Ferdinando Agresta · Fabio Cesare Campanile
Nereo Vettoretto *Editors*

Laparoscopic Cholecystectomy

An Evidence-Based Guide

Forewords by
Luigi Presenti and
Mario Morino

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To Patrizia, Chiara and Rita: without them everything, including this book, would be meaningless.

Ferdinando

To my beloved Tiziana and Simone for their silent support and understanding during all the time I take away from them.

Fabio

To my wife and children, Laura, Giulio and Zeno. And to my patients, main reason and motivation for everyday's work and research

Nereo

Foreword 1

It might appear singular to devote a specific volume to something that one is confronted to in daily practice, scheduled as emergency, because the "topic," or better say the pathology, is one of the most diffuse, one about which articles can be found in almost every specialized journal.

And now a book is published about this "topic," undoubtedly the result of an explosive revolution as laparoscopy has been in surgical procedures.

It is an honor for me to introduce the impressive work done by my colleagues who have tried, after 25 years, to analyze all the current practices and trends in laparoscopic cholecystectomy, with the idea of giving the possibility to us, surgeons, to have all the actual evidences about this topic under hand.

Above this all, besides the evidence, they have never forgotten that the very core of all attempts and improvements is the patient, his/her satisfaction understood as quality of life.

Keeping in mind this core point, another subject must never be forgotten: the young surgeon in training. How to teach and how to learn, what to teach and what to learn, in order to train and grow an expert are main themes authors and editors have here well kept in mind.

This book has to be considered an ambitious work, which surely has reached its goals. As 25 years ago, yet another fuse in order to better understand what has been, and still is, is the revolution brought by laparoscopy in surgery.

Luigi Presenti
President of the ACOI
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Foreword 2

More than a quarter of a century after Philippe Mouret's cholecystectomy and 20 years after the EAES Consensus Conference held in Madrid in 1994 of which I was a member, do we need a new consensus conference on the same topic and above all a text including all the proceedings of such a debate? Yes we do, absolutely.

Medicine, and surgery in particular, is in continuous evolution, and the more a technique is practiced and diffused, the more we need to evaluate its results, its indications, and its technique on the basis of evidence-based medicine. This is the reason why, in my role as the President of SICE, I endorsed with enthusiasm the proposal by Ferdinando Agresta to conduct a consensus on cholecystectomy, and with the same enthusiasm I am introducing to the surgical community this book that has the ambition to go into the details of all the subjects that have been addressed during the consensus.

Gallbladder pathologies are among the most frequent surgical indications in every department of surgery, and laparoscopic cholecystectomy is part of the daily practice of the vast majority of general surgeons; this book contains the scientific basis on which this activity is founded.

The huge success of laparoscopic surgery and its diffusion in the majority of hospitals all over the world does not prevent us to critically analyze every clinical issue in every related pathology; the growing importance of medicolegal issues in the everyday life of the surgeon is only one further reason that will guarantee to this thorough analysis the success that it deserves.

Mario Morino
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Preface

"Long Branch, NJ – United States, 1990. It must have been the end of March; I was a junior surgical resident, making rounds, as every day, on the many patients in the service. It looked like an ordinary day at Monmouth Medical Center; Dr Mark Schwartz, one of the attending surgeons of the Department, just had returned from Tennessee where he attended his training course on laparoscopic cholecystectomy. I will always remember what he stated that day: 'Shortly, every cholecystectomy will be done by laparoscopy', and also I will always remember that I thought he was joking! I knew that he and some other attending physicians from Monmouth went to Nashville, where two surgeons, Reddick and Olsen, were teaching this new technique, but I believed that it was some kind of niche surgery, almost an oddity, not something meant to replace the most common operation in abdominal surgery! How could Schwartz possibly think that taking out a gallbladder through a small tube could be attractive in the everyday practice?

Mouret, of course, had already performed his first laparoscopic cholecystectomy in France, and Perissat, few months earlier, had presented his video at the SAGES meeting, attracting a great deal of interest by the American surgeons, but I was completely unaware of that.

As a matter of fact, a few days later the first laparoscopic cholecystectomy was done at Monmouth Medical Center and many followed. By the summer of 1990, I had performed several laparoscopic operations as first surgeon.

A great excitement spread among surgeons and later that year we started approaching also appendectomies, hernias, colon resections and other operations by laparoscopy. The laparoscopic era had started!

Patients were attracted by the new technique: many came to New Jersey from NYC to have their gallbladder out "with the laser" (actually we often used a YAG laser for dissection in those days); we completed 563 cholecystectomies in 14 months [1]".

The instruments we used in those days were quite simple, but had vivid, zoological, names: duckbill, big bird, whale. They were all straight tools, the curved instruments that could pass through a trocar cannula came later. We used to focus on aspects that seem ingenuous today: achieving a good angle of view with only straight tools and zero degree scopes, never letting go on a detached gallbladder for fear of losing it in the abdomen, assuring the cystic duct with two or three clips.

Almost a quarter of century after the times this memories by Dr. Campanile recalled, and after countless cholecystectomies, we have a much more sophisticated equipment, and our indications have broadened to include almost all cases; alas, have we looked into the evidence that is actually available on laparoscopic cholecystectomy? How much of our practice is evidence driven, and how much is, instead, based on "tradition," habit, or unproved personal preferences?

At the beginning, the explosion of laparoscopic cholecystectomy (and of laparoscopic surgery, in general) has been led by patient preference and surgeon enthusiasm, rather than rigorous scientific scrutiny. J.C. Hunter in an editorial, back in 2001, observed that "Reading's Rule" applies [2]; in other words if two groups look very different, they probably are. As a matter of fact, asking a patient nowadays to be randomized between laparoscopic and open cholecystectomy might be a difficult task, as laparoscopy is clearly perceived as the best treatment and its advantages are widely known.

Hunter noticed that randomized trials on cholecystectomy did not really alter surgical practice [2]. Is this still true today, more than 25 years since the first laparoscopic cholecystectomy? It is a fact that even a meta-analysis proving equivalent outcomes between laparoscopic and small-incision cholecystectomy [3] did not have an impact on our everyday practice. Trials and scientific papers are difficult to construct and even more difficult to read and interpret. However, we must, at least, be aware of the available evidence if we want to make sound clinical choices and act according to the so-called good clinical practice.

The idea of gathering the updated evidence in this book about one of the most frequent operations that general surgeons practice all over the world has been the base for a national consensus conference held under the auspices of several international scientific societies. In this occasion, a panel of Italian experts has met to examine the literature, discuss the topics, and produce evidence-based recommendations, which could be worthwhile for the everyday clinical practice. The reader will find in this book the actual state of the art regarding laparoscopic cholecystectomy, divided into technical and medical issues that summarize the evidence about indications, operating strategy, safety, complications, new technologies, and comprehending details that are generally left to the personal inclination of the surgeon without a real scientific effort to find out what is best. The will to dedicate a chapter of the book to the patients, thanks to the presence in the authors' panel of a foundation called "Chirurgo e Cittadino" (surgeon and citizen), opens a new perspective for the surgeon, where quality of life, examined from the patient's point of view, is a mainstay for the evaluation and the validation both of a correct clinical behavior and the introduction of a new technology.

We hope that our effort will serve, at least, to stimulate the curiosity of surgeons and the improvement of what we do.

Ferdinando Agresta, MD
Fabio Cesare Campanile, MD, FACS
Nereo Vettoretto, MD

Addendum

The authors of this book adopted the following methodology for literature search and appraisal: the primary objective of the search was to identify all clinical relevant randomized controlled trials (RCT) and meta-analysis. Afterwards, other reports, population-based outcome studies, case series, and case reports have been also included. A systematic review based on comprehensive literature search has been made on PubMed according to the following criteria:

Limits Activated: *Humans*, *Clinical Trial*, *Meta-Analysis*, *Practice Guideline*, *Randomized Controlled Trial*, *Review*, *English*, *All Adult*: *19+ years*, *published in the last 20 years. Search details*: [((“*laparoscopy*”[*MeSH Terms*] *OR* “*laparoscopic*”[*All Fields*]) *AND* (“*condition-specific key word* ”[*MeSH Terms*] *OR* “ *condition-specific key word*”[*All Fields*])) *AND* (“*humans*”[*MeSH Terms*] *AND* (*Clinical Trial*[*ptyp*] *OR Meta-Analysis*[*ptyp*] *OR Practice Guideline*[*ptyp*] *OR Randomized Controlled Trial*[*ptyp*] *OR Review*[*ptyp*]) *AND English*[*lang*] *AND* “*adult*”[*MeSH Terms*] *AND* “*1995/1/1*”[*PDat*]: “*2013/12/31*”[*PDat*])].

Then, limits regarding language, age, and publication date and study type have been removed, to search for additional papers. Cross-link control was performed with Google Scholar and Cochrane library databases. The full text paper was obtained for all relevant articles. The papers have been selected and classified on the basis of the highest level of evidence, design of the study, and most recent publication. The 2011 Oxford hierarchy for grading clinical studies according to levels of evidence (LoE) has been used. Studies containing severe methodological flaws have been downgraded as necessary. For each intervention, the validity and homogeneity of study results, effect sizes, safety, and economic consequences have been considered.

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Contents

Laparoscopic Cholecystectomy: Besides the Evidence (What Is Really Done In the World)

1

Ferdinando Agresta, Fabio Cesare Campanile, and Nereo Vettoretto

It does not matter if, thinking to laparoscopy, we speak of "revolution" or "evolution": laparoscopic cholecystectomy (LC) is nowadays considered the gold standard therapy for gallstone diseases, both in scheduled as in emergency cases, and it is done in every hospital setting. The literature about LC might be considered overabundant, and it may be argued that most reports might reflect mainly the results of larger and dedicated centers. At the same time, it is important to find out what is the "true" practice of LC around the world, besides what is "perceived" or "reported."

As editors of a book concerning laparoscopic cholecystectomy, along with the evidence, we wanted to examine the available data from national surveys, audits, and registry.

We have done a research on PubMed – *search details*: [(("*laparoscopy*"[*MeSH Terms*] *or* "*laparoscopic*"[*All Fields*]) *and* ("*cholecystectomy*"[*MeSH Terms*] *or* "*cholecystectomy*"[*All Fields*])) *and* ("*register*"[*MeSH Terms*] *or databse*[*ptyp*] *or national survey*[*ptyp*] *OR audit*[*ptyp*]) *and English*[*lang*] *and* "*adult*"[*MeSH Terms*] *and* "*1995/1/1*"[*PDat*]: "*2014/01/01*"[*PDat*])]. And these are the "practice evidences" we have found.

In the last decades, the number of cholecystectomies increased worldwide. This rising trend is mainly attributable to the diffusion of LC (about 90 % of all the cholecystectomies) even in population where patients are covered by a national health

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system. The question arises if this low threshold for the laparoscopic approach to gallstone disease is always justified by evidence-based medical indications (such as more symptomatic gallstone diseases) [1–3].

The demographics of the Western world is changing: in the last century the general population increased of almost 10 %, but the number of inhabitants older than 65 years increased more than 50 %. Surely, age is an independent negative predictor for outcome after cholecystectomy, especially in an acute setting, where the probability to be operated on during the same admission period ranges from 20 to 57 % [4–6].

However, as reported in a recent study from Denmark, more than 60 % of otherwise healthy octuagenarian patients had a fast and uncomplicated course if undergoing surgery before acute inflammatory complications occurred. Thus, elective laparoscopic cholecystectomy has been recommended also for the elderly when repeated gallstone symptoms have occurred, particularly before the patient experiences acute cholecystitis [7].

It is surprising to find in some national reports that acute cholecystitis (AC) is treated expectantly in almost 50 % of the cases, although several guidelines suggest the surgical therapy as standard. The probability of a subsequent gallstone-related event might reach 30 % in the first year, in those discharged without cholecystectomy. Of these events, 30 % might be for biliary tract obstruction or pancreatitis. When controlling for sex, income, and comorbidity level, the risk of a gallstone-related event is highest for young patients (18–34 years old) [5–8].

The long-term effectiveness of cholecystectomy and endoscopic sphincterotomy (ES) in the management of gallstone pancreatitis has been confirmed by data from the NHS hospitals in England on 5,079 patients. Recurrent pancreatitis after definitive treatment was more common among patients treated only with ES (6.7 %) than among those treated with cholecystectomy (4.4 %) or ES followed by cholecystectomy (1.2 %) ($p \leq 0.05$). Admissions with other complications attributable to gallstones in patients treated with ES alone were similar to those seen in patients who had received no definitive treatment (12.2 vs. 9.4 %) [9].

When surgery is performed, LC is surely the treatment of choice for the acute setting, with more than 80 % of the procedures done with a laparoscopic approach. Primary open cholecystectomy is often chosen by surgeons when the patient is older and has a history of previous abdominal surgery or gangrenous cholecystitis is suspected. The conversion rate ranges from 3 to 30 % [10, 11].

About this last point, a recent population-based analysis of 4,113 patients with acute cholecystitis from the Swiss Association for Laparoscopic and Thoracoscopic Surgery [12] clearly demonstrates that delaying LC resulted in significantly higher conversion rates (from 11.9 % at day of admission surgery to 27.9 % at more than 6 days after admission, $p < 0.001$), surgical postoperative complications (5.7–13 %, $p < 0.001$), and reoperation rates (0.9–3 %, $p = 0.007$), with a significantly longer postoperative hospital stay ($p < 0.001$). These data are confirmed by two other population studies from the United States [13, 14].

On the other hand, if the delayed surgery is prevailing, it has been shown that LC in treating AC cannot show its superiority over the open approach in terms of postoperative complication rate and medical resource utilization [15, 16].

The risk of bile duct injury (BDI) in LC has drawn wide attention from the beginning of the laparoscopic era, after reports of an increase in the incidence of BDI (twice as open cholecystectomy) [17, 18].

The earlier reports, however, are not homogeneous, ranging from 0.1 to 0.45 %, and, what is surprising, with a lower rate reported in national registries than in retrospective multicenter surveys [19–22].

In addition, more recent data from registries are available. In Germany, the Institute for Applied Quality Improvement and Research in Health Care GmbH (AQUA) (commissioned by the Federal Joint Committee to collect and analyze data for quality assurance) has recently published its data: about 90 % of 172,368 cholecystectomies performed for benign disease were performed laparoscopically. Overall (laparoscopic and open approach) an "occlusion or transection of the CBD" was registered in 177 operations (0.1 %); the reintervention rate for all reasons (including BDI) was 0.9 %. The rate of intervention-specific complications requiring treatment after laparoscopically initiated surgery in 2010 was 2.4 % [23].

In Denmark (data from the Danish Cholecystectomy Database), 28,379 patients underwent a cholecystectomy between 2006 and 2009, with complete registration of data in 24,240 patients. A laparoscopic procedure was started in 97.7 % and completed in 92.6 %. A reconstructive bile duct surgery, within 30 days, had to be conducted in 0.1 % (2007) to 0.25 % (2008); another bile duct surgery within 30 days had to be conducted in 0.11 % (2009) to 0.19 % (2007) [24, 25].

In a large retrospectively analyzed Finnish cohort of 8,349 cholecystectomies, 75 BDIs were encountered (0.9 %). The incidence was 1.24 % (20/1,616) for the open and 0.82 % (55/6,733) for the laparoscopic approach. In open surgery, most reported injuries were minor (15/20), while in the laparoscopic cholecystectomies mostly were severe (29 of 55, 14 of them with complete transection or excision of common bile duct) [26]. This data is confirmed by another recent retrospective review of medical record from Kaiser Permanente Northern California (KPNC): 83,449 patients who underwent laparoscopic cholecystectomy (LC) between 1995 and 2008 were included in the study. A cumulative BDI rate of 0.04 % was found, less than a half of what is reported in the Nationwide Inpatient Sample (NIS) (0.11 %). The authors, analyzing the type of injuries, found a trend toward more severe injuries approaching the hilum and fewer distal or minor injuries without significant differences [27].

In conclusion, OC seems to be associated with a higher number of BDI but mostly classified as minor, while LC seems to be associated with less but more severe lesions.

The "critical view of safety" advocated by Strasberg is generally accepted as a safe method to obtain an overview of the key anatomical structures that should be clearly identified before clipping and transecting the cystic duct (we will analyze it in the following chapter). Recent studies report that most surgeons (up to 85 %) stated that they routinely dissect Calot's triangle to provide a critical view of safety, to minimize the risk of bile duct injury during cholecystectomy [28]. Conversely, a recent Dutch survey reported that although it has been included in the *Best Practice for Laparoscopic Cholecystectomy* published by the Dutch Society of Surgery, the concept of a critical view of safety failed to gain wide acceptance in the Netherlands [29].

Several published papers suggest that desirable outcome could be related to the caseload of a hospital or a surgeon. Therefore, volume is often taken as a proxy measure for quality, particularly that for prevalent or possible high-risk procedures, including LC. The reports about this topic in the literature are scanty and have to be taken into consideration very cautiously for the wide variation among hospitals of the same area/region/nation in the management of gallstone disease. A Scottish study reports a lower risk of morbidity and mortality in high-volume centers, significant only for elderly patients and patients with comorbidity. On the other hand, its clinical value seems to be negligible for those at average risk [2, 30].

Nevertheless, patient and hospital demographics do affect the outcomes of patients undergoing cholecystectomy. Although male gender, African American race, Medicare-insured status, and large, urban hospitals are associated with less favorable cholecystectomy outcomes, only increased age predicts increased morbidity, whereas female gender, laparoscopy, and cholangiogram are protective. Increased age, complications, and emergency surgery are predicting factors for mortality, while laparoscopy and intraoperative cholangiogram have a protective effect [31].

Mortality: A low operative mortality of 0.4–0.6 % is reported, but with a 90-day mortality up to 0.8 %. In a survey from Sweden [32], the mortality risk, calculated as standard mortality ratio (SMR), was 1.01 % for the open and 0.56 % for the laparoscopic cholecystectomy. This difference is probably related to the higher risk of the population selected for open cholecystectomy. The recent "Scottish Audit of Surgical Mortality (SAMA)" analyzed the decade 1997–2006 [33]. Gallstone disease was responsible for 790/43,271 (1.83 %) of the surgical deaths recorded, with an overall mortality for cholecystectomy of 0.307 %, endoscopic retrograde cholangiopancreatography (ERCP) of 0.313 %, and cholecystostomy of 2.1 % (12/578). However, the majority of patients who died were elderly (47.6 % ≥80 years or older) and managed conservatively. Deaths following cholecystectomy usually followed emergency admission (76 %) and were more likely to have been associated with postoperative medical complications ($n = 189$) rather than surgical complications. This finding might suggest that enhanced medical management of these patients and attention to the patient pathway – diagnostic as therapeutic – may be necessary to reduce mortality from gallstones [34].

Just a Final Consideration (Not a Conclusion): In the early phase of the laparoscopic "revolution," several large surgical registries have been implemented, but only few of them have been extensively updated. The latter have reported improvements in quality indicators concerning LC, such as the number of unplanned readmission after LC when the procedures were performed by surgeons with appropriate training or the rate of same-day surgery. Moreover, conversion to open surgery is nowadays mainly reported in acute and complicated cases, and it could be possible to wonder if the disposition to "conversion" might be considered a positive factor, for the prevention of major complications (one for all: BDI) [24, 30–40].

As already stated for another disease [41], we wonder if this is the time to find our healthcare policies on multidisciplinary evidence-based guidelines, thoroughly divulgated (by scientific societies), whose results are collected and measured (by the healthcare organizations) and finally audited together (by clinicians, epidemiologists, patients, and healthcare organizations).

Rarely a new technique has been analyzed (even in nonacademic institutions) with such enthusiastic participation, with such a large number of published cases in a long period of time. Besides changing the surgical approach to cholecystectomy, laparoscopy has increased the interest and participation of surgical teams in the scientific evaluation of their work. This may be another benefit of this approach.

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2 Operative Strategies in Laparoscopic Cholecystectomy: Is There Any Evidence?

Fabio Cesare Campanile, Ferdinando Agresta, Nereo Vettoretto, Roberto Cirocchi, and Mario Campli

2.1 Introduction

The laparoscopic revolution in general surgery began between 1985 and 1987, when laparoscopic cholecystectomy was introduced. The development of the technique to perform a cholecystectomy by laparoscopy was the beginning of a radical change that, in a few years, involved general surgeons all over the world. The enormous interest enjoyed by the laparoscopic cholecystectomy spread shortly in all other sectors of general surgery.

During the following years, many surgeons, throughout the world, learned how to perform a laparoscopic cholecystectomy; most surgeons keep practicing the same technique that they had learned in the first place; the technical details they use are a

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matter of personal preference and are not systematically confronted with other propositions. The purpose of this chapter is to examine some of those technical details and find out if there is any evidence in their support.

2.2 Position of the Patient

The first laparoscopic cholecystectomy was performed in 1985 by the German surgeon Erich Mühe, who presented his experience at the Congress of the German Surgical Society (GSS) in April of 1986. However, Phillipe Mouret in Lyon has generally been given credit for developing the first laparoscopic cholecystectomy as we know it today. In 1987, he added a cholecystectomy to a planned laparoscopic gynecological adhesiolysis. Shortly thereafter, François Dubois, in Paris, and Jacques Perissat in Bordeaux began to perform laparoscopic cholecystectomies.

In 1989, Perissat attracted a great interest at the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) meeting with a video on laparoscopic cholecystectomy, and Dubois published the first series on Annals of Surgery in 1990.

Simultaneously to the French, the American surgeons Barry McKernan and William Saye performed the first laparoscopic cholecystectomy in the United States in 1988. Then, Nashville surgeons Eddie Reddick and Douglas Olsen began performing the operation on a regular basis, in their private practice, outside the main academic centers; they also introduced the laser technology and started the first educational program about laparoscopic general surgery. Their educational effort has to be credited for the widespread diffusion of laparoscopic cholecystectomy in the United States, where it was soon regularly adopted: the first large multi-institution clinical series was published in 1991 by the Southern Surgical Group [1]; Cappuccino et al. reported, for the Monmouth Medical Center Laparoscopic Cholecystectomy Group, the first large single institution experience in 1994 [2].

This simultaneous beginning on both sides of the Atlantic explains the coexistence of two techniques, different in several points: French and American (Figs. 2.1 and 2.2). The former approach is common in Europe (especially France and Germany), but the latter is dominant elsewhere.

The position of the patient and the surgical team differs between the two techniques: the patient's legs are divaricated with the surgeon standing between them, in the former, but closed, with the surgeon on the left side of the operating table, in the latter. In both cases, the optical port is at the umbilicus; the operating cannula (for the dissecting instruments) is in the left upper quadrant in the French technique but just below the xiphoid process in the American one. A slight reverse Trendelenburg position and left-sided rotation are enough to allow an easy access to the operating surgeon in the American position, while a steeper reverse Trendelenburg is necessary, in the French position, to bring the operating field closer to the surgeon standing at the pelvis of the patient. The displacement of the liver is trusted to a probe inserted in a cannula positioned just below the costal margin, at the midclavicular line, in the French technique, and the triangle of Calot is exposed by downward and

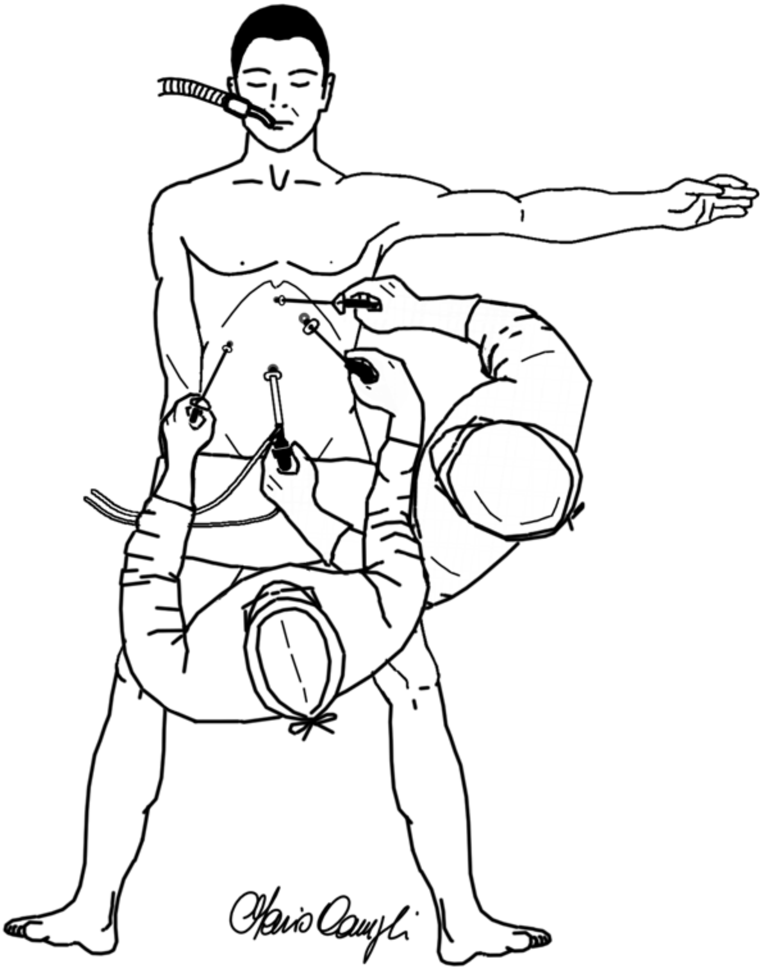

Fig. 2.1 French position

lateral retraction of the gallbladder infundibulum. The American exposure of the surgical field is accomplished, instead, by the assistant who grasps the fundus of the gallbladder, bringing it over the anterior edge of the right lobe of the liver; in this way he rotates upwards the liver itself and exposes the hilum of the gallbladder. In the original American description, the dissection starts at the gallbladder-cystic duct junction, if visible, or high upon the gallbladder otherwise, pulling down the overlying fat until the cystic duct is seen (infundibular technique).

