papilla), if expertise available
  - Insertion of a T-drainage possible

## Choledochal Cysts

### Definition

- Cystic dilatation of the choledochus
- Affects extra- and/or intrahepatic bile ducts
- Mostly indication for surgical therapy

### Epidemiology

- Rare clinical picture: incidence = 1/100.000 to 1/150.000 in western countries
- More common in Japan
- Women: Men = 7–8: 1
- Genetic predisposition

### Pathogenesis

- Abnormal connection between the choledochus and the pancreatic duct
- Reflux of pancreatic juice into distal choledochus = chronic inflammation = slackening of the choledochal wall
- Classification according to Todani/Alonso-Lej

### Clinical Presentation

- Classic triad (only 10% of patients):
  - Pain in the right upper abdomen
  - Icterus
  - Abdominal mass
- Complications (if left long term without surgical treatment)
  - Portal hypertension
  - Cirrhosis of the liver
  - Biliary obstruction
  - Malignant degeneration = 2.5–26%

## Diagnosis

- Lab
  - Liver dysfunction (60% of cases)
- Sonography
- CT/MRI abdomen
- ERCP/percutaneous transhepatic cholangiography (PTC)

## Therapy

- Targets
  - Symptom relief
  - Preventing complications
- Technique = cholecystectomy + resection of the extrahepatic cyst-bearing bile ducts if necessary biliodigestive anastomosis

# 8

## 8.5.3 Gallbladder Carcinoma

### Epidemiology

- Incidental finding in 0.2–0.4% of cholecystectomies
- Proportion of potentially resectable gallbladder carcinomas at the time of diagnosis = 10–30%
- Risk factors:
  - Disposition due to cholelithiasis (1–3%)
  - Porcelain gallbladder (–20%) = indication for surgery even without tumor evidence in imaging
  - Gallbladder polyps = metaplasia-dysplasia pathway and adenoma-carcinoma sequence identified

### Symptoms

- Often asymptomatic
- History of cholelithiasis
- Courvoisier sign = painless palpable enlargement of the gallbladder, if applicable
- Later: Icterus, B-symptomatics

### Diagnosis

#### Sonography

- Mural tumor
- Expansion in the liver bed
- Metastases intrahepatic

## CT Abdomen and Thorax

- Environment diagnosis
- Exclusion of metastases intrahepatic
- OP planning

## Alternative MRI with Magnetic Resonance Cholangiopancreatography (MRCP)

- Exclusion of intrahepatic metastases
- OP planning
- Assessment of the intra- and extrahepatic bile ducts
- If necessary ERCP for the evaluation of the intra- and extrahepatic bile ducts

## TNM Classification and Staging (UICC 2010)

### TNM Classification

- T (tumor)
  - T1 Tumor infiltrates lamina propria or musculature
  - T1a Tumor infiltrates mucosa
  - T1b Tumor infiltrates bile duct muscles
  - T2 Tumour infiltrates perimuscular connective tissue, but no spread via serosa or liver
  - T3 Infiltration of serosa or infiltration of liver and/or other organ such as stomach, colon, pancreas, extrahepatic bile ducts or other organs
  - T4 infiltration of portal vein or hepatic artery or multiple extrahepatic organs
- N (lymph nodes)
  - N0 No regional lymph nodes affected
  - N1 Regional lymph nodes affected
- M (metastases)
  - M0 No distant metastases
  - M1 distant metastases

### UICC Stages According to the TNM Classification (2010)

Stage Ia	T1	N0	M0
Stage Ib	T2	N0	M0
Stage IIa	T3	N0	M0
Stage IIb	T1, T2, T3	N1	M0
Stage III	T4	Each N	M0
Stage IV	Each T	Each N	M1

## Therapy

### Surgical Therapy

- Complete resection = only curative approach

### OP Indication/Strategy

- Extent of surgery depends on TNM stage (see above):
  - T1a cholecystectomy
  - T1b Radical cholecystectomy—resection in the liver bed 3 cm hem apical + lymphadenectomy
  - T2 en bloc resection Couinaud segments IVb and V + lymphadenectomy; 5-year survival 40% vs. 90%
  - T3 Extended right hemihepatectomy + lymphadenectomy
  - T3 with infiltration of an extrahepatic organ or T4 individual decision only; 5-year survival <10%
- If incidental finding after cholecystectomy:
  - Early resection within 2 to max. 4 weeks
  - Goal = Avoid lymphogenic and peritoneal metastasis according to recommendations
- If incidental finding during cholecystectomy:
  - Switch to open procedure
  - Resection according to recommendations
  - If no expertise for liver resection available = early presentation to liver center within 2 to max. 4 weeks
- If gallbladder carcinoma suspected in diagnosis:
  - Either diagnostic laparoscopy in case of frequent early peritoneal metastasis and open resection according to recommendations
  - If no expertise for liver resection available = immediate presentation to liver center
- Early lymphogenic metastasis = extensive lymphadenectomy, ligamentum hepatoduodenale to the truncus coeliacus
- Always excise trocar injection channels to avoid cutaneous metastases

## Adjuvant Therapy

- According to current guidelines
- Preferably inclusion of patients in randomized controlled trials

Malignant diseases of the bile ducts are discussed in the chapter on malignant diseases of the liver with Klatskin tumours (► Sect. 8.2.2).

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