The initial experience demonstrated that the combination of excessive upward traction on the gallbladder and dissection at its infundibulum could be responsible for some common bile duct lesions: the common bile duct can be parallel to the cystic duct, reducing the angle between the two structures, and the choledochus, unduly pulled upwards, can appear in line with the cystic duct and be mistaken for

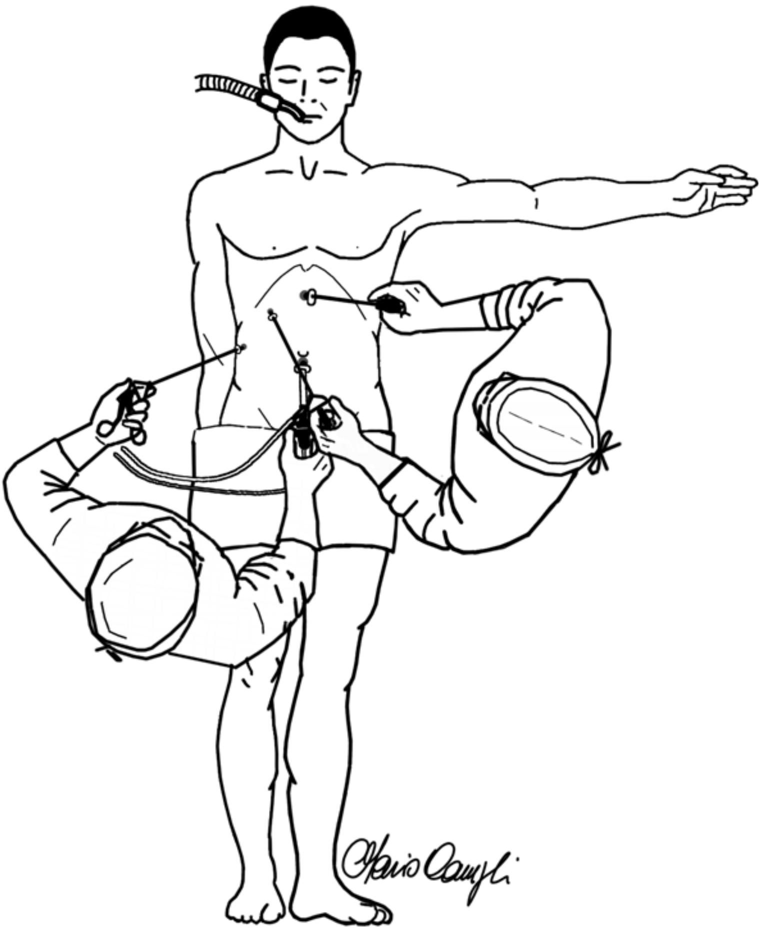

Fig. 2.2 American position

it (Fig. 2.3) [3, 4]. The American technique, then, abandoned the excessive traction on the gallbladder and adopted a lateral retraction of the Hartmann pouch, to keep the cystic duct at an angle with the common bile duct.

On the other hand, the left-sided position of the operating trocar, in the French technique, worried some surgeons. They feared that the passage of the operating instruments from a faraway position towards the surgical fields could provoke some visceral lesion if accidentally introduced without visual control. Therefore, they started adopting the "American" trocar disposition even in an otherwise "French" setting. Beyond description, little has been published about a comparison between the two techniques and how they can affect laparoscopic cholecystectomy performance and outcomes. No evidence-based recommendation can be issued, and the choice is still a matter of personal preference or custom. In particular, no controlled study examined the operative complications of procedures performed with technical details related to these different approaches.

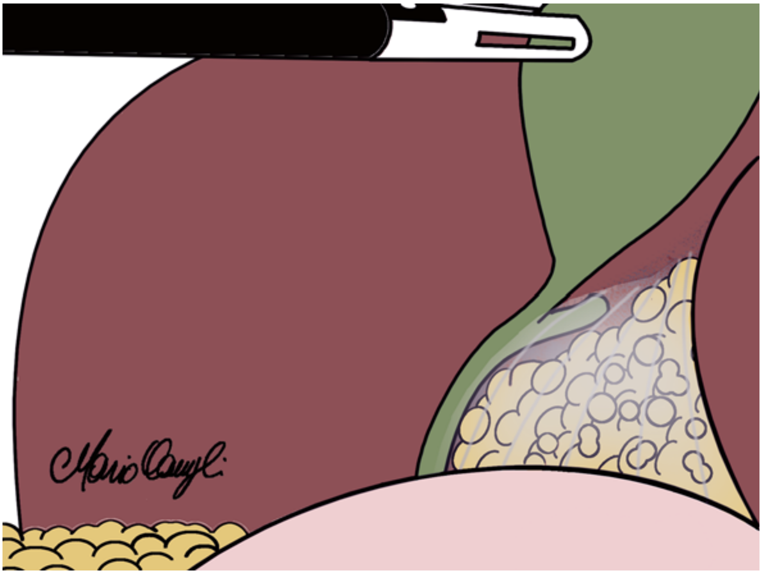

Fig. 2.3 Excessive upward and medial traction can bring the choledochus in line with the cystic duct

One small randomized trial observed that forced vital capacity and forced expiratory volume in 1 s postoperatively were significantly less after laparoscopic cholecystectomy performed according to the American approach and concluded that the French method leads to less impairment of the respiratory function. The authors put the results into relation with the more cranial position of the trocars in the American technique and to the likely different location of the pain. It has to be observed, however, that the American technique presented in the study includes the extraction of the gallbladder through the epigastric port (while it is most commonly extracted through the umbilical port), and the need to enlarge the incision at this level to allow the removal of the organ could have contributed to the unfavorable result. They also reported one duodenal lesion (out of 23 patients) in the "French" group (LoE2) [5].

There may be several other factors in favor or against one or the other technique. The lithotomy position has been associated with complications rarely occurring in the supine position. These include neurovascular injury to the lower extremities, deep venous thrombosis, compartment syndrome, and osteofascial sclerosis [6]. In addition, proponents of the American position observe that the surgeon between the legs of the patient, stands at a greater distance from the focus of the surgical action and back stretching is often necessary to reach the instruments, despite the greater anti-Trendelenburg angle. Besides, the camera and the arm of the camera driver often interfere with a comfortable position of the surgeon pushed backwards when pan out is necessary. On the other hand, the supporters of the French technique maintain that a better triangulation is achievable, and the surgeon does not need to rotate the trunk and reach over the patient to handle the grasping instrument, with a more comfortable upper limb position. Several studies analyzed the ergonomics of the surgeon's posture in relation to the position of the monitor, without specifically referring to the differences among the two most common operating room settings. Instead, the effects of the French and American approach have been compared, in regard to surgeons' learning, performance, and ergonomics, at the Maryland Advanced Simulation, Training, Research and Innovation (MASTRI) Center of the University of Maryland Medical Center [7, 8]. A number of surgeons, at a different level of training, performed four laparoscopic cholecystectomies in a virtual reality surgical simulator. The physical ergonomics were assessed using a tool ("Rapid Upper Limb Assessment, RULA") developed and validated specifically to investigate the exposure of individuals to risk factors associated with work-related upper limb disorders. Mental workload assessment was achieved through the use of the National Aeronautics and Space Administration-Task Load Index (NASA-TLX). A performance evaluation was also obtained, analyzing the report automatically generated by the simulator at the end of each procedure. According to the scores obtained, the position between the legs of the patient appeared to be the most ergonomically sound from both the physical and cognitive point of view. However, the excellent study has some relevant limitations that can introduce some bias in the conclusions. The performance on the virtual simulator does not necessarily reproduce a real-life situation. In particular, the dimensions of the camera equipment and the distance between the surgeon and the "surgical" field appear to be inferior than in a true operating room situation; the surgeon stands much closer to the optical and operating ports of the simulator than to the respective points on real patients because the simulator does not have legs and pelvis. Therefore, the position of the surgeon's body, in the French position, does not appear to be as stretched as in real life. Besides, the shorter camera equipment does not appear to interfere with the surgeon's abdomen, as in real life is often the case. In addition, no data are provided with regard to previous experience of the operators with one or the other examined techniques.

2.3 Technique of Dissection

Since 1990, the beginning of the era of laparoscopic cholecystectomy, Sir Alfred Cuschieri alerted surgeons to be cautious, in order to avoid a rise in surgically induced morbidity [9]. More than 20 years after, the rate of iatrogenic major biliary injury (0.4 %) counts for an almost threefold increase if compared to the traditional open operation (LoE4) [10]. The debate has regained interest since the introduction of new technologies and reduced port surgery for laparoscopic cholecystectomy [11]. An Italian survey confirms an incidence of 0.42 % on major bile duct injuries on 56,591 laparoscopic cholecystectomies, with higher rates in cholecystitis and low-volume practice subgroups (LoE4) [12]. The approach to the gallbladder's pedicle can be of utmost importance for the prevention of these injuries. Three main techniques have been standardized. The oldest and most common approach is the infundibular one, in which the dissection starts from the infundibulum and deepens into Calot's triangle. To allow the correct identification of the cystic duct and artery,

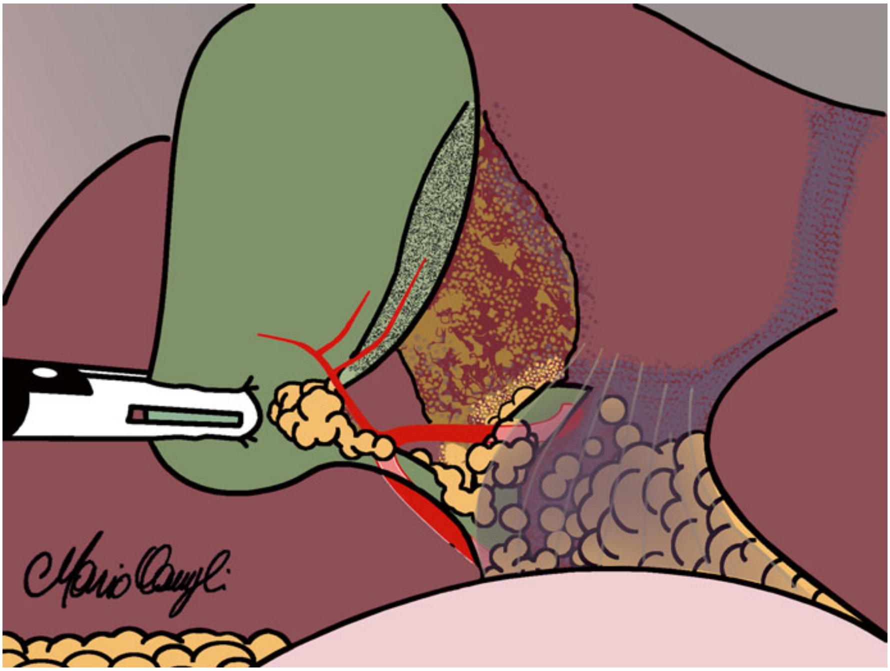

Fig. 2.4 Excessive lateral traction can pull the hepatic artery into the field of dissection

many maneuvers have been analyzed [4]. Identification of the cystic duct at the junction with the gallbladder is considered the first essential step. Many authors consider mandatory the dissection of the cystic duct until the T-junction of the cystic to the common bile duct could be seen (LoE4) [13]. Once the junction of the cystic duct to the gallbladder and common bile duct was identified, a complete dissection of Calot's triangle is deemed safe. Other surgeons preferred to stay away from the risk of injuring vascular or biliary anatomical variants, frequently located in the area medial to the cystic duct, and omitted, therefore, a routine search for the common bile duct junction [4, 14]. As a matter of fact, most common bile duct injuries are related to an unclear anatomy, either due to fibrosis and adhesions or to anatomical variations. The latter are quite common in particular within the triangle of Calot [15, 16]. We already mentioned the possibility that a superior and medial traction of the infundibulum could bring the common bile duct in line with the cystic duct; thus the former could be interpreted as the latter and injured (Fig. 2.3). Also, an excessive lateral traction could bring the hepatic artery in the field of dissection (Fig. 2.4). Another "error trap" to avoid is the misinterpretation of the common hepatic duct for the gallbladder wall in severe inflammation [17]. The extension of the cystic duct dissection medially to the confluence with the common hepatic duct might clarify the biliary anatomy like Katkhouda suggests in the "visual cholangiography" technique (LoE5) [18]. Routine intraoperative cholangiography has been advocated by many authors, although its use, especially in emergency, requires a more

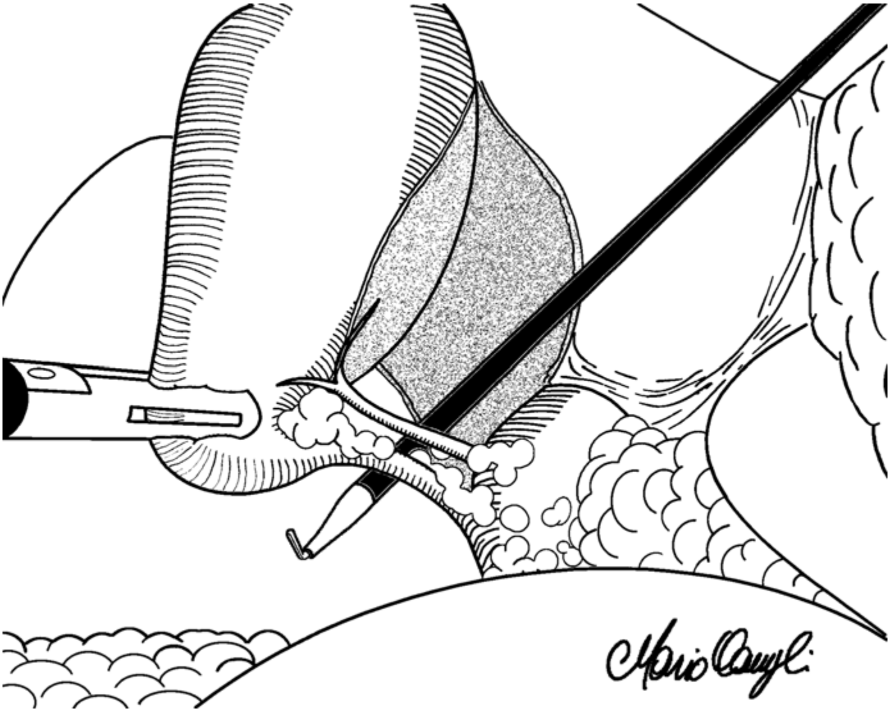

Fig. 2.5 Critical view of safety

complex organization of the operating theater and a good expertise of the surgical team. Alas, it does not seem to prevent biliary injuries, even if it helps their immediate identification (LoE4) [19].

Strasberg, in the early 1990s, introduced the "critical view of safety" (CVS) which involves the dissection of the entire infundibulum from all the fatty tissue, both in its dorsal and ventral aspects (LoE2) (Fig. 2.5) [20]. These principles have been unattended until recent years, in which a standardization of the technique, together with some consistent data confirming Strasberg's hypothesis, has been published (LoE4) [21, 22]. The results seem promising, as in a series of 3,042 patients, where the observed BDI rate lowers of an order of magnitude, thus overwhelming the results of routine cholangiography (LoE4) [23]. The approach is considered viable even for NOTES gallbladder surgery (LoE5) [24]. The validity of the technique has been tested even in acute cholecystitis (performed by entering the inner subserosal layer for dissection) (LoE4) [25]. Even if there is no comparative evidence to prove a reduction in the bile duct injuries with the use of this technique, it is now widely accepted (even in guidelines) as it does not require additive costs or operative time [26]. An evolution of the concept of critical view of safety is the so-called triangle of safety technique (TST). This approach to the infundibulum is described both in the American and the French trocars' position [27, 28]. A cephalad hang-up of the fundus is obtained by a grasper, together with the lateralization

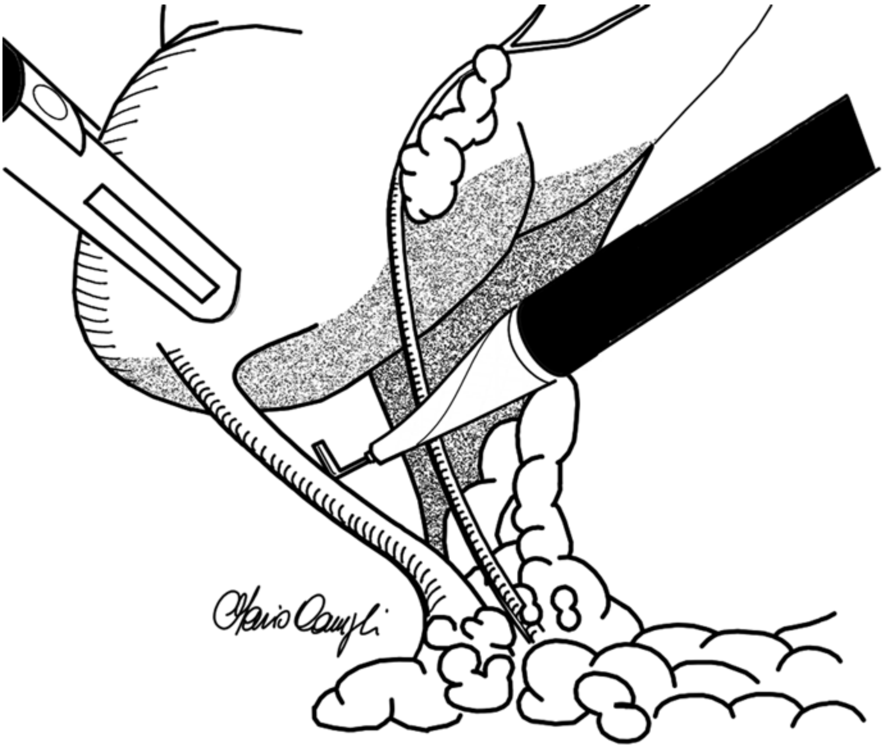

Fig. 2.6 Triangle of safety technique

of the infundibulum. A complete incision of the serosa is performed both in the medial and lateral aspect of the infundibulum and extended upwards almost to the fundus. The medial incision is performed over the vertical fatty line visible on the gallbladder wall; it usually corresponds to the anterior cystic artery which is dissected on the gallbladder surface in order to obtain its medial release. The section of Calot's artery (which connects the cystic artery to the cystic duct) permits access to the critical safety triangle, set between the gallbladder wall on the right, cystic duct inferiorly, and cystic artery on the left. The entire fatty dissection of this triangle and the mobilization of the infundibulum, both anteriorly and posteriorly, permit the visualization of the liver surface through the triangle, well above Rouviere's sulcus (Fig. 2.6) in order to obtain the "critical view." This triangle, which represents the most lateral part of the Calot's triangle, is generally free of biliary and arterial anomalies, thus permitting a safe and quick dissection, without accidental bleedings which might cause, as a consequence, an inadvertent injury to the biliary ducts [29]. The clipping and the section of the duct, next to the gallbladder, the clipping of the artery and the retrograde dissection of the gallbladder complete the operation. The two cited studies (the former retrospective on 491 patients, the latter a case comparison with the infundibular technique on 174 patients) are not powered to draw conclusions on biliary injuries; alas they acknowledge a reduction of the operative time,

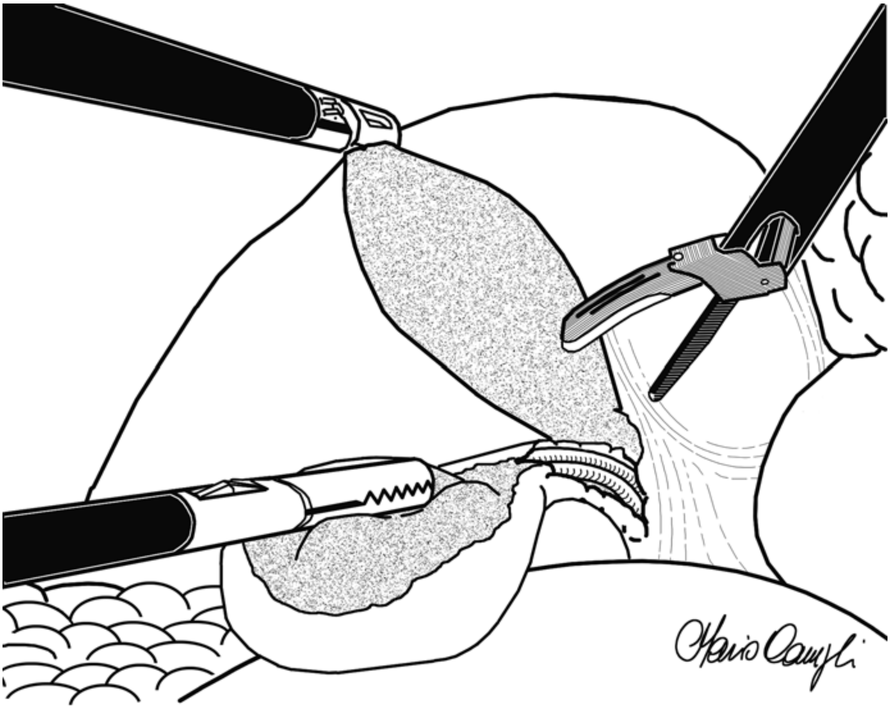

Fig. 2.7 Dome-down or fundus-first technique

a reduction in perioperative morbidity (including intraoperative bleedings), and a null rate of major biliary injuries. These results have been obtained by junior surgeons in both studies, and this reflects increased confidence due to the technique, which probably gives more security to the surgeon, both in inflamed and uninflamed anatomy.

Dissemination of a standardized technique, especially in teaching hospitals and district hospitals or anywhere laparoscopic experience is limited, is desirable. The results of CVS and TST forecast the approach as the future gold standard in the dissection of the gallbladder elements, and further diffusion of the technique is important, especially for training purposes.

During the same period (mid-1990s), another way of laparoscopic dissection was proposed: the "dome-down" or "fundus-first" technique (Fig. 2.7) [30, 31]. Such an "antegrade" strategy was already well recognized as a safe technique for "open" cholecystectomy, especially for difficult situations. The possibility to reduce the risks of damage to the structures in or around Calot's triangle makes this choice particularly popular to reduce the conversion rate for acute cholecystitis (LoE4) [32, 33] and other situations with dense peri-infundibular adhesions or difficult anatomy. The technique involves the dissection of the gallbladder from the liver bed before the dissection of the Calot's triangle is completed. The retraction of the liver is accomplished either grasping the peritoneal flap created between the fundus and the liver or using a liver retractor. The cystic duct and artery are identified after the gallbladder has been completely separated from the liver: usually at this point, as in open surgery, the anatomical relationships are safely clarified (Fig. 2.6). There is a concern, however, regarding the possible lesions to the right hepatic artery, which might be pulled downwards, together with the gallbladder, especially in an inflamed setting (LoE5) [17].

A recent review of observational studies about "difficult" laparoscopic cholecystectomies by Hussain (LoE3) showed that the "dome-down" technique significantly reduced complications and conversion rates in that particular setting [34]. A randomized controlled trial, published in 2004, confirmed that the technique can lower the conversion rate; the report, however, does not provide us with demographic data and clinical details about the study and the control group and its randomization method is not described (LoE3) [35]. Another recent RCT examined the issue of the fundus-down approach in a series of "contracted" gallbladders; lower conversion and complication rates were demonstrated, along with a shorter postoperative stay. Unfortunately, the alternate allocations of the patient to the study and control group prevent this study to be considered a true randomized study (LoE3), but its results are still quite interesting [36].

In the fundus-down technique, the dissection of the gallbladder from the liver bed is generally accomplished without prior ligation of the cystic artery, which could cause increased bleeding. For this reason, many surgeons found that the ultrasound dissection is particularly useful [33, 37]. Cengiz et al. published a randomized controlled trial in which 243 elective patients were randomly assigned to three groups: "conventional" retrograde laparoscopic cholecystectomy with electrocautery, dome-down cholecystectomy with electrocautery, and ultrasound dissector. The fundus-first method had a shorter operating time with ultrasonic dissection (58 min) than with electrocautery (74 min; $p=0.002$). The fundus-first method using ultrasonic dissection produced significantly less blood loss than the conventional method or the fundus-first with electrocautery (12 vs. 36 or 53 ml; $p<0.001$), fewer gallbladder perforations, less pain and nausea, and shorter sick leave (LoE2) [38].

Conclusions

The questions related to the surgical technique for laparoscopic cholecystectomy have been systematically studied only occasionally. However, some evidences about the different choices are available, and we should take them into consideration in our clinical practice. Although laparoscopic cholecystectomy is considered a straightforward "bread and butter" surgical operation, it can be a real challenge in several common instances. The full knowledge of the available operative strategies, their proven benefits and possible downsides, can be extremely advantageous.

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Indications to Laparoscopic Cholecystectomy

3

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3.1 Introduction

The panel of 1994 EAES Consensus Conference on LC answering to the question "Who should undergo an LC?" stated that LC is indicated in symptomatic gallbladder disease patients who are able to tolerate general anesthesia including patients with porcelain gallbladder. On the other hand the panelist identified two special subgroups of patients:

- Symptomless gallstone cases that should be followed up closely (diabetic, sickle cell anemia, those on long-term somatostatin treatment, etc.)
- Patients who required "extreme caution" and an "expert surgeon" (acute cholecystitis, pregnancy, elderly, etc.)

  Finally the absolute contraindications were reported based on the 1994 evidence.

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During the last 18 years LC has been accepted in the surgical and medical community and is the most diffuse laparoscopic procedure worldwide. A large number of papers have been published during this long interval of time and the indications for LC have to be revisited according to the new evidence provided by the literature.

3.2 Asymptomatic Gallbladder Diseases

According to the GREPCO (Gruppo Romano per l'Epidemiologia e la Prevenzione della Colelitiasi) study, cholelithiasis is defined as asymptomatic when gallstones are detected in the absence of gallstone-related symptoms, such as history of biliary pain, or gallstone-related complications, such as acute cholecystitis, cholangitis, or pancreatitis. Other nonspecific symptoms or vague dyspeptic problems, such as epigastric discomfort, dyspepsia, flatulence, nausea, abdominal gurgling noises, or pain outside the right hypochondrium, cannot be considered as symptomatic cholelithiasis and could easily be attributed to other gastrointestinal diseases [1–4] [LoE3].

It is estimated that 10–25 % of the population have gallstones [1, 4–6] [LoE3] and among them 50–80 % are asymptomatic at diagnosis [6, 7] [LoE3] (in Italy 84.9 % of females and 87 % of males) [8, 9]. Several studies report a frequency of symptom development of 10 % after the first 5 years and of 20 % after 20 years [4–6, 10–13] [LoE3-LoE4]. The mean yearly probability of biliary pain is 2 % during the first 5 years, 1 % during the second 5 years, 0.5 % during the third 5 years, and 0 % during the fourth 5 years [11, 14] [LoE4], so the annual risk for severe and non-severe events decreases with time [7, 15] [LoE3]. The annual complication rate of initially asymptomatic patients is 0.3–3 % [7, 16, 17] [LoE3].

The progression of asymptomatic to symptomatic disease is relatively low, and the majority of patients rarely develop gallstone-related complications without first having at least one episode of biliary pain [1, 4, 5, 12, 18] [LoE3-LoE4]. In this view most authors agree that the management of asymptomatic cholelithiasis should be expectant [1, 4, 7, 19, 20] [LoE3]. The evidence of a 24-year follow-up of 134 asymptomatic gallstone patients suggested that only 6 % of patients experienced symptoms that led to cholecystectomy and no adverse events could be ascertained from expectant management of asymptomatic patients [21] [LoE3].

Nevertheless some patients develop potentially severe or even lethal gallstone-related complications, such as cholecystitis or pancreatitis, and some might require emergency operations which are associated with considerable technical difficulties that frequently make conversion to laparotomy mandatory, with higher morbidity and mortality rates than with simple elective laparoscopic cholecystectomy.

In this view Patino and Quintero [1] [LoE3] tried to classify asymptomatic patients into two groups:

(a) Low-risk group for which no therapy is recommended
(b) High-risk group which is more likely to develop complications

The first comprises patients with a functioning gallbladder whose calculi are >3 mm but <2 cm in diameter and radiolucent without concomitant serious diseases.

The second includes patients with stones larger than 2.5 cm and those with small multiple calculi (<3 mm in diameter), biliary sludge, or both, who tend to develop acute cholangitis or pancreatitis.

The authors recommend elective laparoscopic cholecystectomy in asymptomatic patients who fulfill the following criteria:

- Life expectancy >20 years
- Calculi >2 cm in diameter
- Calculi <3 mm in diameter and patent cystic duct
- Radiopaque calculi
- Calcified calculi
- Polyps in the gallbladder
- Nonfunctioning gallbladder
- Calcified gallbladder or "porcelain gallbladder"
- Diabetes mellitus
- Severe concomitant chronic diseases
- Woman <60 years
- Individuals living in regions with a high prevalence of gallbladder cancer

On this basis Sakorafas [6] [LoE3] gave clear and relative indications for selective cholecystectomy in asymptomatic cholelithiasis:

Clear Indications

- Suspicion/risk of malignancy
  Gallstones associated with gallbladder polyps >1 cm in diameter
  Calcified (porcelain) gallbladder
  Some ethnic groups or subjects living in areas with high prevalence of gallbladder cancer associated with gallstones (American Indians, Mexican Americans, Colombia, Chile, Bolivia, Maori population of New Zealand)
  Presence of large (≥3 cm) gallstones
- Asymptomatic cholelithiasis associated with choledocholithiasis
- Transplant patients (before or during transplantation)
- Chronic hemolytic conditions (sickle cell anemia)

Relative Indications

- Increased risk of progression from asymptomatic to symptomatic disease
  Life expectancy >20 years
  Calculi >2 cm in diameter
  Calculi <3 mm and patent cystic duct
  Nonfunctioning gallbladder
- Diabetes mellitus
- Vague dyspeptic symptoms in the presence of gallstones

Questionable Indications

- Patient living in an area remote from medical facilities
- Incidental (concomitant) cholecystectomy during another abdominal operation

In 2009 the conclusion of the Cochrane Review on "cholecystectomy for patients with silent gallstones" [22] [LoE3] was: "there is no evidence in literature to either recommend or refuse surgery to patients with asymptomatic gallstones (no randomized or controlled trial comparing LC vs. no-LC available)." This conclusion was stated in absence of high-quality studies whitout considering the history of gallbladder stone diseases and the high-quality data on long-term follow-up demonstrating the very low percentage of patients developing symptoms and stone-related complications. The same authors stimulated prospective trial to evaluate the ethic issue of the LC morbi-mortality.

In 2012 Duncan and Riall [23] [LoE3] reviewing the evidence-based current surgical practice for calculous gallbladder diseases conclude that prophylactic laparoscopic cholecystectomy for asymptomatic gallstone patients is still not recommended.

Analyzing the latest data available in literature, some of the indications/contraindications reported in EAES consensus document in 1994 have been revisited and new emerging issue has been reviewed.

3.2.1 Microcalculi/Sludge

Recent data suggest an association between acute pancreatitis and small gallbladder stones or sludge, preserved gallbladder motility, and fast cholesterol crystallization [24–30] [LoE3-LoE4]. This association is not unexpected: small gallbladder stones might migrate into the common bile duct easier than larger stones, especially if the gallbladder motility is preserved. Furthermore, small stones might cause a distal obstruction in the common bile duct at the level of the sphincter of Oddi, with subsequent pancreatitis, whereas larger stones might rather lead to a proximal obstruction, with obstructive jaundice without reflux into the pancreatic duct. Colecchia [31] [LoE3] et al. found a relationship between efficient gallbladder emptying and symptom development, while patients with weak gallbladder emptying mainly remained asymptomatic.

3.2.2 Porcelain Gallbladder (PGB)

A recent review by Khan et al. [32] [LoE4] stated that porcelain gallbladder is only weakly associated with gallbladder cancer. Their review showed an association of PGB and gallbladder carcinoma up to 15 %, but they included a study of the 1960s that reported 62 % association of gallbladder carcinoma in PGB subgroup. Excluding this study, the more recent papers report an association of 0–12 % and conclude that prophylactic cholecystectomy is not indicated for porcelain gallbladder alone and that it should be performed only in patients with conventional indications for cholecystectomy considering that most patients with PGB are symptomatic [33–35] [LoE3].

Diffuse intramural calcifications (PGB) (pathological findings) should be distinguished from selective mucosal calcifications. The latest seem to be at higher risk for association with gallbladder cancer [33] [LoE3].

3.2.3 Risk of Gallbladder Cancer (GBC)

Several reviews and other papers investigated on the association between gallstones and GBC. They agree on the fact that there is a great difference in relation to genetic, ethnic, geographical, and life-style factors. Generally there seems to be no indication for prophylactic cholecystectomy in Western countries as the incidence of GBC in gallbladder with stones is quite low (less than 1 % in patients with asymptomatic gallstones). A subgroup of patients with calculi >3 cm (data from 1983) [34] or multiple calculi seem to be at higher risk for GBC, but there is not sufficient evidence yet to advise prophylactic cholecystectomy [6, 7, 15, 21, 27, 35–39] [LoE3].

A population-based Chinese study on 627 biliary tract cancers showed a high relationship of, respectively, 80, 59, and 41 % between gallstones and GBC, biliary duct cancer, and ampulla of Vater cancer. However this study was conducted on Shanghai population, and as stated before there is great variety of GBC incidence in various ethnic groups and China has a much higher GBC incidence than Western Europe [40] [LoE3].

There is no data whether immigrants from high-incidence countries (China, India, Pakistan, Eastern Europe, South America) have the same cancer risk than resident population.

A recent controlled follow-up study on 134 patients (57 men with mean age of 45 years and 77 women with mean age of 46 years) who were asymptomatic in 1983 and followed up for 24 years did not detect any cancer cases [21] [LoE3]. Up to date this is the study with the longest follow-up on asymptomatic gallstone patients.

3.2.4 Incidental Gallstones

It might happen to diagnose gallstone disease during preoperative assessment for other medical/surgical conditions or intraoperatively. In these cases LC is not associated with increased postoperative mortality [40, 41] [LoE3]. Literature agrees on performing incidental cholecystectomy in conjunction with other abdominal procedures as long as the surgeon is comfortable performing it and no prosthetic material is being used [6, 15, 19, 20] [LoE3].

3.2.5 Diabetes

Prophylactic cholecystectomy is not indicated in diabetic patients with asymptomatic gallstones (GS) and cholecystectomy should only be performed in cases of symptomatic cholelithiasis [7, 15, 19] [LoE3]. Diabetic patients should be treated as every other gallstone patient because there is no evidence to support an increased risk of gallstone-related complications.

3.2.6 Patients on Long-Term Somatostatin

Literature confirms that long-term therapy with somatostatin increases gallstone incidence.

No data is available whether these patients are at higher risk of complication than other gallstone population [29, 30, 39, 42] [LoE3]. Patients on long-term somatostatin treatment should be treated as every other asymptomatic gallstone patient. Prophylactic elective laparoscopic cholecystectomy is not recommended.

3.2.7 Transplant Patients

Cardiac transplant recipients with asymptomatic GS disease can be treated by pretransplant cholecystectomy, posttransplant cholecystectomy, or expectant management. It has been demonstrated that nonelective open cholecystectomy for complicated GS disease, in heart transplant recipients, results in high mortality and morbidity rates [46, 47] [LoE3].

Prophylactic posttransplantation LC is the preferred management strategy for post-cardiac transplant patients with asymptomatic gallstones, resulting in decreased mortality and significant cost savings and quality-adjusted life year. No data support the prophylactic elective laparoscopic cholecystectomy in patients candidate or submitted to kidney, pancreas, and pulmonary transplantation [43–48] [LoE3-LoE4].

3.2.8 Sickle Cell Anemia

The incidence of cholelithiasis is reported to be increased in patients with sickle cell disease [49] [LoE4].

Surgery in patients with sickle cell disease is associated with high morbidity (the risk of postoperative complications in these patients ranges from 7 to 32 %) [50, 51] [LoE3-LoE4]. To reduce morbidity, different preoperative transfusion regimens are indicated [50, 51] [LoE3-LoE4]. Laparoscopic cholecystectomy is safe without transfusion in sickle cell disease patients [50, 51] [LoE3-LoE4]. It is known that CO_2 insufflation during LC can result in hypercapnia and respiratory acidosis. These changes, which could precipitate sickling in SCD, are related to the duration of surgery. Shorter operating time at low insufflation pressure makes LC safer in sickle cell disease patients and should be considered the preferred alternative to the traditional open approach [52–56] [LoE3-LoE4]:

3.2.9 Contraindications to LC

Review of literature could not evidence any changes in absolute contraindications for LC. So they remain the same as in the 1994 EAES consensus statement [57].

1. Generalized peritonitis
2. Septic shock from cholangitis
3. Severe acute pancreatitis
4. Cirrhosis with portal hypertension
5. Severe coagulopathy that is noncorrected
6. Cholecysto-enteric fistula

3.2.10 Conclusion

The diffuse ultrasound examination for various abdominal diseases increased in the last decades the diagnosis of asymptomatic gallbladder diseases. High-quality data demonstrate that the majority of patients with asymptomatic gallstones will remain asymptomatic (only 2–4 % will develop symptoms annually) and that the complication rate in asymptomatic patients ranges from 0.3 to 3 % per year. Given the low incidence of symptoms development and complication rate per year in nontreated patients, prophylactic laparoscopic cholecystectomy is currently not recommended as standard treatment.

Nevertheless, according to the conclusion of 2009 Cochrane Review on LC in silent stones, there is no RCT or high-level studies which offer scientific evidence to refuse LC to asymptomatic gallbladder stone patients.

There is no evidence to recommend prophylactic LC in asymptomatic gallbladder stone patients neither for diabetics, patients on long-term somatostatin, nor patients with porcelain gallbladder in Western countries. Also in patients with gallbladder stones >3 cm, there is not enough data available to recommend prophylactic LC to prevent gallbladder cancer.

Nevertheless, recent data suggest that selective prophylactic LC is advisable in some subgroup of patients.

Microcalculi and bile sludge in conjunction with a functioning gallbladder are more likely to predispose patients to calculi migration and subsequent onset of choledocholithiasis and acute pancreatitis.

Incidental diagnosis of cholelithiasis in preoperative or intraoperative setting for other medical conditions can be treated laparoscopically in the same session if it does not add any risk of conversion and no prosthetic material is being used.

As the risk of sickling, in patients suffering from sickle cell anemia, is reduced by a laparoscopic approach, it should be the first choice.

Some ethnic groups and inhabitants of certain geographical areas are more likely to develop gallbladder cancer. Also specific ultrasound findings, like selective mucosal calcifications, increase the risk of gallbladder cancer. These patients could benefit from prophylactic LC.

Cardiac-transplanted patients with asymptomatic cholelithiasis should undergo LC.

3.3 Obesity

Once considered a relative contraindication (Consensus EAES 1994) [57] [LoE3] nowadays obese patients (BMI >30) are approached by LC using the same indications as nonobese. This change is mainly based on data with low level of evidence as literature lacks RCTs or studies with high statistical power. On the other hand the bulk of the available data suggest that obesity, even morbid obesity (BMI>40), does not result in an increase in morbidity, mortality, conversion rates, or perioperative complications when compared to nonobese population [58–64, 66–78] [LoE4] (Table 3.1).

There are few published papers comparing outcomes of LC in obese versus nonobese, but several studies investigate obesity as a risk factor for conversion. Unlike

Table 3.1 Published series of obese patients

	Number of patients	Obesity as risk factor for conversion	Increased complication rates	Increased operation time
Hutchinson et al. [61]	587	Yes		
Fried et al. [62]	1,676	Yes		
Phillips et al. [63]	841	No	No	No
Schrenk et al. [68]	1,300	No	No	Yes
Angrisani et al. [58]	?	Yes	No	Yes
Liu et al. [64]	500	Yes		
Alponat et al. [69]	783	No		
Gatsoulis et al. [70]	145	No	No	Yes
Brodsky et al. [71]	215	No		
Ammori et al. [67]	864	No (trend NS)	No (trend NS)	No (trend NS)
Kama et al. [72]	1,000	No		
Rosen et al. [59]	1,347	Yes[a]		
Livingston et al. [66]	Nationwide	Yes		
Tayeb et al. [73]	1,249	No		
Simopoulos et al. [74]	1,804	No	No	Yes
Sidhu et al. [75]	603	No	No	Yes
Lipman et al. [76]	1,377	No		
Chandio et al. [60]	324	Yes[a]		
Chang et al. [77]	627	No	No	No
Farkas et al. [78]	1,027	No	No	

[a]Not independent, in association with acute cholecystitis

the paper of Angrisani [58] [LoE4], all studies comparing obese versus nonobese could not identify that high BMI (>40) is an independent risk factor for conversion to open surgery [63, 67, 68, 70, 74, 75, 77, 78] [LoE4]. All studies demonstrated that obesity is not associated with higher perioperative complication rates [58, 63, 67, 68, 70, 74, 75, 77, 78] [LoE4].

Furthermore, Rosen [59] [LoE4] and Chandio [60] [LoE4] found a relationship between BMI and higher conversion rates only in case of acute cholecystitis. Therefore obesity per se cannot be considered a risk factor for LC in symptomatic gallstone patients.

The remaining papers [58, 61, 62, 64] [LoE4] that report obesity as independent risk factor for conversion to open cholecystectomy were published in the second half of 1990. The explosion of laparoscopic bariatric surgery during the last 10 years changed the attitude of surgeons.

A recent review by Hussain [65] [LoE4] (2011) stated that the triad of obesity, acute cholecystitis, and previous upper abdominal surgery leads to higher morbidity, a longer operating time, and a higher conversion rate (only obesity independently predicted higher conversion to open cholecystectomy in patients with acute cholecystitis) which was also stated by former studies [59, 60] [LoE4].

In conclusion, comparative data (LC in obese vs. nonobese) demonstrate that obesity per se does not increase conversion rates, mortality, and perioperative complication rates. Therefore elective LC can be considered a safe approach to obese patients with symptomatic gallstone disease.

3.4 Pregnancy

It has been demonstrated that laparoscopy can be performed safely during any trimester of pregnancy with minimal morbidity to the fetus and mother [79–91] [LoE2-LoE3-LoE4].

The significant morbidity and mortality associated with untreated benign gallbladder diseases in the gravid patient favors surgical treatment [79, 84, 87–89, 92–94] [LoE2-LoE3-LoE4].

LC is the treatment of choice in the pregnant patient with benign gallbladder diseases [79, 95] [LoE2-LoE3].

Patients with symptomatic gallstones who were treated conservatively have shown a 92 % recurrence rate when symptoms were present in the first trimester, 64 % when symptoms were present in the second trimester, and 44 % when symptoms were present in the third trimester. This data support an early surgical approach to gravid patients with symptomatic gallstones [79, 95] [LoE2-LoE3].

The delay in surgical management results in increased rates of hospitalizations, spontaneous abortions, preterm labor, and preterm delivery compared to those undergoing cholecystectomy [79, 93, 96] [LoE2-LoE3-LoE4]. Nonoperative management of symptomatic gallstones in gravid patients results in recurrent symptoms in more than 50 % of patients, and 23 % develop acute cholecystitis or gallstone pancreatitis [79, 84, 97] [LoE2-LoE3-LoE5]. Gallstone pancreatitis results in fetal loss in 10–60 % of pregnant patients [79, 89] [LoE2-LoE3]. Gravid patients candidate to LC should be placed in the left lateral recumbent position to minimize compression of the vena cava and the aorta [79, 92] [LoE2-LoE5].

There has been much debate regarding abdominal access in the pregnant patient with preferences toward either a Hasson technique or Veress needle. Because the intra-abdominal domain is altered during the second and third trimester, initially accessing the abdomen to create the pneumoperitoneum via a subcostal approach has been recommended. If the site of initial abdominal access is adjusted according to fundal height and the abdominal wall is elevated during insertion, both the Hasson technique and Veress needle can be safely and effectively used [79, 82, 84, 89, 95, 98] [LoE2-LoE3-LoE4].

3.5 Elderly

Life expectancy continues to increase in Western countries and the incidence of gallstones increases parallel with age [99] [LoE4]. Gallbladder disease is the most common indication for abdominal surgery in the elderly and therefore cholecystectomy is the most commonly performed surgical procedure [100, 101] [LoE4].

All examined studies demonstrated that LC is indicated for elderly patients with uncomplicated gallbladder stone disease, as results are better than those obtained with open cholecystectomy (OC) regarding morbidity, length of surgery, and mean postoperative hospitalization with more discharges to home [102–107] [LoE2-LoE3-LoE4]. Nevertheless Tucker et al. in a recent case-match study, based on American College of Surgeons National Surgical Quality Improvement Program database, stated that elderly patients were more likely to undergo OC compared to younger age group, concluding that LC is safe but underused in the elderly [108] [LoE3].

LC in older patients is associated with increased rates of conversion to laparotomy, longer operation time, longer hospital stay, and increased rates of operative complications, such as bile duct injury and hemorrhage, than when performed in younger patients [109, 110] [LoE2-LoE4]. These differences are probably due to the evidence that elderly patients are more likely than the younger ones to have had prior abdominal upper surgery or longstanding gallstone disease with chronic inflammatory changes and adhesions in the right upper quadrant. Moreover, elderly experience a high incidence of choledocholithiasis and gallstone pancreatitis and a higher frequency and severity of associated cardiopulmonary disease [101, 111] [LoE4].

Kim et al. stated that perioperative outcomes in the elderly seem to be influenced by the severity of gallbladder disease, and not by chronologic age [100] [LoE4].

On the basis of these observations, early elective LC should be encouraged in symptomatic elderly patients before the development of complicated cholelithiasis [100, 101, 112] [LoE4]. Such approach may serve ultimately to lower conversion to open cholecystectomy (OC), reduce the incidence of acute presentations with common bile duct stones, and possibly lower complications and mortality [101] [LoE4].

In conclusion LC can be performed with acceptable morbidity in extremely elderly, like octogenarians, with complicated gallstone disease, although it should be considered and encouraged also for this age group of patients when gallstone disease is still uncomplicated, because early treatment could further improve outcomes. However octogenarians have a higher rate of conversion to OC, more complications, and higher mortality rates [99–101, 112–114] [LoE4].

3.6 Gallbladder Polypoid Lesions (GPL)

The treatment and surveillance of GPL is still controversial as a result of the lack of RCTs [115] [LoE2]. There is no evidence from randomized clinical trials to either recommend surgery or not for patients with GPL smaller than 10 mm [116] [LoE2].

For patients with GPL associated with pain, nonrandomized trials have shown that LC offers good pain relief in more than 90 % of the cases [117] [LoE4]. The primary goal in GPL management is to prevent gallbladder carcinoma, even though it is a rare condition [118] [LoE2].

Any surgeon has to balance the risk of malignancy (ranging between 45 and 67 %) in polyps between 10 and 15 mm in size [119–122] [LoE3-LoE4] and the risks associated with LC.

The ultrasound (US) evidence of multiple polyps per se is not considered an indication for surgery [115] [LoE2].

In patients with age ≥60 years, sessile polyp morphology, and polyp size ≥10 mm, a generous approach to endoscopic ultrasound (EUS) or multislide CT for accurate characterization should be advised [118] [LoE2].

Table 3.2 Risk factors predicting malignancy [128]

Authors	Patients	Year	Risk factor
Yang et al. [123]	182	1992	Size >10 mm, single, stone, age >50 years
Kubota et al. [124]	47	1995	Sessile shape, rapid growth, isoechogenicity
Collett et al. [125]	38	1998	Size >10 mm
Terzi et al. [120]	100	2000	Age >50 years, size >10 mm, stone
Mainprize et al. [119]	38	2000	Size >10 mm
Yeh et al. [121]	123	2001	Age >50 years, size >10 mm
He et al. [126]	244	2002	Age >50 years, size >10 mm
Sun et al. [127]	194	2004	Size >10 mm, age >50 years, sessile, stone or cholecystitis, biliary colic, decreased gallbladder emptying function due to polyp
Chattopadhyay et al. [122]	23	2005	Size >10 mm
Park et al. [128]	689	2008	Age >57 years, size >10 mm
Saleh et al. [129]		2008	Size >10 mm, age >50 years, concurrent gallstones, single, symptomatic
Andrén-Sandberg [118]		2012	Age >50 years, size >10 mm, fast growth, sessile or wide-based polyps, polyps with long pedicles, concurrent gallstones, polyps in the gallbladder infundibulum, abnormal gallbladder wall ultrasound
Marangoni et al. [115]		2012	Size >10 mm
Morera-Ocòn [130]	26	2012	Size >10 mm

Authors indicate as risk factors in patients with gallbladder polyps the following characteristics (Table 3.2) [118–130] [LoE2-LoE3-LoE4]:

- Polyps with diameters greater than 10 mm [118–123, 125–130] [LoE2-LoE3-LoE4]
- Fast-growing polyps [118, 124], sessile polyps or wide-based polyps [118, 124, 127] [LoE2-LoE4], and polyps with long pedicles [118] [LoE2]
- Patients aged over 50 years [118, 120, 121, 123, 126, 127, 129] [LoE2-LoE3-LoE4-LoE5] and with concurrent gallstones [118, 120, 123, 127, 129] [LoE2-LoE4-LoE5]
- Polyps of the gallbladder infundibulum or abnormal gallbladder wall ultrasound [118] [LoE2]

If there are no signs of malignancy, for polyps 6–9 mm in diameter, a US examination is recommended after 6 months. If the US examination does not show any significant changes, a new US examination is recommended after 12 months. No further follow-up in case of stable lesion is recommended [118] [LoE2].

GPL smaller than 6 mm do not require follow-up in the absence of suspicion of malignancy [118, 131] [LoE2-LoE4].

A GPL greater than 18 mm has a high likelihood of gallbladder cancer: open cholecystectomy, partial liver resection, and lymph node dissection are advised [120] [LoE4].

Based on the literature review, we propose the following flowchart for gallbladder polypoid lesions management (see Fig. 3.1).

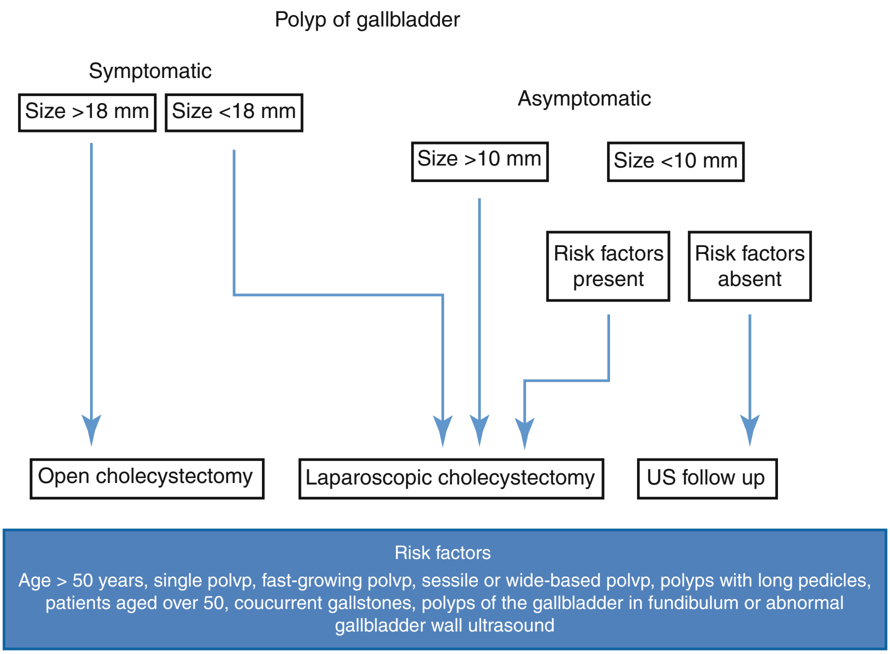

Fig. 3.1 Decision making flow-chart in patients with GPL

3.7 Cirrhosis

Cholelithiasis in patients with cirrhosis occurs twice as often as in general population. Despite cholecystectomy is the most frequently performed surgical procedure for patients with liver cirrhosis, there are few studies about laparoscopic cholecystectomy (LC) in those patients. The studies are small, heterogeneous in design, and include almost exclusively patients with Child-Pugh class A and B. There are poor data about LC outcome in Child-Pugh class C [132] [LoE1].

However, three systematic reviews (including a total of 4,211 patients) and four meta-analysis of RCTs (including a total of 1,138 patients) comparing outcomes of open cholecystectomy (OC) versus LC for symptomatic cholelithiasis in Child-Pugh A or B cirrhotic patients show fewer overall postoperative complications, a shorter hospital stay, shorter operative time, and faster resume of a regular diet for the LC group than for the OC group [132–139] [LoE1-LoE2-LoE3].

Because of the high risk of liver failure and heavy hemorrhage in Child-Pugh C patients, the indications for surgery in this subset of cirrhotic patients should be evaluated very carefully and surgery avoided unless clearly indicated [140] [LoE4]. In such patients cholecystostomy or percutaneous drainage of the gallbladder as alternative options should be considered [140] [LoE4].

The severity of cirrhosis is a major determinant in the decision-making process on the optimal approach [135] [LoE2]. Both Child-Pugh and MELD scores were used to predict postoperative morbidity and mortality in patients with liver cirrhosis [134] [LoE1]. Review of the literature showed that cirrhotic patients who undergo non-hepatic surgery exhibit postoperative morbidity and mortality rates strongly related with the severity of cirrhosis and the nature of the surgical procedure [134] [LoE1].

The increased risk for a major complication, however, demands more attention than usual.

The morbidity rates for OC in patients with cirrhosis are reported to be between 30 and 35 % while for LC between 13 and 33 %. However, mortality after OC varied between 0 and 7.7 % [134, 135, 139, 141] [LoE1-LoE2-LoE3].

Some studies report a 3.4-fold higher risk of mortality for cirrhotic patients undergoing cholecystectomy when compared to non-cirrhotic patients [134, 142] [LoE1-LoE3].

Long-term complications after cholecystectomy for cirrhotic patients, such as abdominal wall hernias and adhesions, are not assessed in literature, but it is demonstrated that they occur less frequently after laparoscopic cholecystectomy than open cholecystectomy in patients with a non-cirrhotic liver. In the hypothesis of future surgery, for example, liver transplantation, cirrhotic patients could even take greater advantage of this fact [133] [LoE1].

3.8 Gallbladder Dyskinesia

Acalculous gallbladder disease represents a clinical entity which is not clearly defined and incorporates chronic and/or acute inflammation, gallbladder and/or biliary dyskinesia, intrinsic motility disorders, and functional disorders of biliary flow [143–146] [LoE4]. Nonetheless, gallbladder dyskinesia, in the absence of gallstones or polyps, is a challenging clinical entity in laparoscopic era.

Gallbladder dyskinesia is a motility disorder of the gallbladder (acalculous) associated with intermittent right upper quadrant pain (classic symptoms) [147] [LoE4]. More recently Corrazziari and Cotton published a flowchart to assess the diagnostic criteria and treatment options [148] [LoE4].

The incidence of negative US examination in patients complaining about biliary pain differs between the two sexes, ranging from 7.6 % in males to 20.7 % in females [149] [LoE5].

There are three hot topics concerning the management of this clinical entity:

1. Diagnostic criteria
2. Validation of the cholecystokinin-hepatoiminodiacetic hepatobiliary scintigraphy test (CCK-HIDA) or similar dynamic test to measure gallbladder motor disorder
3. Indications to laparoscopic cholecystectomy and outcomes

Preoperative diagnostic evaluation should include serial dynamic ultrasonography, upper ultrasound-endoscopy (to rule out microlithiasis), and dynamic cholescintigraphy [144, 150–153] [LoE3-LoE4].

CCK-HIDA scintigraphy is considered by many authors as the first specific test (high specificity) for gallbladder dyskinesia [153, 154] [LoE4]. Its increasing utilization coupled with decreasing utilization of other preoperative evaluation methods may indicate increasing physician awareness of the disease and appropriateness of the CCK-HIDA scintigraphy as a predictor of postoperative success after cholecystectomy [143, 150, 153] [LoE4]. In 2003 DiBaise et al. [155] [LoE3] in their systematic review concluded that the quality evidence of the 23 papers selected was lacking precluding a definitive recommendation regarding its use. In 2010 the Rome Committee stated that CCK-HIDA scintigraphy is not a standardized test and may be conducted differently in different institutions. Moreover the extent to which the results predict the surgical outcome remains controversial. Finally, reproduction of pain on injection of cholecystokinin (CCK) has been considered to indicate gallbladder motor disorder, but this is not a reliable predictor of favorable surgical outcome. Recently an evidence-based review [156] [LoE3] concludes that despite the widespread acceptance of CCK-HIDE provocative test and its standardization, high-quality data indicating efficacy of cholecystectomy in the treatment of this condition are still lacking.

Clinical signs and symptoms still remain the most important criteria for some surgeons for patient selection to surgical treatment [152–170] [LoE3-LoE4-LoE5]. While few nonrandomized clinical studies have demonstrated a discriminatory ability of the impaired gallbladder ejection fraction (<35 %) in predicting the symptoms relief after cholecystectomy [152–154, 157, 158, 160–162] [LoE3-LoE4-LoE5], other published studies have not confirmed this [155, 163] [LoE3]. Carr et al. reported the results of a prospective nonrandomized concurrent cohort study on the treatment of gallbladder dyskinesia (defined as negative ultrasound examination and ejection fraction <35 % after CCK stimulation) based upon typical and atypical biliary symptoms. This study demonstrated that classic biliary symptoms are more predictive of success after cholecystectomy in patients with gallbladder dyskinesia than are atypical symptoms. The resolution of symptoms in the "classic symptom group" was 97 % versus 57 % in the "atypical symptom group." The ejection fraction was not significantly different between the two groups [164] [LoE4]. Actually 5–27 % of gallbladder dyskinesia cases are approached by LC (majority in females) [149, 165, 166] [LoE3-LoE4-LoE5].

LC alleviates symptoms in about 50 % of unselected patients with chronic acalculous cholecystitis/biliary dyskinesia with minimal morbidity, and patients who suffered symptoms for a longer period of time preoperatively were more likely to be satisfied [149, 151, 167] [LoE4-LoE5].

In 2005 Ponsky et al. [168] [LoE3] included in their systematic review and meta-analysis of 5 studies (275 patients, 1963–2003) reporting data and follow-up on efficacy of cholecystectomy versus no treatment in patients with gallbladder dyskinesia. The meta-analysis showed 98 % symptomatic relief in cholecystectomy-treated group versus 32 % in the control group (no treatment). However, the analysis was lacking in high-quality paper. Pathologic examination of the removed gallbladder demonstrates acalculous chronic cholecystitis in 67–95 % [158] [LoE5].

In 2009 Gurusamy et al. [169] [LoE3] underlined in the conclusions of their Cochrane Review that the evidence for benefits and harms of cholecystectomy in the treatment of gallbladder dyskinesia is based on a single small randomized controlled clinical trial (21 patients, 11 open cholecystectomy vs. control) being therefore at risk of bias. Randomized clinical trial in laparoscopic era is advocated.

In quality of life terms, the usefulness of laparoscopic cholecystectomy is similar in patients with calculous or acalculous gallbladder disease, thus making its surgical indication reasonable [152] [LoE3]. LC should be offered as elective treatment to those patients who understand the magnitude and potential success and failure of LC.

In conclusion, the diagnosis of gallbladder dyskinesia is based mainly on clinical signs and symptoms with typical biliary pain, especially after meals, negative serial US examinations and EUS and a positive CCK stimulating test. The CCK-HIDA scintigraphy seems to be predictive for gallbladder dyskinesia if ejection fraction is <35 %, but it is not predictive for surgical outcomes. Both patients presenting with typical and atypical biliary symptoms will benefit from cholecystectomy, but there is greater benefit for patients with typical biliary symptoms, regardless of the entity of reduced ejection fraction. In this view, LC should be proposed to patients with gallbladder dyskinesia suffering from typical symptoms. A wait and see policy is recommended for patients with atypical symptoms. But if symptoms persist, they can be sent to LC after a careful interview, explaining pros and cons and the insecure success and deciding together with the physician.

Abbreviations

BMI	Body mass index
CCK	Cholecystokinin
CCK-HIDA	Cholecystokinin-hepatoiminodiacetic acid
EUS	Endoscopic ultrasound
GBC	Gallbladder cancer
GPL	Gallbladder polypoid lesion
GS	Gallstones
LC	Laparoscopic cholecystectomy
OC	Open cholecystectomy
PGB	Porcelain gallbladder
RCT	Randomized controlled study
SCD	Sickle cell disease
US	Ultrasound

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Biliary Tree Stones

4

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4.1 Introduction: Definition and Epidemiology

Choledocholithiasis, or stones in the common bile duct (CBDS), can be classified as primary, forming initially in the bile ducts, or secondary, originating in the gallbladder and passing into the bile ducts. In Western countries, bile duct stones are most commonly secondary, and bile duct stones are found in 8–18 % of patients with symptomatic gallstones. Coexistent gallbladder and common duct stones are correlated with increasing age, Asian descent, chronic inflammatory conditions

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(primary sclerosing cholangitis, acquired immunodeficiency syndrome, parasites), and possibly hypothyroidism.

Primary bile duct stones can also form, but their incidence in Western countries is low. Previous studies have implicated bacterial infection and biliary stasis as important factors in formation of primary duct stones [1]. Bacteria have been found in mixed pigment stones, and bile infection appears to precede stone formation [2]. Parasitic infection has also been associated with primary duct stones, primarily in Asia.

Secondary choledocholithiasis may be asymptomatic or associated with symptoms and complications similar to those seen with gallbladder stones. Bile duct stones may be discovered incidentally in the evaluation of suspected gallstones. Patients may become jaundiced with persistent obstruction; however, the biliary obstruction is usually incomplete.

Several risk factors, including clinical, biochemical, and imaging variables, can help predict the presence of common bile duct stones [3–5]. Clinically, an increasing age and a history of fever, cholangitis, or pancreatitis are risk factors for choledocholithiasis. Elevations of serum bilirubin, aspartate aminotransferase, or alkaline phosphatase are also independent positive predictors. However, US is not a sensitive or specific diagnostic tool for the presence or absence of common duct stones. A dilated common bile duct on US is a useful predictor [3]. Statistical models incorporating a combination of clinical, laboratory, and imaging variables are more accurate in predicting bile duct stones than any individual risk factor. Other imaging techniques, such as magnetic resonance cholangiography, CT cholangiography, or endoscopic ultrasound (EUS), have been developed to detect common bile duct stones more accurately [6, 7]. In a patient with gallbladder stones being evaluated for elective cholecystectomy, or in a patient with known gallbladder stones presenting with acute pancreatitis, when and how the common bile duct should be imaged and the timing of therapeutic intervention remain areas of active investigation and are covered in detail in the next four articles in this supplement.

The last 30 years have seen major developments in the management of gallstone-related disease, which in the United States, alone, costs over six billion dollars per annum to treat. Endoscopic retrograde cholangiopancreatography (ERCP) has become a widely available and routine procedure, while open cholecystectomy has largely been replaced by a laparoscopic approach, which may or may not include laparoscopic exploration of the common bile duct (LCBDE). In addition new imaging techniques such as magnetic resonance cholangiography (MR) and EUS offer the opportunity to accurately visualize the biliary system without instrumentation of the ducts. As a consequence clinicians are now faced with a number of potentially valid options for managing patients with suspected CBDS.

4.2 Symptom Pattern

Signs and symptoms of choledocholithiasis are due to the presence of stones that prevent the normal bile passage through the CBD. The stones can consist of pigments or more frequently of cholesterol, and they can migrate into the CBD from the gallbladder or develop directly inside it due to the bacterial action [8].

The stones generally arrive to the terminal portion of CBD causing its dilation and the increase of upstream bile pressure. The normal pressure inside CBD is 15 cm H_2O whereby the flow slows if the pressure exceeds 15 cm H_2O and up to a complete stop when it reaches 30 cm H_2O [8].

CBDS can arise both in people with intact gallbladder and with cholecistectomy [9]. Approximately 95 % of patients with CBDS also have gallbladder stones, while only 15 % of patients with gallbladder stones have also cholelithiasis [3]. The main symptoms are abdominal pain, fever, jaundice, nausea, vomiting, and up to the development of cholangitis or pancreatitis. Typically an increase of total bilirubin (TB), alkaline phosphatase (AF), γ-glutamyltransferases (γ-GT), and liver function enzymes is found [8].

Bilirubin increases because of biliary excretion hurdle, while alkaline phosphatase increase is due to an enhancement in the enzyme synthesis by the canalicular epithelium. Normally the alkaline phosphatase rise precedes and is more rapid than that of bilirubin and does not correlate to the cause of obstruction or its entity. Usually bilirubin level is around 2–5 mg/dl [9, 10].

Some authors proposed that the higher the level of the AF, the greater is its predictive value [11]. However, both AF and TB are independent predictors of CBDS [12, 13].

The symptoms are mainly influenced by different factors such as the rapidity of the obstruction and the bacterial contamination degree. In case of acute obstruction, acute abdominal pain and jaundice are present; on the other hand, only itching or mild jaundice is found in the gradual obstruction. The physical examination could be normal if there is intermittent obstruction, but in the presence of prolonged obstruction, biliary cirrhosis with typical alterations of chronic hepatopathy can develop [12].

A new iatrogenic CBDS form is growing in literature, considered as a late complication of endoscopic sphincterotomy. It has an incidence around 12 % in a study focused on the long-term consequences of endoscopic sphincterotomy. The stone composition suggested an action of the chronic bacterial colonization of the CBD as principal cause [8].

4.3 Diagnostic Evidence

The diagnosis of CBDS is based on the fusion of clinical suspicion with biochemical tests. Unfortunately, none of these alone allows to reach a certain diagnosis. This is the reason why the further step is the radiological and/or endoscopic imaging. In rare cases the diagnosis is incidental, during investigation performed for other reasons.

Diagnostic techniques available are several:

Transabdominal ultrasonography is the first-level investigation. This is a noninvasive procedure, widely available, and low cost. It has a sensitivity of 22–65 % and specificity of 70–98 %. The possibility of CBDS detection is influenced by patient-related factors including the number, size, and site of stones; bloating; body habitus; and possible presence of metallic clips in patients who had previous cholecystectomy [14].

Endoscopic ultrasonography is a minimally invasive procedure with a risk similar to a routinary gastroscopy [15]. It is very sensitive in confirming the presence of CBDS. It is operator dependent and has a 95 % of agreement with diagnostic ERCP. The sensitivity is 85–97 % and the specificity is 90–95 %. It is not widely spread [16].

Intraductal sonography is a technique based on images obtained from a transducer at the catheter tip that is inserted through a duodenoscope. It is operator-dependent and has a sensitivity of 97–100 %. The limitations of the procedure are due to difficulty to distinguish stones, sludges, and air bubbles in addition to limited durability of the probe [17].

Laparoscopic intraoperative ultrasonography can be performed as diagnostic tool during laparoscopic cholecystectomy using laparoscopic ultrasound probes. It has a sensitivity of 80–83 % and specificity of 99–100 %. The main limitations are the difficulty to perform the procedure and to evaluate correctly the intrahepatic portion of the CBD and the operator dependence [9].

Intraoperative cholangiography allows to perform a cholangiography inserting a catheter through the cystic duct during cholecystectomy. It has a sensitivity of 75–100 % and specificity of 97–100 %. The main limitations are due to a prolongation of the operative time and x-ray exposure.

Intravenous cholangiography is based on intravenous injection of contrast medium followed by a radiographic imaging of the biliary tree. It has a sensitivity of 48–50 % and specificity of 95–97 %. Nowadays it is no more used because of the lack of accuracy in patients with high bilirubin levels, risk of allergic reaction or renal impairment, and x-ray exposure [9].

Helical computed tomography cholangiography is a CT scan of the biliary tree after intravenous injection of contrast medium. It has a sensitivity of 71–85 % and specificity of 88–97 % and has the same intravenous cholangiography limitations [9].

Endoscopic retrograde cholangiopancreatography (ERCP) is both an endoscopic and a radiological invasive procedure, developed about 30 years ago, which may be both diagnostic and therapeutic. The diagnostic investigation consists in the passage of a catheter through the endoscope until the ampulla of Vater. The cannulation of the interested duct permits to inject contrast medium and perform a cholangiography. It is the "gold standard" technique for the diagnosis of biliary or pancreatic disease with a sensitivity of 71–85 % and specificity of 88–97 % [9]. It is a technically demanding procedure with a failure rate between 3 and 12 %. This depends on the type of treated disease, availability of well-trained team, and endoscopist's skills. The complication rate is about 5–6 % and the death rate ranges from 0.0089 to 0.01. The most frequent complication is pancreatitis, followed by bleeding, perforation, and cholangitis. Risk factors for pancreatitis are age less than 60 years, incomplete removal of stones, and the use of precut papillotomy. This procedure cannot be performed in patients with Billroth II or Roux-en-Y reconstruction after gastric surgery, sclerosing cholangitis, pancreatic pseudocyst, or previous post-ERCP serious complications [17].

Magnetic resonance cholangiopancreatography (MRCP) is a selective or partially selective MRI of the biliary-pancreatic tree developed in 1991. It is based on heavily T2-weighted images which show a contrast between the background and stationary fluids. The bile, in fact, has a high signal intensity compared to that of the parenchyma. The contiguous slices acquired can be reconstructed using maximum intensity projection (MIP) to obtain a composite image that can be analyzed from different angles [17]. It has a sensitivity of 85–100 % and specificity of 91–97 % [9]. No preparation is required, but the patient's fasting 2–4 h before the exam reduces the fluid in the gastric antrum and duodenum increasing, instead, the biliary tree and gallbladder filling [18]. The limitations of this procedure are the difficulty to identify small stones, even if sizes up to 2–3 mm are normally displayed. Further limitations are MRI related such as claustrophobia, pacemakers, hemodynamic instability, ferromagnetic material, and obesity which reduces both the quality of the images and the possibility to enter into the scanner. It is important that these machines are less than 8 years old and have periodic software updates.

The two principal diagnostic procedures performed after transabdominal ultrasound, as second step imaging, are MRCP and ERCP whereby it is essential to identify patients who may benefit from one or the other investigation. MRCP and ERCP have different contraindications whereby they can be considered complementary. MRCP can be performed in patients who cannot perform ERCP because it would be risky or impossible. On the other hand, when there is the high suspicion of an obstacle susceptible to endoscopic treatment, it could be useful to perform directly ERCP avoiding further procedure and reducing costs. This is the reason why performing routinary MRCP before ERCP is not justifiable [19]. Moreover MRCP is estimated to cost about 30–50 % of ERCP. MRCP associated with MRI also enables a broader assessment of the surrounding organs leading to evaluate possible stenosis of the upstream biliary tract and a complete staging of the disease especially for malignancies [20].

The decision-making proceeding must be based on a risk stratification to have CBDS among patients with symptomatic gallbladder stones. The American Society for Gastrointestinal Endoscopy proposed a strategy to stratify these patients [21].

The predictors of choledocholithiasis can be divided in three groups [3, 5, 22, 23]:

Very Strong
- Transabdominal US evidence of CBDS
- Clinical ascending cholangitis
- Bilirubin level >4 mg/dL

Strong
- Transabdominal US evidence of dilated CBD >6 mm with gallbladder in situ
- Bilirubin level between 1.8 and 4 mg/dL

Moderate
- Alteration of liver function test, different from bilirubin
- Age >55 years
- Clinical gallstone pancreatitis

The likelihood of choledocholithiasis based on clinical predictors is divided in three groups [16–21]:

High

Presence of any among the "very strong"

Presence of both "strong"

Low

Absence of predictors

Intermediate

All other patients

4.4 Therapeutic Decision Making

4.4.1 Endoscopic Treatment

The endoscopic management of common bile duct stones (CBDS) has been considered, for a long time, the first-line therapy. There are several endoscopic therapeutic options currently used in the treatment of CBDS.

The endoscopic sphincterotomy (ES), firstly introduced by Classen and Demling in 1974, is the most commonly used therapy for the treatment of CBDS and consists in severing of the deep muscle layers of the sphincter of Oddi. This technique is actually accepted as the first step in the clearance of CBDS. The goal of this procedure is to cut the biliary sphincter facilitating the stone passage and extraction and allows to remove small- or medium-sized stones in a single step. The risks of ES include perforation, infection, bleeding, and acute pancreatitis [24].

The aim of the endoscopic papillary balloon dilation (EPBD) is to dilate the sphincter of Oddi. This procedure may be performed after biliary sphincterotomy allowing the removal of very large CBDS or without ES allowing to preserve the sphincter of Oddi function and to reduce the bleeding rates if compared to ES alone [25]. The endoscopic balloon dilatation of the biliary sphincter should be considered an alternative to ES in selected patients with small-sized and few common bile duct calculi and high risk of post-ERCP bleeding (coagulopathy, anticoagulation therapy, etc.), but because of the high incidence of post-procedural pancreatitis, routine stone extraction by balloon dilatation should be avoided (EL Ia) [26].

Mechanical lithotripsy (ML) firstly described by Rieman in 1982 includes a variety of techniques that, through endoscopic devices, are capable of breaking big stones into smaller pieces. At the moment this procedure is the first-line therapy when conventional techniques cannot extract the stones.

The laser lithotripsy (LL) is able to break big stones through a pulsed laser energy applied to the stone via a fiber. This procedure offers a good outcome, above all in the management of refractory stones, even if it is not free of risks. The use of biliary stents, instead, is generally reserved to refractory stones and is not a first-line therapy.

Literature suggests that the endoscopic treatment of CBDS, compared to surgical intraoperative removal of CBDS, is safe without differences in efficiency, morbidity, and mortality (EL Ia) [27, 28] and that an adequate and careful selection of patients undergoing ERCP is recommended to reduce complication rate following endoscopic sphincterotomy (EL III); the risk factors for complications following ERCP include young age less than 60 years, female gender, and comorbidities like coagulopathy, thrombocytopenia, and previous failed clearing of biliary stones [29–31]. On the other hand, ERCP/ES is considered a safe and effective procedure in elderly patients without overall complication rate increase [32, 33]. It is recommended to perform an early ERCP and ES within 72 h of symptom presentation in severe acute biliary pancreatitis with persistent biliary obstruction or cholangitis (EL Ib) [34–36]. In septic patients with acute cholangitis, an early endoscopic biliary decompression is indicated, while open surgery should be considered an inappropriate therapeutic option (EL Ib) [37, 38]. Patients affected with concomitant gallbladder and common bile duct stones are not adequately treated by endoscopic sphincterotomy alone, but subsequent cholecystectomy is recommended, apart from high-risk patients (EL Ib) [39].

4.4.2 Surgical Treatment

Before the laparoscopic era, the gold standard for the treatment of gallstones and common bile duct stones was open cholecystectomy, choledochotomy, stone extraction, and T-tube placement. In the laparoscopic era, the best treatment for common bile duct stones (CBDS) is still a matter of debate. When the presence of CBDS is symptomatic, the decompression of the common bile duct (CBD) and the removal of the stones are mandatory. Endoscopic techniques can help in the management of these patients, thanks to endoscopic sphincterotomy, papillary dilation, nasobiliary drainage, and biliary stenting. For many years, the subject of debate among surgeons was whether it was right to treat CBDS without removing the gallbladder: recent studies have clarified this concept, suggesting benefits for a planned subsequent cholecystectomy [36, 37].

CBDS can be surgically treated in a single-stage procedure or in a two-stage procedure.

The single-stage procedure includes two options.

The first one includes the laparoscopic cholecystectomy (LC) plus a laparoscopic common bile duct exploration (LCBDE) with stone extraction trough a trans-cystic or a trans-choledochotomical way. Single-stage LC combined with LCBDE is associated with significantly shorter hospital stay and lower costs of hospitalization [38–40], but the laparoscopic CBD exploration may be difficult in the presence of marked inflammation of CBD or in the presence of a small CBD less than 7 mm, and the technique may be complex with a long operation time and postoperative complications [28, 41].

Laparoscopic trans-cystic or trans-choledocal clearance is an effective and appropriate technique, in patients suffering from gallstones and common bile duct stones, with clearance (85–95 %), morbidity (4–16 %), and mortality rate (0–2 %) comparable to endoscopic approach (EL Ia). The trans-cystic approach appears to be a good option for small stones preserving the Oddi's sphincter; meanwhile, laparoscopic choledocholithotomy is more indicated in the presence of stones larger than 6 mm or in the presence of a small cystic duct (<4 mm), of multiple stones, of a proximal ductal stones inside the common hepatic duct, or unfavorable cystic duct anatomy (small, friable, low common bile duct junction) [27, 42]. There is an increased risk of biliary complications (bile leakage, T-tube displacement) and prolonged hospital stay in case of stones that cannot be managed trans-cystically requiring a choledochotomy. Therefore, in patients in which laparoscopic trans-cystic stone clearance appears unsuccessful, intraoperative or postoperative endoscopic sphincterotomy may be a good approach, especially in the presence of small diameter common bile duct and inflamed tissues.

The second option for a single-stage procedure is the "rendezvous" technique that includes the laparoscopic cholecystectomy plus an intraoperative endoscopic retrograde cholangiopancreatography (ERCP) and a concomitant endoscopic sphincterotomy (ES) [43, 44]. Several studies have demonstrated the safety and efficacy of this technique, even if it requires considerable organizational efforts, specific instrumentation, skilled laparoscopic surgeon, skilled endoscopists, and an adequate nursing staff training [43, 45]. It is important to consider that postoperative unsuccessful of ES would require a surgical reintervention.

On the other hand, the "two-stage" management remains another possible strategy in the treatment of CBDS and includes a preoperative ERCP plus ES followed by LC or LC followed by postoperative ERCP plus ES [42, 43]. In this treatment strategy, the preoperative identifications of patients with concomitant CBDS are important [45]. Several studies have demonstrated that the conversion rate from laparoscopic cholecystectomy to open cholecystectomy was higher after ES than in laparoscopic cholecystectomy performed without preoperative ES. The laparoscopic cholecystectomy planned early after ES may reduce this risk [46, 47]. It is demonstrated that ERCP after LC is successful as the laparoscopic choledochotomy, when the trans-cystic stone extraction has failed [38, 39]. Despite if the preoperative or postoperative ERCP plus ES before the laparoscopic era was the treatment option for choledocholithiasis in patients with residual stones after cholecystectomy or in patients who were considered unfit for surgery, during the early experience with LC, preoperative ERCP and ES became the preferred treatment for suspected CBDS; meanwhile, postoperative ERCP became the favorite treatment for stones discovered during cholecystectomy or after surgery. Although relatively rare events, complications related with ERCP may be life threatening including pancreatitis (1.3–6.7 %), gastrointestinal bleeding (0.3–2.0 %), and duodenal perforation (0.1–1.1 %) [48]. Furthermore, ERCP/ES led to a disruption of the Oddi's sphincter that may allow duodenobiliary reflux and bacterobilia into the bile duct with possible stone recurrence and neoplastic mucosal changes [49]; this risk should be taken into account in young patients with CBDS, and for this reason, further trials are required. Postoperative ERCP, based on intraoperative detection of choledocholithiasis by cholangiography, is more suitable and cost-effective than preoperative ERCP, reducing unnecessary procedure rate, but requires surgical reintervention if ES fails.

In the last years there has been a gradual improvement in surgical procedures in order to reduce pain and hospital stay. Even if open surgery, compared to endoscopic sphincterotomy, appears to be associated with less mortality and more successful clearance rate, in the laparoscopic era, it should be considered a second option reserved to specific clinical situations. The indications for open surgery are failed or not feasible laparoscopic or endoscopic common bile duct clearance, surgical team not experienced in advanced laparoscopy, and lack of local sources. The authors suggest to be more appropriate, when choledocholithiasis is found during an open procedure, in performing common bile choledochotomy instead of deferring stone removal to postoperative ERCP (LE Ib) [50].

In Fig. 4.1 a tentative of decision-making algorithm is reported.

4.5 Decision-Making Statements

Moving from the abovementioned evidences, we can conclude some statement concerning the decision-making approach of CBDS. First of all, the result of ERCP is definitively established to be as safe as the LCDE (*GR strong*). Moreover, ERCP should be more efficiently performed preoperatively to the cholecystectomy (*GR moderate*). Again, it is clear that ERCP alone is not a sufficient treatment when gallbladder stones are coexisting (most of the case). In such cases a subsequent cholecystectomy would be recommended (*GR strong*), a part from the cases of high-risk patients. Moreover, when facing a patient with cholangitis or severe acute biliary pancreatitis with persistent biliary obstruction, ERCP should be early performed within 72 h (*GR moderate*).

On the other hand, concerning the total laparoscopic approach, we suggest to try a trans-cystic removal whenever it is technically feasible, but the trans-CBD is acceptable too (*GR moderate*). In the latter case, the primary closure of CBD is as effective as T-tube drainage in the prevention of complications (*GR moderate*). Finally, intraoperative cholangiography is recommended for those patients with suspected, non-preoperatively confirmed CBDDS (*GR moderate*).

4.6 Decision-Making Algorithms

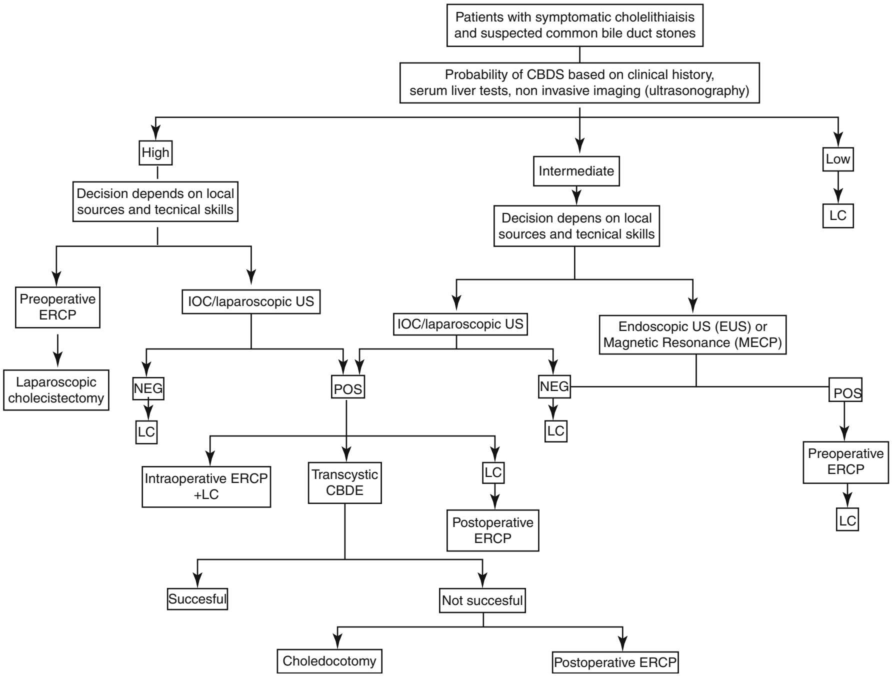

Fig. 4.1 The flow-chart shows the decision-making process in case of symptomatic cholelithiasis associated to the clinical or instrumental suspicion of common bile duct stones

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5 Laparoscopy and Acute Cholecystitis: The Evidence

Fabio Cesare Campanile, Alessandro Carrara, Michele Motter, Luca Ansaloni, and Ferdinando Agresta

5.1 Introduction

Acute cholecystitis is a relevant healthcare problem. Between 3 and 10 % of all patients with abdominal pain have acute cholecystitis [1].

Cholelithiasis accounts for more than 90 % of causes of acute cholecystitis [2, 3]. About 10–15 % of the adult population of Western countries have gallstones [4–7]. About 700,000 cholecystectomies are performed annually in the USA [8]. In Italy more than 101,000 cholecystectomies have been performed in 2011, 90 % of them laparoscopically [9]. About 10–30 % of cholecystectomies are performed for acute cholecystitis [10].

The laparoscopic approach was initially considered being contraindicated for acute cholecystitis, but it has been adopted later, as experience increased, gradually overtaking open cholecystectomy as the preferred procedure even in an acute setting.

The severity of the disease may range from a mild, self-limited illness to a severe, potentially life-threatening illness.

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Between 50 and 70 % of the cases of acute cholecystitis occur in aged patients [11], and steady increase in life expectancy during the past years will make the problem even more relevant in the future. High prevalence of comorbidities in elderly, as well as increased incidence of complications, sepsis, and severe forms of cholecystitis in this population, often causes a serious surgical emergency.

Several international guidelines addressed the issue of diagnosis and treatment of acute cholecystitis [12–15].

5.1.1 Diagnostic Criteria

Diagnosis of acute cholecystitis relies on a combination of local clinical signs, systemic signs of inflammation, and imaging findings. Very similar sets of criteria, able to achieve almost 100 % specificity, have been suggested in the EAES guidelines of 2006 [16] and the Tokyo Consensus Meeting Guidelines [13]; both can be used in the clinical practice.

The EAES guidelines adopted a scheme validated by a systematic review: (a) acute right upper quadrant tenderness for more than 6 h and ultrasound evidence of acute cholecystitis (the presence of gallstones with a thickened and edematous gallbladder wall, positive Murphy's sign on ultrasound examination, and pericholecystic fluid collections) or (b) acute right upper quadrant tenderness for more than 6 h, an ultrasound image showing the presence of gallstones, and one or more of the following: temperature above 38 °C, leukocytosis, and/or C-reactive protein level greater than 10 mg/L [17].

The Tokyo Consensus Meeting, in 2007, focused on a set of diagnostic criteria that are summarized in Tables 5.1 and 5.2 [18]. The same panel, however, in the 2013 revision of their guidelines, agreed that the proposed criteria were ambiguous and difficult to use, and a definite diagnosis could not be supported in current practice without positive diagnostic imaging studies [13].

The guidelines issued in 2013 included Tc-HIDA scan among the imaging techniques to be taken into consideration and proposed a set of severity assessment criteria that formed the basis for their therapeutic strategy [13].

5.1.2 Indications for Laparoscopy

The safety of laparoscopic cholecystectomy for acute cholecystitis has been shown in several studies. Two randomized trials (LoE2) [19, 20], a population-based outcome research (LoE3) [21], and numerous comparative studies demonstrated that laparoscopic cholecystectomy is associated with faster recovery and shorter hospital stay than open cholecystectomy. The US population-based outcome research showed also lower morbidity and mortality for the 6 years examined [21]. A third randomized controlled study demonstrated that the laparoscopic cholecystectomy caused less surgical trauma and immunosuppression (by measuring serum C-reactive protein and tumor necrosis factor-α (TNF-α) secretion of peripheral blood

Table 5.1 Diagnostic criteria for acute cholecystitis

(A) Local signs of inflammation 1. Murphy's sign, (2) RUQ mass/pain/tenderness
(B) Systemic signs of inflammation 1. Fever, (2) elevated CRP (>3 mg/dl), (3) elevated WBC count
(C) Imaging findings: imaging findings characteristic of acute cholecystitis
Definite diagnosis (Tokyo Guidelines 2007) [18] 1. One item in A and one item in B are positive
2. C confirms the diagnosis when acute cholecystitis is suspected clinically
Definite diagnosis (Tokyo Guidelines 2013) [13] 1. One item in A + one item in B + C
Suspected diagnosis (Tokyo Guidelines 2013) [13] 1. One item in A + one item in B

Modified from Yokoe et al. [13, 18]
Note: acute hepatitis, other acute abdominal diseases, and chronic cholecystitis should be excluded

Table 5.2 Imaging findings of acute cholecystitis

Ultrasonography findings (EL 4) Sonographic Murphy's sign (tenderness elicited by pressing the gallbladder with the ultrasound probe) Thickened gallbladder wall (>4 mm; if the patient does not have chronic liver disease and/or ascites or right heart failure) Enlarged gallbladder (long axis diameter >8 cm, short axis diameter >4 cm) Incarcerated gallstone, debris echo, pericholecystic fluid collection Sonolucent layer in the gallbladder wall, striated intramural lucencies, and Doppler signals
Magnetic resonance imaging (MRI) findings (LoE2–4) Pericholecystic high signal Enlarged gallbladder Thickened gallbladder wall
Computed tomography (CT) findings (LoE4) Thickened gallbladder wall Pericholecystic fluid collection Enlarged gallbladder Linear high-density areas in the pericholecystic fat tissue

From Hirota et al. [18]

mononuclear cells) and also confirmed that it was associated with a shorter hospital stay [22]. This evidence supported the EAES recommendation that laparoscopic cholecystectomy be the treatment of choice for acute cholecystitis (EAES Consensus Conference about laparoscopic approach to acute abdomen [12] and EAES Consensus Conference about laparoscopic cholecystectomy, held in 2013).

It cannot be excluded, of course, that the better outcome of the laparoscopic cholecystectomy be related to the medical staff attitude toward expectation of faster recovery rather than to true physiopathological changes (expectation bias). The trial published by Johansson in 2005 was designed to avoid this bias and included a blind

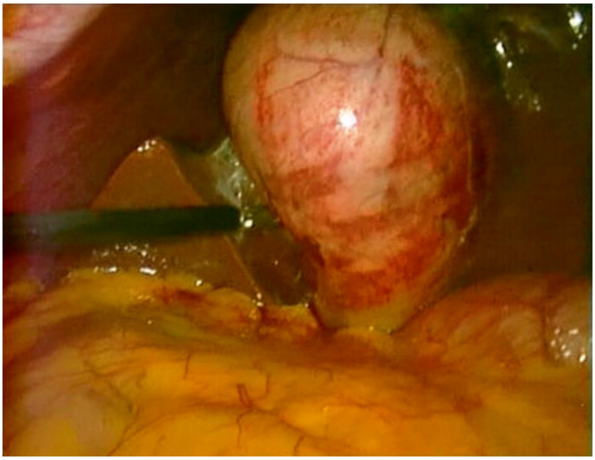

Fig. 5.1 severe cholecystitis: empyema

assessment of outcomes: the wounds were concealed to both patients and postoperative care staff, unaware of the surgical access received by the patient. They showed a very similar postoperative course but still demonstrated a shorter postoperative hospital stay for the laparoscopic group [20].

The preference for laparoscopic cholecystectomy is confirmed by the panel of the Tokyo guidelines, first published in 2007 and recently updated [14], but it is actually limited only to the mildest forms of the disease, excluding most of the severe forms. We will discuss later such a cautious approach and the issue of a therapeutic decision making based on the severity of the local inflammation or the patient general condition as it involves every aspect of the treatment of acute cholecystitis.

Here, it is important to state that review of the literature shows that local inflammatory conditions do not preclude the indication for laparoscopic cholecystectomy (Fig. 5.1). The trial of Kivuloto et al. [19], mentioned above, specifically included gangrenous cholecystitis. Furthermore, a recent review of prospective and retrospective series of severe cholecystitis (gangrenous, empyematous, or perforated) (LoE3) [23] did not show an increase in local postoperative complications and confirmed that laparoscopic cholecystectomy is to be considered an acceptable indication for severe cholecystitis despite a demonstrated threefold conversion rate. The patients examined in the review, and treated by laparoscopic cholecystectomy, would have been instead directed to other treatments by the Tokyo guidelines scheme.

Subtotal cholecystectomy also appears to be an acceptable alternative solution in case of intense inflammation and increased risk of damage to Calot triangle structures (LoE3) [24, 25].

Another subgroup that deserves a separate analysis is the elderly population. The number of elderly with acute cholecystitis has been increasing over the years; earlier reports suggested increased morbidity and higher conversion rate for laparoscopic cholecystectomy in elderly [26]. However, the acute biliary disease appears to be more severe in the older patients and overall prevalence of comorbidities is higher, making it difficult to extrapolate data from series involving both acute and chronic gallbladder disease [27, 28] or comparing younger versus older patients [29, 30].

Several prospective and retrospective comparative studies examined laparoscopic versus open surgery for acute cholecystitis in elderly patients demonstrating a reduction in the length of hospitalization [31–33] and morbidity either unchanged [31] or improved [32–34] (LoE3).

5.1.3 Timing of Surgery

In the pre-laparoscopic era, randomized controlled trials comparing early versus delayed open cholecystectomy had found that early surgery was associated with a lower complication rate and a briefer hospital stay [35–38]. In the 1990s, however, it was suggested that early treatment of acute cholecystitis by laparoscopic cholecystectomy could be related to an increased risk of conversion and complications, in particular bile duct injury [39]. Since then, the optimal timing of surgical treatment of acute cholecystitis has been extensively debated. A systematic review of the literature found seven randomized controlled trials [40–46] examined in 5 meta-analysis (LoE1) [10, 47–51] comparing early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Six of those seven papers were RCTs (LoE2), but one of the systematic reviews [51] included a nonrandomized study (LoE3) [45].

All the studies agreed that early treatment reduces total hospital stay, without an increase in complication or conversion rates. In particular, rate of bile duct injury seems to be higher in the delayed treated patients, but the difference was not statistically significant due to the small numbers analyzed in the trials [10, 50].

Four further RCTs (LoE2) were not included in any systematic review because they were published later [52–55]. Three of them reported similar results between the two groups; the large trial by Gutt confirmed the superiority of the early cholecystectomy [54].

The definition of time interval for early or delayed surgery, however, varies among the studies: surgery is considered “early” either 4 or 7 days of the onset of symptoms, and planned delay of treatment after index admission may vary between 6 and 12 weeks. In the studies of Chandler [43], the group of delayed treatment included patients operated after resolution of symptoms or within 5 days if the symptoms failed to resolve; those patients would be considered in the “early” group in the rest of the trials; this study has not been included in 3 out of 5 systematic reviews.

The Cochrane review published by Gurusamy and Samraj [50] pointed out that 17.5 % (range 13.9–25 %) of patients included in the delayed surgery groups required urgent surgery during the interval period, for failure of conservative treatment or recurrent symptoms after discharge, and in this subset the conversion rate was 45 %. These data could further support early surgery.

After those studies, several case series were published and confirmed the value of early surgery. However, population-based outcome researches [56–61] showed that practice patterns remain variable worldwide.

Four cost-utility analyses focused on early versus delayed cholecystectomy for acute cholecystitis. Only one of them, performed in a prospective randomized trial, found no significant difference in the cost or outcomes of early laparoscopic cholecystectomy versus delayed treatment, with the latter favored by the incremental cost per additional QALY; however, patients operated on for biliary colic were included in that trial [62]. A model-based economic evaluation and two recent additional analyses found that early surgery is less expensive and results in better quality of life than delayed treatment [63–65].

If the advantages of early laparoscopic cholecystectomy are well defined, the optimal amount of delay for surgery after the onset of symptoms is not completely clarified in the above mentioned studies and deserves a more precise definition. One case series reviewed the issue of the amount of delay between the onset of symptoms and surgery and examined its relation to the conversion rate: the earlier the operation, the lower the risk of conversion. The incidence of conversion is lowest (9.5 %) if surgery is performed within 2 days from the onset of symptoms, rises to 16.1 % if surgery is done within 4 days. After that term, the conversion rate is similar to that of delayed surgery (38.9 %) (LoE4) [66]. However, if one recent observational study confirmed those findings [67], others did not [68–70] (LoE4). A subgroup analysis performed by Gurusamy on the data of his Cochrane review [52] did not show a statistically significant difference between the patients treated less than 4 days from the onset of symptoms and those of the studies including also patients with a longer delay. One large population-based studies, mentioned above, examined the association between outcomes and preoperative length of hospital stay (used as a surrogate marker for the onset of symptoms); their patients were divided into six different groups according to the delay of surgery after hospital admission: group 1, operated on the day of admission; group 2, 1 day after hospital admission; group 3, 2 days; group 4, 3 days; group 5, 4 or 5 days; and group 6, on or after day six. There was no significant association between preoperative length of stay and postoperative mortality or overall morbidity. However, patients hospitalized for two or more days before surgery sustained longer operative times and were significantly more likely to require open cholecystectomy than patients operated on the day of admission. As the time point of surgery is delayed (day of admission versus six and more days after admission), significantly more patients undergo a longer operation and were more likely to be converted to a laparotomy [56]. Similar results were found in the study by Brooks on a total of 5,268 patients [61].

A definitive conclusion on this issue has yet to be reached; however, the available literature allows us to state that cholecystectomy should be performed as early as possible after the onset of symptoms, without evidence of a clear cutoff delay, after which the outcome is significantly worse. Further studies could clarify this issue.

Only one retrospective trial examined the results of early versus delayed treatment in the aged, finding no outcome difference between the two groups [71]. Riall et al., recently, examined a sample of the US Medicare Claims Data System and found that 75 % of the patients aged 66 years and older, urgently or emergently admitted to an acute care facility for a first episode of acute cholecystitis, received an early cholecystectomy (71 % laparoscopic and 29 % open). The diffuse use of early laparoscopic cholecystectomy in elderly patients confirms that most US surgeons trust that early laparoscopic cholecystectomy should be offered, for acute cholecystitis, even in that age group. The same analysis showed that lack of definitive treatment during initial hospitalization in elderly patients is associated with 38 % gallstone-related readmission rate over the subsequent 2 years (with only 9.5 % of the patients undergoing an elective outpatient cholecystectomy), compared with 4.4 % in patients who underwent early treatment (LoE3) [72].

5.1.4 Percutaneous Cholecystostomy (PC)

Severe comorbidities in elderly or other unstable patients can, however, make early anesthesia or surgery itself too risky. Several alternatives have been proposed for emergency treatment in septic high-risk patients unfit for emergency surgery: conservative treatment (LoE2) [73], tube cholecystostomy followed by early laparoscopic surgery (LoE2) [74] or by delayed surgery (LoE4) [11], and cholecystostomy not followed by surgery (LoE4) [75].

Among the alternatives proposed for the emergency treatment in septic high-risk patients, percutaneous tube cholecystostomy (followed or not by surgery) is extensively reported in the recent literature. In particular the abovementioned Tokyo guidelines consider the percutaneous drainage as mandatory in the severe grade of acute cholecystitis and also suggest its use in the moderate grade, in order to overcome the technical difficulties of an inflamed gallbladder. However, percutaneous gallbladder drainage has never been proven to be an effective alternative to early surgery; the evidence on its role is still lacking.

No randomized controlled trial is yet available on the use of gallbladder drainage in acute cholecystitis. Winbladh et al. published a systematic review with a particularly detailed examination of 53 papers about cholecystostomy as an option in acute cholecystitis (LoE3). The average level of the papers examined in their study is rather poor, and the results are nonhomogeneous. Acknowledged these limitations, the review found no evidence to support the recommendation of percutaneous drainage rather than straight early emergency cholecystectomy even in critically ill patients. Early cholecystectomy actually seems to be a better option for treating acute cholecystitis in the elderly and/or critically ill population [76]. The comparison of the mortality rate after PC (15.4 %) with that after acute cholecystectomy (4.5 %) in similar series shows a significant difference ($p < 0.001$) in favor of acute cholecystectomy.

After their review, about 13 retrospective and 2 prospective series have been further published, confirming that the groups considered in the studies, their inclusion criteria, the results, and even the conclusions reached by different authors are largely nonhomogeneous. Bearing in mind these limitations, the reported in-hospital mortality for cholecystostomy varies between 4 and 50 %

(vs. 4.5 % reported for cholecystectomy), and its morbidity ranges between 8.2 and 62 %.

At the present time, percutaneous cholecystostomy cannot be recommended as part of a routine protocol for treatment of acute calculous cholecystitis, but only considered as a possible alternative to reduce anesthesiology risk in a small subset of patients unfit for emergency surgery due to their severe comorbidities. A randomized controlled trial (CHOCOLATE trial) has been planned to attempt to clarify the largely conflicting evidence [77].

5.1.5 Severity Tailored Approach

If the advantages of early laparoscopic cholecystectomy in an unselected population are clarified by the evidence reported above, it can be argued that still it could be possible to improve the overall outcome tailoring the treatment according to the severity of the condition and to the patient status.

The question arises if early surgery, in particular laparoscopic, is indicated for every acute cholecystitis. What is the best treatment for the frailer patients and the more advanced forms of inflammation? Should the clinical decision making take into account a grading system for the severity of the disease and the illness of the patient? As a matter of fact, the heterogeneity of patients, comorbidities, and environment in which this disease presents make the diagnosis, and the subsequent therapeutic procedures, very difficult to standardize; the severity of inflammation and its life-threatening potential are also strongly determined by the general condition of the patient, and the choice of a surgical treatment cannot disregard this aspect [78].

The severity assessment criteria, included in the Tokyo guidelines, take into consideration both general and local factors and classify acute cholecystitis into three severity degrees. An acute cholecystitis is defined “severe” if the condition has developed organ dysfunction and “moderate” if local inflammatory condition (marked leukocytosis, palpable tender mass, onset of symptoms >72 h, gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis) may increase the probability of local complications (“criteria predicting when conditions might be unfavorable for cholecystectomy in the acute phase”). If none of these conditions are present, the cholecystitis is classified as “mild”[13, 18].

Based on that scheme, the Tokyo guidelines recommend early cholecystectomy only in the mild forms (grade I), in which a laparoscopic cholecystectomy is likely to be easy. In the moderate cases, they maintain that medical therapy with or without early gallbladder drainage (surgical or percutaneous) followed by delayed cholecystectomy is indicated, except in “experienced” centers. Cholecystostomy is also preferred for patients placed in the “severe” grade by their organ dysfunction.

Such severity-based classification, however, has not been validated by studies showing an improved outcome after its introduction, and actually a retrospective series failed to find any significant benefit [85].

The severity tailored approach of the Tokyo guidelines ends up in a large use of delayed cholecystectomy, despite the amount of literature against its use. Today, early laparoscopic cholecystectomy is the gold standard, established (as examined above) by evidence level 1 meta-analysis.

Furthermore, several reports show that early cholecystectomy is safe and effective even in the severe forms of the disease (LoE3) [23, 79, 80], (LoE4) [81] or in the elderly population (LoE4) [71, 72, 82].

Finally, a definitive conclusion about the use of percutaneous cholecystostomy has yet to be drawn as discussed above.

Aside from the Tokyo scheme, several clinical scores for the evaluation of surgical risk for acute conditions are available [83], but none is validated for acute cholecystitis. Weighting the risk of early surgery for acute cholecystitis against a well-established risk score could help in identifying those patients with reduced functional reserve who could benefit from a treatment alternative to surgery. The overall outcome of the treatment of this condition could be improved. This selection is not going to be straightforward, until we can achieve a more complete assessment of the results of the alternative treatments available, including morbi-mortality, functional status, and quality of life beyond hospital stay: de Mestral et al., in an elderly population treated by percutaneous cholecystectomy (890 patients among 27, 718 acute cholecystitis between 2004 and 2011), showed that besides a 5 % in-hospital mortality, an additional 18 % of patients had died by 1 year and less than 50 % had received the planned cholecystectomy. An overall 49 % of patients had at least one gallstone-related emergency department evaluation or hospital admission 1 year after discharge [60].

The need for further investigations aimed to a patient-related and evidence-based algorithm that can be related to the clinical and therapeutic decision making for acute cholecystitis remains.

5.1.6 Is Acute Cholecystitis Actually Treated by Laparoscopic Cholecystectomy?

The surgical approach suggested by the Tokyo guidelines appears to be extremely cautious if compared to the findings available in the literature. The EAES Consensus Conference statements are much more assertive in suggesting that laparoscopic cholecystectomy is the treatment of choice for acute cholecystitis and should be performed as soon as possible after the onset of symptoms. Despite the limited surgical indications, the introduction of the Tokyo guidelines seems to be able to increase the adoption of early laparoscopic cholecystectomy as reported by Asai [84].

A Japanese study, based on a large administrative database, examined the records of 6,080 patients with acute cholecystitis from 777 hospitals (68 academic and 709 community hospitals) between April and December of 2008. It is rather surprising to find that only 35 % of those patients received surgery at some point of their hospital course (mean length of stay 20.2 ± 18.2 days). Among the patients who did not receive gallbladder drainage, most likely the mildest forms, only 50.5 % received early surgery and an additional 13.2 % had cholecystectomy later than 4 days after the hospitalization [58]. After all the introduction of their paper reveals a preconceptual nonsurgical attitude when states that antimicrobial therapy is the mainstay of therapy for acute cholecystitis followed by drainage if the patient fails to improve.

If the Japanese database showed a low cholecystectomy rate for acute gallbladder disease, Western population-based studies reported rates higher but still inferior to the expectations if the indications provided by the literature are to be considered. A report by Csikesz et al., based on the US National Hospital Discharge Survey, demonstrated that the cholecystectomy rate on the first admission was 40 % in the years between 2000 and 2005 [21]. Sandzén et al., on a similar Swedish database, examined between 1988 and 2006, reported that surgery was performed during the index admission in 32.2 % of cases [59]. Only the study on the Medicare Claims Data System, published by Riall et al., reported an overall 75 % cholecystectomy rate during the first admission [72] between 1996 and 2005. It has to be specified that, unlike the Japanese study, the time frame taken into consideration by these reports includes years in which the use of laparoscopy was not widespread.

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di Chirurgia (SIC), Società Italiana di Chirurgia d'Urgenza e del Trauma (SICUT), Società Italiana di Chirurgia nell'Ospedalità Privata (SICOP), and the European Association for Endoscopic Surgery (EAES). Surg Endosc 26:2134–2164. doi:10.1007/s00464-012-2331-3
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Number of Trocars, Types of Dissection, Exploration of Bile Duct, Drainage and Analgesia

6

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Laparoscopic cholecystectomy is a gold standard, but at this time several aspects of technique are not homogeneous, and there are many differences in terms of indications, instruments, technologies involved, and surgical techniques employed. So we decide to examine specifically the literature about five main topics, trying to solve some concern existing about.

A literature search has been done in PubMed starting from 2000 to 2013 with the following limits and filters: adult, clinical trial, review, and English language. The PICO (population, intervention, comparison, outcome) system was applied for the Mesh (Medical Subject Headings) search whenever possible. Analogous search has covered the Cochrane Collaboration database and the Trip database in order to gather all the remaining evidence, synopses, and guidelines on the topic. The search strings used are the following:

local anesthesia[All Fields] OR "*anesthesia, local*"*[MeSH Terms] AND* "*cholecystectomy, laparoscopic*"*[MeSH Terms] OR laparoscopic cholecystectomy[Text Word];*"*analgesia*"*[MeSH Terms] OR analgesia[Text Word] AND* "*cholecystectomy, laparoscopic*"*[MeSH Terms] OR laparoscopic cholecystectomy[Text*

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F. Agresta et al. (eds.), *Laparoscopic Cholecystectomy*,
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Word];"pain"[MeSH Terms] OR pain[Text Word] AND "cholecystectomy, laparoscopic"[MeSH Terms] OR laparoscopic cholecystectomy[Text Word];("cholecystectomy, laparoscopic"[MeSH Terms] OR ("cholecystectomy"[All Fields] AND "laparoscopic"[All Fields]) OR "laparoscopic cholecystectomy"[All Fields] OR ("laparoscopic"[All Fields] AND "cholecystectomy"[All Fields])) AND (("drainage"[MeSH Terms] OR "drainage"[All Fields] OR "drain"[All Fields]) OR ("drainage"[MeSH Terms] OR "drainage"[All Fields]));"three port" [All Fields] OR "port"[MeSH Terms] AND "cholecystectomy, laparoscopic"[MeSH Terms] OR laparoscopic cholecystectomy[Text Word];"four port"[MeSH Terms] OR "port" [Text Word] AND "cholecystectomy, laparoscopic"[MeSH Terms] OR laparoscopic cholecystectomy[Text Word];"Three four port";[Text Word] AND "cholecystectomy, laparoscopic"[MeSH Terms] OR laparoscopic cholecystectomy[Text Word];"Trocar" [All Fields] "cholecystectomy, laparoscopic"[MeSH Terms] OR laparoscopic cholecystectomy[Text Word];Intraoperative[All Fields] AND (("cholangiography A total of 215 items came out, 3 RCT and 1 Metanalysis and 2 Retrospective and/or prospective cohort studies were analyzed"[MeSH Terms] OR "cholangiography"[All Fields]) OR ("cholangiography"[MeSH Terms] OR "cholangiography"[All Fields] OR "cholangiogram"[All Fields]));"laparoscopic cholecystectomy"[All Fields] AND ((Cystic[All Fields] AND duct[All Fields]) OR (Cystic[All Fields] AND ("arteries"[MeSH Terms] OR "arteries"[All Fields] OR "artery"[All Fields])) OR (Metallic[All Fields] AND ("surgical instruments"[MeSH Terms] OR ("surgical"[All Fields] AND "instruments"[All Fields]) OR "surgical instruments"[All Fields] OR "clips"[All Fields])) OR (Absorbable[All Fields] AND ("surgical instruments"[MeSH Terms] OR ("surgical"[All Fields] AND "instruments"[All Fields]) OR "surgical instruments"[All Fields] OR "clip"[All Fields])) OR (Absorbable[All Fields] AND ("Nat Mater"[Journal] OR "Materials (Basel)"[Journal] OR "materials"[All Fields])) OR (("ultrasonography"[MeSH Terms] OR "ultrasonography"[All Fields] OR "ultrasonic"[All Fields] OR "ultrasonics"[MeSH Terms] OR "ultrasonics"[All Fields]) AND ("instrumentation"[Subheading] OR "instrumentation"[All Fields] OR "devices"[All Fields] OR "equipment and supplies"[MeSH Terms] OR ("equipment"[All Fields] AND "supplies"[All Fields]) OR "equipment and supplies"[All Fields])) OR Endo-Gia[All Fields] OR Endo-loop[All Fields] OR (Monopolar[All Fields] AND ("electrocoagulation"[MeSH Terms] OR "electrocoagulation"[All Fields] OR "electrocautery"[All Fields])) OR (electrothermal[All Fields] AND monopolar[All Fields] AND sealer[All Fields]) OR (electrothermal[All Fields] AND bipolar[All Fields] AND sealer[All Fields])) AND Randomized Controlled Trial

A total of 5,323 articles come out, respectively:

- 225 for three- versus standard four-port technique
- 1,738 for techniques of dissection from the liver bed and occlusion of cystic duct and artery
- 2,314 for intraoperative cholangiography
- 826 for drainage
- 220 for analgesia

Four independent researchers screened the titles and abstracts and subsequently applied the previously described limitations in order to select and extract in full text the pertinent articles, respectively:

- 3 RCT and 1 meta-analysis and 1 retrospective and/or prospective cohort study were analyzed for three- versus standard four-port technique.
- 5 RCT, 4 meta-analysis, 5 cohort studies, and 3 editorials for techniques of dissection from the liver bed and occlusion of cystic duct and artery.
- 8 RCT and 5 systematic reviews, 10 retrospective and/or prospective cohort studies, and 2 editorials for intraoperative cholangiography.
- 4 RCT, 2 meta-analysis, and 2 editorials for drainage.
- 19 RCT and 12 meta-analysis and 6 editorials for analgesia.

The papers have been classified for evidence strength following the Oxford CEBM 2011 scheme.

6.1 Three- Versus Standard Four-Port Technique

Standard laparoscopic cholecystectomy is mainly done by using four trocars. With increasing surgeon experience, laparoscopic cholecystectomy has undergone many refinements including reduction in port size and number. It has been argued that the fourth trocar may not be necessary, and laparoscopic cholecystectomy can be performed safely without using it. Several studies have reported that three-port laparoscopic cholecystectomy is technically feasible and safe. Further, in the era of laparoscopic surgery, less postoperative pain and early discharge are the major goals to achieve better patient care and cost-effectiveness. It is difficult to compare the two surgical techniques because there is no standardization especially in trocar size and position.

There are one meta-analysis of randomized clinical trials and one prospective randomized study that agree in affirming that there are no significant differences between the three-port group and four-port group in terms of operating time, success rate, and postoperative hospital stay; the second study finds some advantages in the three-port technique such as less pain, less costs, and fewer scars [1, 2] (LoE 1). The three-port laparoscopic cholecystectomy technique is safe and has no increase in bile duct injuries [3] (LoE 2).

Cerci C et al. and Dhafir Al-Azawi et al. in their studies state that there is no need of preoperative clinical and ultrasound patient selection, because the three-port technique was found to be safe when performed on acute and chronic cholecystitis and always reached the same results in terms of operating time, conversions, complications and postoperative pain, and time of discharge [4, 5] (LoE 3).

In conclusion, the three-port technique has similar outcomes with conventional four-port technique. There is no evidence of any advantage of this technique versus the traditional one, but at the same time there are no clear limits to its wide applicability in elective procedures. There was also some evidence of shorter hospital stay with 3-port technique, but length of hospital stay is largely determined by local policy, and increasingly 3- and 4-port technique cholecystectomies are performed as day-case procedures. Therefore, this reduces the impact of any positive effect of the 3-port technique on length of hospital stay.

6.2 Techniques of Dissection from the Liver Bed and Occlusion of Cystic Duct and Artery

The occlusion of the cystic duct is one of the main steps of laparoscopic cholecystectomy. Usually it has been done by metal clips, but it could be done by several methods (absorbable clips, clipless with ultrasonic dissector, with stapler, and so on). Currently, monopolar electrosurgical energy is the most commonly used energy undertaken for dissection of the liver bed. However, its application is associated with numerous risks, such as biliary compilations and thermal injuries. The application of ultrasound within the harmonic frequency range, which limits lateral energy spread reducing the risk of distant tissue damage compared with high-frequency electrosurgery, has been suggested as an alternative to conventional electrosurgical energy.

Traditionally, we use nonabsorbable metal clips to occlude the cystic duct permanently. The simple clips used are U-shaped pieces of titanium which were tightly closed around the duct using a 5-mm or 10-mm applicator. Usually three large clips were applied, and the cystic duct was sheared between the proximal and middle clips. However, applying multiple clips is neither feasible nor safe for dilated (>1 cm) and difficult cystic ducts, for example, in patients affected by Mirizzi syndrome type I, acute cholecystitis, acute cholecystitis with acute cholangitis, and biliary pancreatitis. Clip-related complications were a problem with metallic clips [6] (LoE 2).

The surgeon should proceed with ligation only when the cystic duct and artery are clearly identified and encircled. The use of metal clips, absorbable clips, or ties is up to the individual preference of the surgeon. Once the artery and cystic duct are divided, the surgeon should rule out the presence of further tubular structures before proceeding with the separation of the gallbladder from the liver bed. During dissection of the gallbladder from the liver bed, the surgeon should carefully look for accessory (Luschka) ducts. These ducts should be ligated and not just divided with electrocautery to avoid postoperative bile leakage. Any open subvesicular duct should be treated with sutures. Any thin continuous tubular structure running on the liver bed should be opened. If it bleeds, it can be diathermed. If it is of biliary origin (Luschka duct), it should be ligated [7] (LoE 1). Hem-o-lok clips is not a very safe method to control vessel and cystic duct during laparoscopic cholecystectomy, because the clips can fall down into common bile ducts and clip migration can lead to hemorrhage and bile leakage [8] (LoE 4).

6.2.1 Absorbable Materials

The use of absorbable materials (absorbable locking clips, endoloops, or suture transfixion) to occlude the cystic duct has been suggested as an alternative for metal clips for various reasons. Locking absorbable clips come as part of a disposable cartridge and are easy to use and apply; they consist of an outer rigid body of polyglycolic acid that slides over a soft pliable polyglyconate inner clip. Once applied, they are not easily dislodged. There is a reduced inflammatory reaction to absorbable clips, as compared with metallic clips [9] (LoE 2). A study conducted by Yano H. et al., to examine the usefulness and safety of absorbable clips in laparoscopic cholecystectomy, based on 328 patients treated with absorbable clips and 444 with metal clips, suggests that absorbable clips are as safe and effective as standard metal clips for vessel and duct ligation in laparoscopic cholecystectomy [10] (LoE 2). Laparoscopic cholecystectomy with intracorporeal ligation of cystic duct was very safe and economical, above all for management of enlarged cystic duct. Using this technique a surgeon should have sufficient experience to do intracorporeal knot by practicing in an endo-box first [11] (LoE 4). For a dilated and difficult cystic duct >1 cm, an alternative is applying laparoscopic intracorporeal interrupted or continuous sutures using absorbable or nonabsorbable material to close the cystic duct, as in the open procedure. However, this method is technically demanding and time-consuming [6] (LoE 2). In a recent review of 2010, three trials including 255 patients were qualified for this review; Gurusamy KS et al. concluded that they are not able to determine the benefits and harms of different methods of cystic duct occlusion because of the small sample size, short period of follow-up, and lack of reporting of important outcomes in the included trials. Adequately powered randomized trials with low risk of bias and with long periods of follow-up and assessing all of the important outcomes for patients and professionals are necessary [12] (LoE 1).

6.2.2 Monopolar Electrocautery of the Cystic Artery

There is an increasing trend among surgeons to use monopolar electrocautery for control of the cystic artery during laparoscopic cholecystectomy. Although many feel that electrocautery is an unsafe method of controlling the cystic artery because of concerns over both adequacy of hemostasis and collateral tissue damage. Katri et al. report their experience with the use of monopolar electrocautery to control the cystic artery during laparoscopic cholecystectomy. The study included 158 laparoscopic cholecystectomies. The artery was controlled using monopolar electrocautery in 114 patients (77.5 %) and by metal clips in 33 patients (22.5 %). The authors believe that the monopolar electrocautery is safe and effective for control of the cystic artery during laparoscopic cholecystectomy. A good visualization of the cystic artery and careful use of cautery are essential to achieve these results. The size of the artery was the only factor identified in this study to affect the decision; electrocautery was used safely and efficiently to control small and medium (<3 mm) cystic arteries [13] (LoE 3). Kavlakoglu et al. in their study reported that the use of diathermy or electrocautery is one of the important factors that causes bile duct damage. Therefore, the injury is named as diathermy-induced bile duct injury [14] (LoE 2).

6.2.3 Ultrasonic Devices

Skepticism still exists in using ultrasonic shears as the sole instrument for laparoscopic cholecystectomy. A prospective randomized study has shown the safety and superiority of ultrasonically activated scalpel in laparoscopic cholecystectomy in terms of dissection and sealing of cystic artery and duct without any increase in intraoperative and postoperative complications. The ultrasonically activated scalpel has a cutting and coagulation effect similar to electrocautery but is devoid of many harmful effects that occur for the lateral spread of electric current. Ultrasonic shears generate temperatures ranging from 80 to 100 °C, compared with 200 °C or more with conventional electrocautery. The depth of penetration of ultrasonically generated heat is nearly 1.5 mm, which reduces the chances of injury to important structures such as bile ducts and arteries. A prospective, randomized study of Sudhir Kumar Jain et al. shows decreased postoperative pain and analgesic requirement and shorter hospital stay with the use of ultrasonic scalpel [15] (LoE 2). Some authors published their work with a recommendation that ultrasonic shears can effectively ligate cystic duct up to 6 mm in diameter. The cystic duct and common bile duct status were confirmed preoperatively by ultrasonography [16] (LoE 1). Ultrasonic dissection is safe and effective, and it improves the operative course of laparoscopic cholecystectomy by reducing the incidence of gallbladder perforation [17] (LoE 2). Ultrasonically activated scalpel used as a single working instrument allows the use of a two-working-trocar technique, with better cosmetic results and more patient satisfaction in follow-up [18] (LoE 3). Catena F et al. in a prospective analysis claim that the use of harmonic scalpel, without adversely affecting postoperative morbidity rates, appears to correlate with reduced rates of laparoscopic-open conversion during video-laparo-cholecystectomies (VLCs) in case of acute cholecystitis. Given this evidence, the harmonic scalpel may be more suitable for technically demanding cases than monopolar diathermy [19] (LoE 2). Cengiz Y. et al. performed ultrasonic fundus-first dissection; the cystic artery was divided with the ultrasonic shears; the cystic duct was clipped; the use of electrocautery has been associated with a higher white cell count and slower return to preoperative values than ultrasonic dissection. It creates a larger zone of tissue damage and more loss of nerve function. The degree of tissue damage, with subsequent inflammation and edema, may affect the level of pain and nausea after surgery [20] (LoE 1). Huscher CGS et al. in a prospective randomized trial showed that the use of ultrasonic dissection during laparoscopic cholecystectomy seems to reduce the risk of common bile duct injuries and biliary complications. Nevertheless, a learning curve in the use of ultrasonic-activated devices is required, and significant differences in postoperative major complications and biliary complications between the expert and the surgeon-in-training subgroups were shown [21] (LoE 3). Ultrasonic devices have been used successfully to achieve closure and division of the cystic duct and artery; however, they are considered expensive and not used widely during laparoscopic cholecystectomy [13] (LoE 3). A recent meta-analysis reveals a possible benefit associated with the use of ultrasonic energy over monopolar electrical energy in laparoscopic cholecystectomy. The data indicate that ultrasonic energy is as safe and effective as electrosurgical energy and potentially might be safer in laparoscopic cholecystectomy. However, cost-effectiveness needs to be established in well-structured cost-benefit analysis before its use can be recommended for general application [22] (LoE 1).

6.2.4 Endo-GIA

The cystic duct is sometimes inflamed, edematous, fibrous, and too large to be managed safely and easily in the condition of cystic duct stone. Dilated cyst duct was defined as cystic duct diameter >1.0 cm. Endo-GIA is effective and practical in selected patients and should be the preferred treatment in dilated and difficult cystic duct. However, the following important safety points must be noted. First, the dilated cystic duct was cleaned until the anatomy was clear both to prevent misinterpreting it as common bile duct and both to create the adequate space to apply an Endo-GIA. Second, an adequate length of cystic stump is required to prevent common bile duct side wall injury. This protects against common bile duct partial injury and ensures safe closure of the cystic duct [6] (LoE 2).

6.3 Intraoperative Cholangiography

Intraoperative cholangiography (IOC) was performed for the first time by Mirizzi in 1931 during open cholecystectomy in a female patient with gallbladder hydrops [23, 24]. Since then, IOC has been advocated to reduce the risk of biliary injuries and of retained stones in the common bile duct (CBD). While this debate is still going on fervently, other techniques to delineate biliary tree anatomy are also being investigated and reported in the medical literature. These relatively innovative techniques include fluorescent cholangiography, laparoscopic ultrasonography, and preoperative MRI cholangiography. These approaches have shown some promising results, but IOC is still probably the most commonly used investigating adjunctive procedure for cholecystectomy.

Even in the era of laparoscopic cholecystectomy, there remain ongoing controversies regarding the role of routine versus selective IOC, because there are no prospective randomized trials nor meta-analysis showing a significant decreased incidence of bile duct injury when IOC is routinely used.

In 2012 Sajid et al. [25] published a meta-analysis of four randomized controlled trials [26–29] (LoE 2) reporting that routine cholangiography during cholecystectomy is helpful for perioperative bile duct stone detection and for readmission rate reduction, but is associated with significantly longer operative time and more perioperative complications; bile duct injury rate was the same in cholecystectomy with or without cholangiography (LoE1).

In 2011, Ford et al. [30] published a meta-analysis of eight randomized controlled trials [26–29, 31–35] concluding that there is no robust evidence to support or abandon the use of IOC to prevent retained CBD stones or bile duct injury; none of the trials analyzed, alone or in combination, were sufficiently powered to demonstrate a benefit of IOC routine use (LoE 1).

There are several large, retrospective population-based studies showing that the incidence of bile duct injury is higher in patients undergoing cholecystectomy who did not have IOC performed.

In 2011 Buddingh et al. [36] published a meta-analysis of six retrospective, large, population-based studies [37–42], each with 10,000 or more patients, that compared the incidence of bile duct injuries (BDI) in cholecystectomies explicitly performed using IOC to that in cholecystectomies explicitly performed without IOC. From this meta-analysis, the odds ratio (OR) for BDI when using IOC was 0.67 (range = 0.61–0.75), demonstrating a well-established relationship between IOC and a lower incidence and increased early detection of BDI; the authors concluded that IOC is recommended to be performed routinely (LoE 3).

If many investigators [37–40, 43] advocate the routine use of IOC (LoE 3), the cost-effectiveness and efficacy of this approach have been questioned by others [41, 42, 44–46] (LoE3). Metcalfe and colleague [47] in 2004 reviewed eight retrospective series of laparoscopic cholecystectomies (total of 6,024 patients) with routine IOC and nine series (3,268 patients) with a selective IOC policy; in this study the rates of complete CBD transection were not significantly different between the two groups, although a larger proportion of BDI was identified intraoperatively when routine IOC was used (LoE 3).

More recently, in 2013, Sheffield and colleague [48] published an interesting retrospective cohort study based on the reports of all Texas Medicare claims data from 2000 to 2009; of 92,932 patients undergoing cholecystectomy, 37,533 (40.4 %) underwent concurrent intraoperative cholangiography and 280 (0.30 %) had a common duct injury. The common duct injury rate was 0.21 % among patients with intraoperative cholangiography and 0.36 % among patients without it; controlling confounders with instrumental variable analysis, there was no statistically significant association between intraoperative cholangiography and common duct injury (OR, 1.26 [95 % CI, 0.81–1.96], $p = .31$). The authors concluded that routine IOC is not effective as a preventive strategy against common duct injury during cholecystectomy (LoE3).

An important issue is the role of IOC in the intraoperative detection of an eventual bile duct injury. Ludwig and colleague [49] in 2002, analyzing results from a cohort of 3,27,523 patients from 40 published case series, reported a significantly lower rate of CBD injury in case of LC and routine IOC compared to LC with selective IOC (0.21 % vs 0.43 %, $p < 0.05$); with routine use of IOC, 90 % of all injuries could be diagnosed intraoperatively, which corresponded to a detection rate twice as high as with the selective use of IOC (90 % vs 44.5 %, $p < 0.05$). The authors concluded that liberal use of IOC helps to reduce the incidence of CBD injuries and minimize the severity of injury, facilitates intraoperative detection, and improves the outcome of affected patients. It still remained unproven whether the general use of IOC may be recommended on these bases (LoE 3).

There is an additional issue related to the routine versus selective IOC debate. If surgeons are not sufficiently trained to perform intraoperative cholangiography, they may be not able to properly interpret the findings and may waste too much time for this procedure.

In conclusion, IOC itself cannot prevent a bile duct injury, but the additional information gained, especially in a difficult cholecystectomy associated with anatomic ambiguity, may lower the risk and can provide its early detection and repair if an injury has already occurred. The role of IOC has been extensively investigated, and several national surveys have been published. The results are controversial, often biased by retrospective data collection, poor data quality (mostly based on questionnaires or data codes), and impossibility to determine the intent of IOC use at the time of intervention (routine or to protect against injury, to detect CBD stones, or for suspected injury). Whether this procedure should be performed routinely is still an active subject of debate, but several of the larger retrospective studies have indicated that despite the increased time in operative procedure and materials needed, routine IOC may be cost-effective by reducing the severity of BDI and the cost of the treatment of retained stones. However, a truly causal relationship between routine IOC and reduced BDI has yet to be conclusively established, which leaves the issue unresolved, probably forever.

6.4 Drainage

Drains are used after laparoscopic cholecystectomy to prevent abdominal collections and to help the surgeon in the management of bleeding and biliary injuries. However, drain use may increase infective complications and delay discharge. The value of surgical drainage in laparoscopic cholecystectomy is an issue that is not resolved clearly.

The SAGES Guidelines [50] (LoE 1) reported that while use of drain postoperatively after laparoscopic biliary tract surgery is at the discretion of the operating surgeon, recent studies including a randomized controlled trial and meta-analysis of six randomized controlled trials found that drain use after elective laparoscopic cholecystectomy increases postoperative pain and wound infection rates and delays hospital discharge; the authors further stated that they could not find evidence to support the use of drain after laparoscopic cholecystectomy. Drains are not needed after elective laparoscopic cholecystectomy and their use may increase complication rates. Drains may be useful in complicated cases particularly if choledochotomy is performed.

The Cochrane Database of Systematic Reviews [51] (LoE 1) found no evidence to support the use of drains in laparoscopic cholecystectomy. Drains are used after laparoscopic cholecystectomy to prevent abdominal collections. However, drain use may increase infective complications and delay discharge. Drain use after elective laparoscopic cholecystectomy reduces early postoperative pain but increases wound infection rates and delays hospital discharge. We could not find evidence to support the use of drain after laparoscopic cholecystectomy.

In the EAES consensus conference on laparoscopic cholecystectomy of 1994, drainage is not required during laparoscopic cholecystectomy [52] (LoE 1). The drain was not useful in elective, uncomplicated LC [53] (LoE1).

The routine use of a drain in noncomplicated laparoscopic cholecystectomy has nothing to offer; in contrast, it is associated with longer hospital stay [54] (LoE 1). The effect of subhepatic drain on postoperative pain is controversial. Significant reduction of postoperative pain in patient without drain insertion with respect to those with subhepatic drains was reported in the trial of Tzovaras et al. [55] (LoE 1).

Kazuhisa et al. found that the mean VAS scores were significantly greater in the drain group than in the non-drain group at 24 and 48 h especially in women. On the contrary, Tzovaras et al. suggested that the routine use of a drain in elective laparoscopic cholecystectomy has nothing to offer and it is associated with increased pain. Gurusamy et al. and Tarik et al. and Gouda El-Labban reports showed no significant differences in postoperative nausea and vomiting between drain and no drain groups [51, 54, 56] (LoE 1). Postoperative pain was intensified by the insertion of a drainage tube after LC. This tendency was stronger in women [56] (LoE 1).

The insertion of a subhepatic drain after elective laparoscopic cholecystectomy increases postsurgical pain and prolongs hospital stay and does not prevent the occurrence of intra-abdominal abscesses [57] (LoE 2).

Hawasli and Brown found that there were minor but not statistically significant differences between drain group and non-drain group in terms of postoperative severity and duration of the abdominal pain and shoulder pain [58] (LoE 2).

In conclusion, we can confirm that there is no evidence of any advantage resulting from the use of drainage and then routine use of drain is not necessary after elective laparoscopic cholecystectomy.

6.5 Analgesia

Postoperative pain has been an important limiting factor for ambulatory LC. To date, the exact mechanism of pain has not been clarified. The use of intraperitoneal local anesthetics and the use of a local anesthetic applied to the port wounds provide some benefit in pain reduction, but their results are controversial.

The origin of pain after laparoscopic cholecystectomy is multifactorial with pain arising from the incision sites (somatic pain), from the gallbladder bed (visceral pain), and as a consequence of a pneumoperitoneum. Many researchers have suggested that the combination of somatovisceral local anesthetic treatment reduces incisional, intra-abdominal, and shoulder pain in laparoscopic cholecystectomy. Pain after laparoscopic cholecystectomy carries a high interindividual variability in intensity and duration and is largely unpredictable. Pain is most intense on the day of surgery and on the following day and subsequently declines to low levels within 3–4 days. However, pain may remain severe in approximately 13 % of patients throughout the first week after laparoscopic cholecystectomy.

Boddy et al. identified several factors that may influence the benefits of intraperitoneal local anesthetic (IPLA), namely, dose, concentration, timing, site, spillage of bile and blood, instillation in the head-down versus supine position, and volume of residual gas left in the abdomen [59] (LoE 1). Kahokehr at al. described the results of a meta-analysis of 30 RCTs. Various methods of IPLA in laparoscopic cholecystectomy (LC) have been described. There is benefit to be gained in terms of pain reduction, analgesia use, and blunting of endocrine response after LC. Clinical heterogeneity was high due to the variation of IPLA protocols. We conclude that the use of IPLA is beneficial to reduce pain in LC, and further trials in this area are not needed. An effective and safe dose seems to be 20 ml of 0.5 % bupivacaine applied to the dissection bed prior to pneumoperitoneum release [60] (LoE 1).

True Bisgaard found that the complexity of pain after laparoscopic cholecystectomy suggests that effective treatment of postoperative pain should be multimodal. Based on a critical analysis of current literature, the regimen includes preoperative single dose of dexamethasone, incisional local anesthetics (at the beginning or at the end of operation, depending on preference), and regular use of NSAIDs or COX-2 inhibitors combined during the first 3–4 postoperative days, including the day of surgery. Prophylactic treatment of postoperative opioids is not recommended because of the many potential side effects. Short-acting opioids should be used only [61–64] (LoE1).

Yeri Ahn concluded that dexamethasone 8 mg i.v. should be given preoperatively. Preoperative administration of NSAIDs or COX-2 inhibitors is indicated, and pre-incisional local anesthesia to wounds and peritoneum should be used. Intraperitoneal LA was shown to be beneficial in seven of nine trials. In two trials, in which no difference emerged, LA was administered at the end of the procedure [65–70] (LoE 1).

Gupta concluded that preemptive intraperitoneal instillation combined with trocar site LA should be used [67] (LoE 1). Karaaslan et al. showed the effect of LA to be greatest when it was administered at the commencement of pneumoperitoneum [69] (LoE 1).

Opioids provide effective treatment of postoperative intense pain. However, to accelerate recovery and avoid side effects, routine use of opioids is not recommended in patients after laparoscopic cholecystectomy. Postoperative short-acting opioids should be used when needed to supplement basic analgesic treatment. Better outcomes are using PCA [61, 71] (LoE 1).

Pneumoperitoneal pressure of <9 mmHg may be useful in reducing postoperative pain scores even in combination with local anesthesia [65, 72] (LoE 1).

Alkhamesi et al. showed aerosolized LA to be more effective than injected intraperitoneal LA. Aerosolized intraperitoneal local anesthetic is an effective method for controlling postoperative pain. It significantly helps to reduce opiate use and contributed to rapid mobilization leading to short hospitalization and possible reduction in treatment costs [73] (LoE 1).

Pre-incisional LA has been shown to be superior to post-incisional infiltration. Two trials showed that the combination of intraperitoneal and incisional LA is superior to either method alone and reduces PONV. Preinsertion of local anesthesia at the trocar site in laparoscopic cholecystectomy significantly reduces postoperative pain and decreases medication usage costs [74] (LoE 2).

Pre-incisional transversus abdominis plane (TAP) block revealed good analgesic outcome, but our understanding of the TAP block and its role in contemporary practice remains limited [75–77] (LoE 2–3).

We can conclude that a multimodal approach to postoperative pain after laparoscopic cholecystectomy is strongly recommended, pre-incisional local anesthesia to wounds and peritoneum instillation should be used to relief pain and facilitate a faster hospital discharge, and finally, opioids provide effective treatment of postoperative intense pain, but to accelerate recovery and avoid side effects, their routine use is not recommended.

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Complications: How to Prevent and Manage Them

7

Piero Narilli, Annalisa Di Filippo, Mario Campli, Michele Motter, and Alessandro Carrara

7.1 Bile Duct Injuries

7.1.1 Introduction

A quarter of century from the first laparoscopic cholecystectomy (LC) and more about 20 years after it was established the gold standard for gallbladder removal, a rate of biliary duct injuries (BDI) is still reported with a range from 0.25 to 0.74 % for major BDI and from 0.28 to 1.7 % for minor BDI [1, 2] (survey) [3–10] (LoE4) [11–14] (LoE3). The accepted incidence for total BDI is nowadays attested in about 0.4 % [1] (survey) [12, 15] (LoE3) and seems to remain constant despite advances in this surgical field.

Nowadays only knowledge of risk factors and efforts to understand causes may help the surgeon to decrease BDI incidence. Patient features, as age or sex, and local factors, as acute or chronic inflammation, anatomic variations, previous abdominal surgery and hemorrhage, are associated in literature with BDI, but because of a small number of cases it is not always possible to provide data for the relevance of these factors.

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7.1.2 Identification of Calot's Triangle Structures

Misidentification of structures within the Calot's triangle is the most frequent cause of BDI [16] (LoE4) so that a correct and conclusive identification of cystic and common bile duct (CBD) may help to prevent injuries. With this goal, routine use of intraoperative cholangiography (IOC) is often advocated, although the efficacy and cost-effectiveness are nowadays discussed. In our systematic review CBD injury risk during LC was similar with or without routine IOC, even if IOC was reported helpful in perioperative CBD stone detection [17] (LoE1). No routine IOC was associated with shorter operative time and fewer perioperative complications. The IOC may be adopted for patients undergoing LC when clinical, biochemical, or radiological features are suggestive of CBD stones [17] (LoE1). In a recent population-based cohort study, early detection of BDI using IOC led up to an improved survival [14] (LoE3). The EAES guideline that routine IOC cannot be recommended even if it allows early identification of BDI, as long as it is correctly interpreted, is still valid. To visualize the junction of cystic duct and CBD with the aim to decrease the incidence of BDI, routine use of intraoperative laparoscopic ultrasound (IOUS) was also proposed. Hashimoto M. et al. referred 94 % of intraoperative valid identifications of biliary structures in 200 enrolled patients during LC before IOC [18] (LoE3). Machi J. et al. reported 96 % of successful IOUS in 200 patients during LC, whereas, in selected cases (3.5 %), IOC was needed with no false-positive detection of the identified 20 bile duct stones [19] (LoE3). Even if this technique may be useful to select patients needing IOC and to detect stones, the effectiveness of routine IOUS as an alternative to usual methods for identification of anatomic structures of Calot is nowadays unclear and not strongly recommended.

7.1.3 Critical View of Safety (CVS)

The effort to standardize an approach to the cystic artery and duct brought Strasberg et al. [20] (LoE2) to outline the "critical view of safety" (Figs. 7.1, 7.2, 7.3, and 7.4). Although there is only limited evidence from clinical studies to back this technique, the EAES guidelines recommended to perform this strategy [21]. A more detailed description of the evidence available on CVS is in Chap. 2.

7.1.4 About Conversion

Despite the advances in training and increased clinical experience, conversion rates reaching 10 % are still reported [22] (LoE4). Needful prompt conversions are mandatory to avoid complications, but few studies have investigated the causes of conversion. Lengyel et al. recently claimed that conversion, in many circumstances, is performed "electively" due to an "anticipated" difficulty, with a longer hospital stay and higher costs [23] (LoE4) [24] (LoE3). Furthermore, to identify the timing and the main reasons for conversion, they concluded that the conversion was elective in

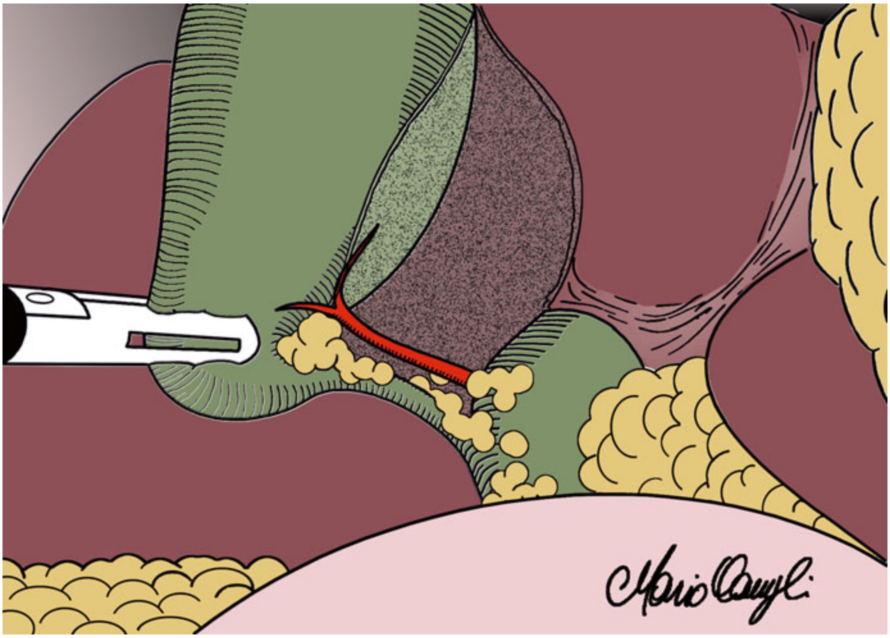
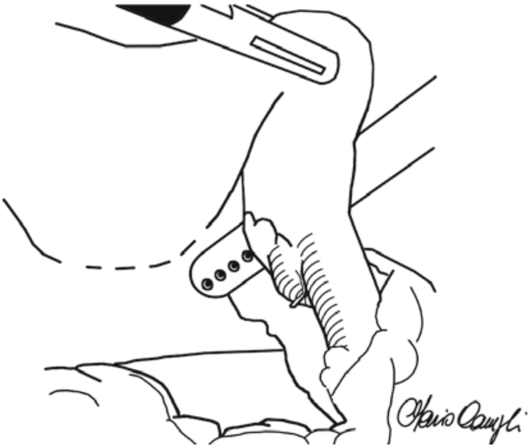


Fig. 7.1 Critical view of safety: gentle grasper traction exposes structures in Calot's triangle



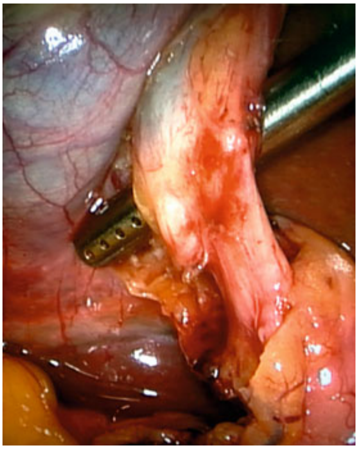


Fig. 7.2 Underpassing cystic duct and artery to obtain the critical view of safety avoids bile duct injuries

91 % of the examined cases. In about half of these cases, conversions were performed without a genuine attempt at laparoscopic dissection and the inserted trocars were fewer than four [22] (LoE4). Despite, several limitations of the study (small sample size, degree of laparoscopic training, experience of the surgeons), the authors believe that all laparoscopic cases should be genuinely attempted, the

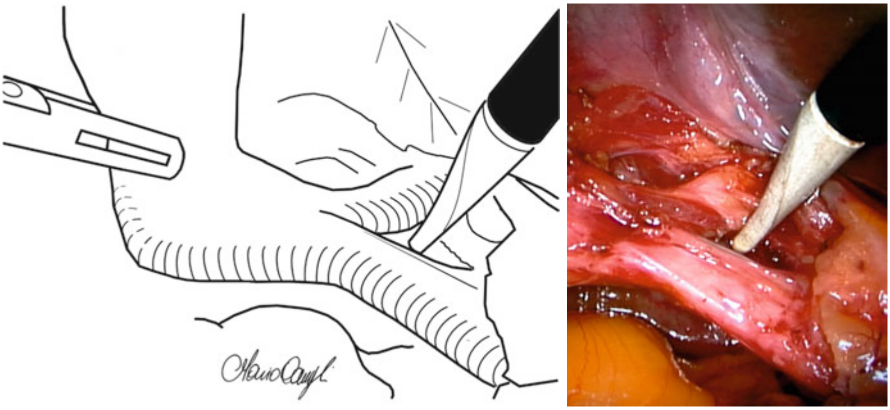


Fig. 7.3 Accurate isolation of each anatomical structure

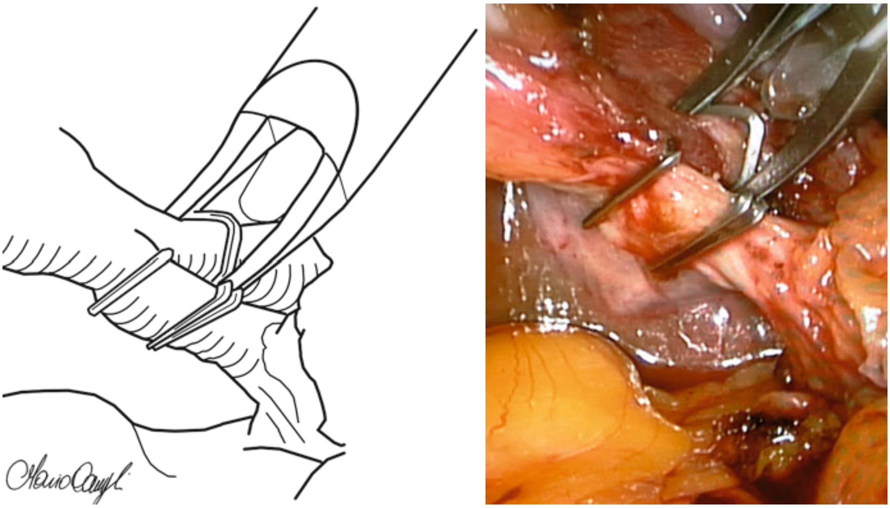


Fig. 7.4 Clipping and dividing structures in Calot's triangle only after a clear identification

correct number of ports placed, and some effort made at dissection. With decreasing experience in open cholecystectomy, this procedure does not always seem to be a "safe" alternative.

7.1.5 Partial Cholecystectomy

In the case of a difficult LC (e.g., in acute cholecystitis wherein dissection of Calot's triangle is challenging due to severe adhesions or inflammation), a change in surgical strategy such as anterograde or partial cholecystectomy or even drainage may be more practical than conversion. Since surgical skill and experience play an

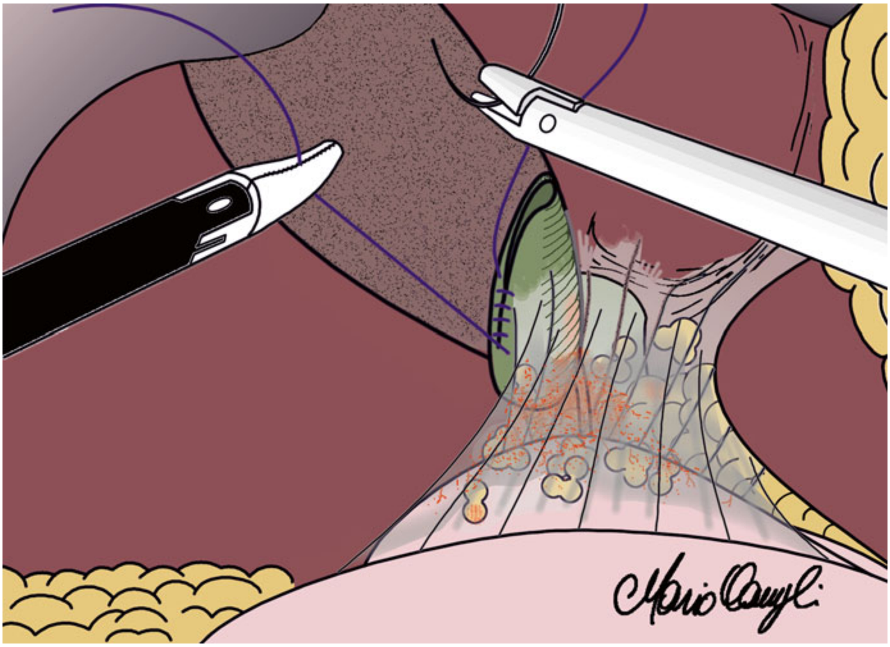


Fig. 7.5 Partial cholecystectomy

important role, a different surgical strategy may be especially valuable for less experienced surgical teams. An alternative approach to conversion aimed at preventing BDI is laparoscopic partial cholecystectomy (Fig. 7.5). The safety and efficacy of this procedure are unclear. Literature concerning LPC is poor. Henneman et al. [25] (LoE3), in 625 patients suffering from acute cholecystitis who received partial (subtotal or incomplete) cholecystectomy, reported a median hospital stay of 4.5 days and one case of BDI. Without firm conclusions, closure of the remnant gallbladder pouch, cystic duct, or both seems favorable, minimizing the need for ERCP, reducing the amount of leaks and the associated hospital stay, and lowering the rate for recurrent symptoms of gallstone disease and for the risk of BDI. Also Davis et al. in a recent retrospective case-control study evaluated this technique in a series of patients with acute cholecystitis. They reported a half postoperative complication with no BDI after this strategy, suggesting partial cholecystectomy as an alternative approach to conversion. Furthermore, this technique with removing necrotic portions of the gallbladder may prevent empyema formation [26] (LoE4).

7.1.6 Intraoperative Management

A single-institution retrospective analysis of a large series of patients with diagnosis of BDI sustained during LC was recently published where 88 % of the patients receiving on-table repair during surgery had a favorable evolution. The authors concluded that the intraoperative diagnosis of BDI is a very important topic with lower morbidity and mortality rates [27] (LoE4). Even though only case series and expert opinions in management were published in the medical literature, there is a growing body of literature supporting the importance of early referral to a tertiary care hospital to treat BDI with a multidisciplinary approach [28–31] (LoE4) [32] (LoE3) [33] (LoE2). And so the EAES guidelines [21] recommend that "nevertheless no high-quality evidence dealing with this question was identified from clinical studies, the management of BDI should be performed by surgeons who are experienced in this field."

7.2 Abscesses

The incidence of abscesses in LC is very low. In a large national survey of 77604 LCs [34], the reported abscess incidence was 1/13,000 complications. Bile leakage and gallstone spillage remain the most frequent causes of abscesses after surgery [35–45] (LoE4) [46] (LoE3). Untill now only case reports or case series are published in examined literature, and therefore it was not possible to perform a systematic review according to the criteria of the best evidence-based literature.

7.2.1 Incidence

The incidence rate of unretrieved gallstones in the peritoneal cavity is high (2.4–50 %) [43, 47] (LoE4) [48] (LoE3); nevertheless severe complications are rarely described. The incidence of infection-related complications was reported in 0.1–0.3 %. Abscesses were generally located in the abdominal wall or in the subhepatic space, but less frequently anywhere in the abdomen and more likely in the setting of acute cholecystitis [49] (LoE3).

7.2.2 Management

In a retrospective analysis on 10,174 LCs, only 0.08 % required reoperation for abdominal abscess with no mortality. Since gallbladder perforation and stone spillage occur during the dissection (75 %) or the removal (25 %) of the gallbladder, caution in removing from the hepatic fossa is suggested, avoiding hurried traction to Hartmann's pouch [46] (LoE3). Less frequent causes include gallstone spillage during gallbladder retrieval across the umbilical port, especially if it is not recovered in an endobag, and so the use of this device is recommended [46] (LoE3). The number and the size of lost stone seem to be a risk factor for abscess growth. More than 15 stones or stones larger than 1.5 cm were found in more than 40 % of these patients [46] (LoE3). The kind of the stones seems to be an important factor: in the pigmented-type stones (black, brown, mixed), bacterial contamination was present in 83 % compared to 33 % in cholesterol calculi [46] (LoE3). It is suggested to send a sample of bile and/or a retrieved stone for microbiological analysis, because pathogens are usually the same as those that cause subsequent infections [46] (LoE3). Extensive peritoneal lavage is widely recommended, but care must be taken to not spread gallstones into more inaccessible sites, making retrieval even more difficult. Placing the irrigating instrument beyond the stones so that they are flushed into view can be helpful [48] (LoE3). Authors emphasize the need for removal of as many calculi as possible during laparoscopy [50] (LoE3). However, they advised conversion to an open procedure only in patients with too many gallstones left in the peritoneal cavity, especially when bacteriobilia is suspected or confirmed by Gram stain of the bile. They also noted that percutaneous drainage of intra-abdominal abscesses in most of the patients was ineffective if the inciting gallstones were not removed [50] (LoE3). There is no indication for converting the laparoscopic procedure to a laparotomy purely on the basis of spilled stones, but documenting spilled stones in the operation note and informing the patient about stones' spillage and its unlikely consequences should be useful. The surgeon should be alert to the possibility of abscess formation and other complications because early recognition of intraperitoneal gallstones is essential in the diagnosis and further treatment of symptomatic patients [45] (LoE4).

7.2.3 Antibiotic Prophylaxis and Therapy

In a recent Cochrane Systematic Review [51] (LoE1), Sanabria et al. concluded that there is no sufficient evidence to support or refuse the use of antibiotic prophylaxis to reduce surgical infections in low-risk patients undergoing elective LC.

In a recent randomized trial of 166 patients who suffered from accidental perforation of the gallbladder during elective LC, there was no significant association between antibiotic treatment and surgical wound infection [52] (LoE2). No patients developed residual abscess. In a multivariate analysis, diabetes mellitus, age over 60, operation time lasting more than 70 min, and ASA 3 were identified as independent factors significantly associated with the onset of surgical wound infection ($p < 0.001$) [52] (LoE2). The authors concluded that routine administration of an antibiotic to patients experiencing accidental perforation of the gallbladder during LC is not necessary. They recommend antibiotic prophylaxis, immediately before surgery, for patients with associated risk factors [52] (LoE2).

7.3 Hemorrhages

Vascular injuries during LC may more often occur during dissection of the Calot's triangle structures [53] (LoE4) [54] (LoE3). Unfortunately the clinical relevance and impact of vascular injuries may be dramatic for the surgeon and above all for the patient. The knowledge of the mechanism by which hemorrhages occur represents a fundamental way to diminish the risk of incontrollable bleeding during LC.

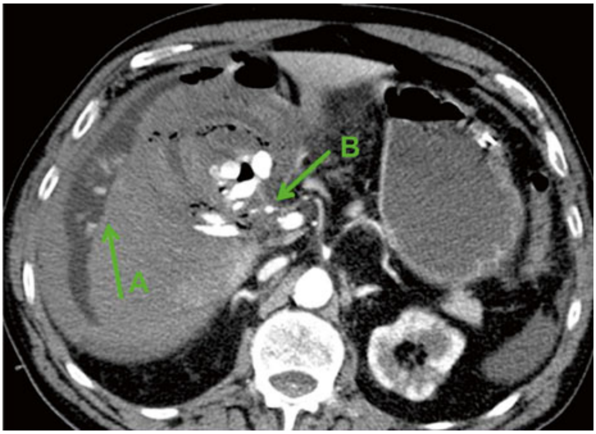


Fig. 7.6 Severe postoperative hypotension after LC: large perihepatic hematoma (*A*) and active bleeding of the gallbladder bed (*B*) (Courtesy of G. Gualdi – "Sapienza" University, Rome)

Recent literature still reports incidence data derived from systematic studies of the 1990s: the small number of cases and the wide extent of the confidence interval do not permit to obtain reliable updated incidence rate of bleeding in LC; furthermore, there is no uniform classification about major or minor bleeding. Maybe the real incidence of relevant hemorrhages during LCs is underestimated [54, 55] (LoE3).

Copious bleeding from the liver bed accounts for about 88 % of hemorrhages during LC [54] (LoE3) [56] (LoE4), while the right hepatic artery (RHA) injuries represent less than 12 % of cases [57, 58] (LoE3), with an overall rate of uncontrollable hemorrhages requiring open conversion ranging from 0.1 to 8 % [56, 59] (LoE4) [54, 60] (LoE3) (Fig. 7.6). Coagulation defects may be responsible for uncontrollable hemorrhage, and preoperative blood assessment must be carefully evaluated, and caution must be posed about the use of nonsteroidal anti-inflammatory drugs because of enhanced bleeding diathesis from poor platelet adhesiveness [61] (LoE4). Higher bleeding rate is reported in cirrhotic patients (26 vs 3.1 % in not cirrhotic patients) because of damaged liver function [62] (LoE3).

The common hemorrhage of the liver bed is often a borderline condition depending on the different caliber of the involved vessels. It frequently comes from small vascular branches so that direct pressure to the gallbladder bed via a laparoscopic instrument may arrest the hemorrhage [63] (LoE4), but surgeons have to keep in mind that a middle hepatic vein or an aberrant cystic artery (CA) may be also involved [63–65] (LoE4). The portal vein injury, often associated with hepatic artery injury (HAI), is the third highest ranking injury, although it is considerably less common (4 %) [66] (LoE4) [67] (LoE3).

CA bleeding may become a serious complication during LC, with an increasing risk of overlap vascular or biliary structures injuries, that may impose conversion to open surgery. The CA has many possible position, number, and origin with the RHA being the most common, and the knowledge of anatomical variations of the CA may help the surgeon to avoid hemorrhage [68] (LoE4).

The RHA, which is located in 82 % of the cases in the Calot's triangle ([69] Atlas), is the most common major vascular structure damaged during dissection of this anatomic space (90 %) [58] (LoE3). Stewart et al. [66] (LoE4) described how the RHA may be misidentified as the CA. The source of the error depends upon the common bile duct incorrectly identified as the cystic duct: in this case the transection of the common bile duct exposes the RHA, which is often clipped, based on the wrong assumption that it is a posterior CA. These mistakes emphasize the importance of identifying the CA and dividing it close to the gallbladder. The "fundus-first" technique, suggested for acute cholecystitis [70] (LoE4), may lead to a possible injury to the RHA, which might be retracted downwards, along with the gallbladder [71] (LoE4). For incontrollable hemorrhage, even if only few data are available on the real incidence of bleeding complications, the rate of conversion to open surgery was reported in about 8 % of the cases (meta-analysis from 39 studies for a total of 15,596 patients) [60] (LoE3).

Among patients with bile duct injury (BDI) during LC, the incidence of RHA injury was reported from 12 to 25 % [34] (survey) [71] (LoE4). Higher incidence was reported in the review by Pulitanò and colleagues [58] (LoE3) where 38 % of cases were combined with HAI. In cases of BDI and concomitant HAI, the arterial supply to the bile duct is often completely interrupted, further increasing the risk for potential ischemic stricture of the remaining right biliary tree as well as a high risk for hepatic necrosis. The sensitivity of the bile duct to ischemic injury is well described and might contribute to the increased morbidity after biliary reconstruction [58] (LoE3).

7.3.1 Hemostatic Agents

Many adjunctive local hemostatic agents are frequently proposed to favor bleeding control in liver surgery, but no strong evidence exists about their real efficacy during LC. Because their actual effectiveness is not yet extensively studied in large randomized, controlled prospective studies, the current indications for usage, both in hemorrhage and bile leakage, are not clear and mostly based on the individual surgeon's preference. Routine use of local hemostatic agents is not recommended.

7.4 Bowel Injuries

The incidence of all bowel injuries (BI) during LC is very low, and it was reported in literature from 0.07 to 0.5 % [54, 72, 73] (LoE3), but excluding lesions for trocar insertion or Veress needle, the specific LC-related causes are seldom referred and ascribe mainly to dissection, adhesiolysis [54] (LoE3), electrocautery burns, and tearing during retraction [74] (LoE4). BI comprise a severe complication when they do occur and may remain undetected during the operation [54] (LoE3). The injuries most frequently involve the small intestine, followed by the colon, duodenum, and stomach [75] (Chapter of book). Careful patient selection, control of the integrity of the isolation of the instruments, and no out-of-sight activities can diminish overall complication rates. Limited injuries to serosa may not require any treatment [76] (LoE4), while full-thickness lesions need immediate repair either laparoscopically [73] (LoE3) or with conversion to laparotomy. Since bowel injuries may remain undetected during the operation, any patient with signs of peritonitis, sepsis, or increased abdominal pain after laparoscopic surgery must promptly be investigated [72] (LoE3).

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New Technologies

8

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The evolution towards mini-invasiveness in surgery has opened new strategies in the way of performing laparoscopic cholecystectomy (LC), which have recently gained attention. Cholecystectomy has often been the field for the initial application of new technologies, since it remains the most common operation in abdominal surgery, mostly performed in the elective setting. Still, even if nowadays laparoscopic cholecystectomy is considered the "gold standard" since 1992, its indubitable advantages are still burdened by a slight but significant rise in the rate of major biliary injuries, which is certified around 0.42 % [1], which consists of a two- to fourfold rise in the rate reported in the literature for open cholecystectomy. Major concerns regarding the widespread of new technologies in LC should consider these data, and the university, the scientific societies, and the health providers

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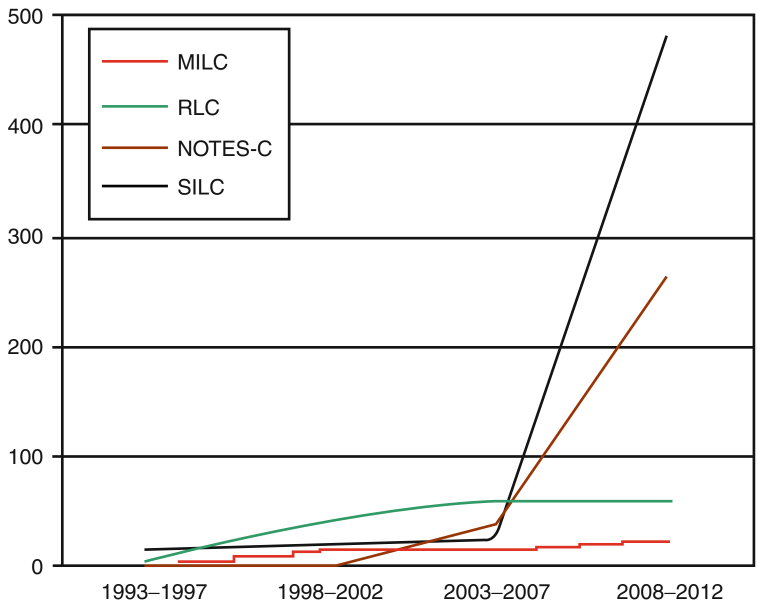

Fig. 8.1 Number of articles retrieved in PubMed concerning the new technologies for laparoscopic cholecystectomy

should ascertain the safety issues before considering a new surgical operation to be done outside clinical trials. This concept has not always been fulfilled, and some of the operations that we consider in this chapter have gained spread between surgeons, mostly due to a strong pressure by the industry of new surgical devices and instruments [2]. Also, reports on cost-effectiveness should be part of a surgical health policy, and the relatively few papers and health technology assessment reports on the subject are not the most cited references when analyzing a new technology [3].

We have taken into consideration four alternatives to standard 4-port LC, one strictly regarding the technological aspect (robotics) and three other aspects focused on reduced port surgery (mini-laparoscopy, single-access laparoscopy, and surgery through natural orifices). A literature search has been done in PubMed, Cochrane Library and Tripdatabase starting from 1994 through March 2013 and the papers have been classified for evidence strength following the Oxford CEBM 2011 scheme. The results in terms of quantity of studies published in PubMed are summarized in Fig. 8.1; the major interest in single-incision access for cholecystectomy is directly followed by studies in the field of natural orifice surgery, where the curves are still in the rising area, while the number of articles concerning mini-laparoscopy and robotics is slowly growing, but their number is far lower than the former.

8.1 Robotic Laparoscopic Cholecystectomy (RLC)

The question if a robotic assistant (RLC) could ameliorate the standard 4-port laparoscopic cholecystectomy (LC) has been highlighted by a recent meta-analysis of randomized controlled trials, where the authors put together both "camera only robotic assistants" (EndoAssist, Aesop, Passist) and fully robotic remote systems (Zeus, da Vinci). A detailed and systematic review of the literature revealed that there were six randomized clinical trials including 560 patients. One trial involving 129 patients did not state the number of patients randomized to the two groups. Of the remaining 431 patients in the remaining five trials, 212 patients underwent laparoscopic cholecystectomy with the help of robot assistant, and 219 patients underwent the same procedure with the help of a human assistant. All the trials were at high risk of bias and errors due to play of chance. Mortality and surgical complications were reported in only one trial with 40 patients. There was no mortality or surgical complications in either group in this trial. Mortality and morbidity were not reported in the remaining trials. Quality of life or the proportion of patients who were discharged as day-patient laparoscopic cholecystectomy patients were not reported in any trial. There was no significant difference in the proportion of patients who underwent conversion to open cholecystectomy or in the operating time between the two groups. Since the presumed lowering of errors due to a robotic assistant was not demonstrated, we can state that no significant advantage comes from a RLC over standard LC [4] (LE2).

The main drawback of advanced robotic surgery is the associated cost. Obviously, from the perspective of the cost requirements, an investment in this technology can only be justified if the costs are reasonable and a significant benefit is demonstrated regarding patient outcome. A prospective case-matched study was conducted on 50 consecutive patients, who underwent RLC (da Vinci robot, Intuitive Surgical) between December 2004 and February 2006. These patients were matched 1:1–50 patients with conventional laparoscopic cholecystectomy, according to age, gender, American Society of Anesthesiologists score, histology, and surgical experience. End points were complications after surgery, conversion rates, operative time, and hospital costs. No minor, but 1 major complication occurred in each group (2 %). No conversion to open surgery was needed in either group. Operation time (skin to skin, 55 min vs. 50 min, $p = 0.85$) and hospital stay (2.6 days vs. 2.8 days) were similar. Overall hospital costs were significantly higher for robotic-assisted cholecystectomy $7,985.4 (SD 1,760.9) versus $6,255.3 (SD 1,956.4), $p < 0.001$, with a raw difference of $1,730.1(95 % CI 991.4 –2,468.7) and a difference adjusted for confounders of $1,606.4 (95 % CI 1,076.7–2,136.2). This difference was mainly related to the amortization and consumables of the robotic system. In conclusion, RLC showed no benefits in clinical outcome over LC. The costs for RLC were significantly higher than for LC because of extensive expenses for the robotic system itself and its consumables and is, therefore, not justifiable [5] (LE3).

The role of RLC as a start-up for more difficult tasks in robotics was studied by Jayaraman et al. [6]. There were 16 procedures in the robotic arm and 20 in the laparoscopic arm. Two complications (da Vinci port-site hernia, transient elevation of liver enzymes) occurred in the robotic arm, whereas only one laparoscopic patient (slow to awaken from anesthetic) experienced a complication. None was significant. The mean time required to perform robotic cholecystectomy was significantly longer than laparoscopic surgery (91 vs. 41 min, $p < 0.001$). The mean time to clear the operating room was significantly longer for robotic procedures (14 vs. 11 min, $p = 0.015$). They observed a trend showing longer mean anesthesia time for robotic procedures (23 vs.15 min). Regarding learning curve, the mean operative time needed for the first 3 robotic procedures was longer than for the last 3 (101 v. 80 min); however, this difference was not significant. They concluded that RLC can be performed reliably, but, owing to the significant increase in operating room resources, it cannot be justified for routine use. Their experience, however, was far to demonstrate that RLC is one means by which general surgeons may gain confidence in performing advanced robotic procedures (LE3).

Vidovszky et al. [7] investigated the learning curve of the procedure. Interestingly, they did not experience a significant change in robotic operative time, changing from 38.2 ± 22.9 min for the first 16 cases (stage 1) to 32.5 ± 12.7 min for the last 16 cases (stage 3). These data suggested that the learning curve to master the robotic technique is short for a relatively simple procedure, such as cholecystectomy. The total robotic operative time was influenced primarily by the difficulty of the dissection, which varied from patient to patient. They found, however, that the total operating time ("skin to skin") improved from their initial 16 cases (85.6 ± 25.7 min) to the final 16 cases (68.2 ± 17.1 min), but this improvement represented primarily the improvement in setup time(LE4).

All the robotic trials available in literature have been performed in elective, non-inflamed cases: the role of RLC in acute cholecystitis is still to be studied.

Single-site surgery might reveal as a fascinating application for robotics: in fact the technical possibilities might bypass the limitations of a single-entry site. Since Desai's first operation in cadavers [8], Intuitive Surgical International (Sunnyvale, CA, USA) has developed a single-site platform for the da Vinci robot in 2010 [9]. Technical problems are still present, but studies have established its feasibility in urology, gynecology, and digestive surgery [10] (LE2).

The largest series about single-site robot-assisted laparoscopic cholecystectomy (SSRLC) was published by Pietrabissa et al. [11]. The primary goal of the study from an efficacy standpoint was completion of the procedure without conversion. The primary goal in terms of safety was freedom from major adverse events such as serious intraoperative injury or death. Other goals and focal points included measuring the times required to complete the procedure and analyzing the effect of the learning curve on the different recorded times. In addition to collecting data about the procedure, at the completion of the study, an 11-item questionnaire was administered to each of the 5 operating surgeons to gather their technical and clinical opinions about robotic single-site technology. Two patients underwent conversion. No major intraoperative complications occurred, but there were 12 minor incidents (7 ruptures of the gallbladder and 5 cases of minor bleeding from the gallbladder bed). Mean total operative time was 71 (±19) min, with a mean console time of 32 (±13) min. No significant reduction in the operative times was observed with the increasing of each surgeon's experience. The technique was judged more complex than standard 4-port laparoscopy but easier than single-incision laparoscopy as the robotic view, exchange of left-right hands, and triangulation allow an operation more comparable to standard LC(LE 4).

A reduction in the SSRLC operative time has been demonstrated in more recent case–control studies but still not comparable to standard LC times, due to docking and robot assembly [12, 13] (LE3).

Future implications of research should better study the role of RLC in the setting of costs, while randomized controlled trials to compare SSRLC to LC are awaited in order to establish a role for this procedure in selected patients especially in those centers where robotic surgery is routinely performed and that carry a great expertise.

8.2 Mini-Laparoscopic Cholecystectomy (MILC)

Mini-laparoscopic cholecystectomy (MILC) is a safe and technically feasible procedure for the treatment of gallstone disease and an alternative to single-port surgery (SPS). LC made through reduced 2- to 5-mm ports has gained a wide attention at the end of 1990s and at the beginning of 2000, as soon as the industries put new instruments in commerce especially for 2–5-mm trocars, including devices like scissors, forceps, and clip appliers. The three 5-mm trocar MLC allows the same surgical procedures to be undertaken as for the conventional approach.

The main goal was to achieve, with the use of reduced ports, less pain and a better cosmesis while keeping the same standards of work as in standard LC. It has regained attention after the onset of SILC, which carries the same goals in reducing mini-invasiveness, as an alternative method [14]. To this regard, in a meta-analysis of MILC versus LC, mini-laparoscopic cholecystectomy without intraoperative cholangiography (IOC) was successfully performed in a number of studies using a combination of three 3-mm ports with either 10-mm or 12-mm ports in study populations with variable exclusion criteria (LE2). Consistently with these observations, McCormack et al. successfully performed MILC with routine IOC using one 5-mm and three 3-mm ports in 89 % of consecutive elective cases of cholecystectomy, eliminating the likelihood of selection bias and demonstrating that IOC can be sufficiently performed as an adjuvant to the MILC technique when deemed appropriate based on surgeon judgment or preference. Most of the cases are described as using the standard trocar positions and keeping the larger trocar at the umbilical level (which serves for the extraction): the combinations in the articles retrieved vary from 3 to 4 trocars and various combinations of 2-, 3-, and 5-mm trocars, 5–10-mm cameras, and so on. Indeed a standardization of MILC has not yet been reached. A recent Cochrane review [15] (LE1) summarizes 13 RCTs comparing MILC to LC and finds a high rate of success (87 %). Pain was significantly lower in MILC and there was a better cosmetic satisfaction. Alas, the analyzed RCTs lack primary information on safety issues and are all at high risk of bias (incomplete blinding, outcome data and selective reporting). So, although morbidity and mortality are not significantly different in the two arms, its application outside selected trials is not recommended. Some criteria for selection of the patients and costs are eligible from the largest case series on MILC on 932 patients [16] (LE4); most patients reduced the operative trocar from 10/12 to 5 mm and the umbilical trocar to 5 mm, such as to have a 5-mm 3-port LC. A selection of 45 patients (elective cases, women with a low BMI) have undergone a 3-mm 3-port LC, and the fragility of instruments is enhanced as a costly issue.

From a financial perspective, previous studies [14] showed that there was no cost difference associated with the use of 3-mm ports and other MILC instruments compared to conventional instrumentation based on our accounting and cost allocation records. Further advantages of the proposed technique consist of cosmesis and also in a decrease of operative trauma. The latter might result in a reduced incidence of incisional hernias and possible complications (hemorrhages) at the site of trocars' insertion.

Lately, MILC has regained interest in the literature, as a possible alternative to single-incision technique, which is associated with loss of triangulation and decreased maneuverability, making the procedure technically demanding [17]; future randomized trials are welcome for a comparison of outcomes between the two methods.

The lack of standardization of the technique (how many 5-mm or 3-mm ports) is still a concern and further studies should aim at standardizing the operation. On the basis of the literature data, an all three 5-mm trocar MLC is feasible, effective, and easy to perform (without any increase in technical difficulties). The technique provides acceptable and comparable results concerning the operative time, the postoperative morbidity, and hospitalization as those already reported for conventional laparoscopy. Instead, the 3-mm MLC should only be considered in a small group of selected patients (young, thin, scheduled) and mainly for cosmetic reason. Sparing patients a wider skin incision at the trocar sites might reduce postoperative pain, increase prompt recovery of gastrointestinal functions, shorten hospitalization, help contain health-care costs, and increase cosmesis [18]. Still these benefits are not considered as primary without a strong information on its safety and clinical and economic benefits. This would also permit a more precise calculation of the costs of MILC and of the instruments required. The selection of a subgroup of patients which would mostly benefit from this approach is also an important issue to be studied in future trials.

8.3 Single-Incision Laparoscopic Cholecystectomy (SILC)

Single-incision laparoscopic surgery (SILS) is so called as it reduces to one skin incision the entry port to the abdomen. SILS is a step forward in the direction of mini-invasive surgery, and in recent years, its efficacy and security have been proved in operations on humans. The most "surgical" alternative to NOTES has started in 1997 [19] but had a boost starting from 2008 to 2010, together with the commercialization of new port devices, which allowed to solve the main problems of the single access: the creation of a stable transabdominal platform and the triangulation of instruments in the operating field. New articulated or curved instruments and new access devices were created in order to perform LC with the instruments passing through a single incision (or, in the beginning, multiple contiguous incisions) generally placed in the umbilicus. The umbilicus is the most used access point in this kind of surgery, because of the presence of a natural scar, which makes the procedure virtually scarless. Cholecystectomy, as it is the most frequent elective operation in surgery, was the mainstay of the technique, which has nowadays interested many surgical operations. There is a lot of literature on this subject, and it's the only new technology which has clinical guidelines [20] and a health technology assessment [21] written back in 2010. Then, the evidence was low and the advisors' committee suggested its use only in controlled clinical trials and by experienced laparoscopic surgeons who had received specific training in the procedure. Since then numerous randomized controlled trials have been conducted, and at least 5 meta-analyses of RCTs have been written in 2012 comparing SILC to LC and collecting 200–400 patients per arm [22–26] (LE1). The only ascertained significance, in accordance to all the studies, regards the time required to perform an SILC, which always results significantly longer with a weighted mean difference of 9–17 min. This parameter is often used as an index of an increased difficulty of the procedure, and its stabilization serves as a proxy to determine the learning curve: a pilot study from China [27] done by a single experienced surgeon showed a normalization of the operating time after 20 procedures (LE4), and another study from the USA evidenced the cutoff after 10 procedures [28] (LE4). Another claim of SILC was a better perceived cosmesis: the results of the meta-analyses seem to confirm it, but the evaluation scales and times were very heterogeneous in the analyzed trials, thus requiring confirmation in future studies. Another hope of the surgeons was a lowering of the postoperative pain in SILC, but no significant difference has ever been evidenced in the cited reviews. An interesting survey [29] (LE 4) asked 281 young women about their laparoscopic cholecystectomy (done in the previous 2 years); fewer than 50 % of patients recalled the number of incisions they had, and the more painful site was reported to be the umbilical incision by 2/3 of the patients. This puts some questions concerning the hypotheses of SILC benefits. The two operations have also no statistical differences regarding hospital stay or return to normal activity, morbidity, incisional hernias, or conversion to open surgery. The RCTs did not, alas, have the appropriate power to investigate differences in complications, as biliary injuries (which are the most feared and serious adverse effects of cholecystectomy) have very low rates in LC (0.4 %) [1]. A systematic review has been dedicated specifically to the calculation of bile duct injuries in a pool of 2,626 patients from 45 different studies [30] (LE2) and found a 0.72 % rate, significantly higher than LC. We concern, although, that the majority of the case series comprehended the learning curves. More definite data are awaited from large multicentric randomized trials, like the European MUSIC (MUlti-port vs. Single-port Cholecystectomy – http://music.world.it/). The costs of SILC can be higher and are especially related to single-port devices and operating room subcharges [31] (LE 2) by means of 2,000 $ (on 79 pts), even if this data is not confirmed by lower evidence studies [32] (LE 3). Costs might be reduced with the use of "home-made" devices for single-port entry [33] (LE 4), like the glove port, as shown in Fig. 8.2.

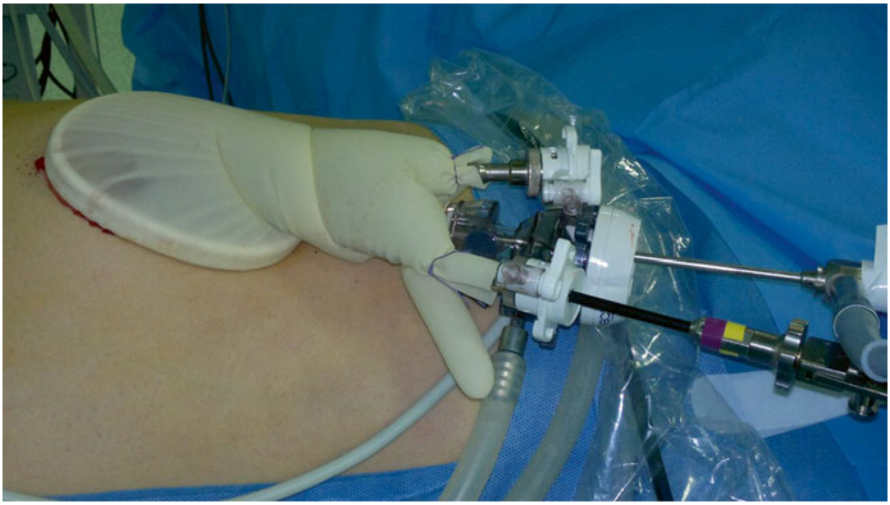

Fig. 8.2 Glove port for single-site surgery

Implications for research will need to focus on standardized and well-designed RCTs, in order to assess any advantage in terms of quality of life and cosmesis, which seem to be the only real advantages of SILC in order to select patients who would benefit from it.

8.4 Natural Orifice Cholecystectomy (NOTES-C)

The concept of access to the abdominal cavity by entering through natural orifices has been called to the attention of the surgical community since the first reported clinical cases in 2007 but has been conceived since 2004 in animal studies by Kalloo in 2004 in his report of peritoneoscopy and transgastric liver biopsy in a porcine model [34]. That same year, Rao and Reddy simultaneously performed peritoneoscopies and genital organ procedures using flexible endoscopes introduced perorally and in 2007 reported the first transgastric human appendectomy, which generated widespread interest in clinical applications of NOTES [35]. As for transgastric cholecystectomy, it was also in 2005 that Swanstrom's and Parks' teams successfully performed transgastric cholecystectomy and cholecystogastrostomy using flexible endoscopes in the animal model [36, 37]. Two years went by before any interest in clinical applications arose, and it was thanks to the use of the transvaginal route. The clinical transvaginal approach for NOTES was not preceded by extensive animal experimentation, since the accessibility and safety of this access route had been proven through the use of culdoscopy in gynecology and of the vaginal route to extract surgical specimens [38]. In early March 2007, Zorron's team performed the first series of transvaginal NOTES cholecystectomies in four patients, based on the previous experimental trials [39]. A short time later, Bessler successfully performed a hybrid transvaginal cholecystectomy with three abdominal laparoscopic entry ports [40], and in April 2007, Marescaux performed the purest NOTES cholecystectomy in a patient using a single abdominal entry port [41]. Since then clinical series of NOTES-C in humans have been published, although two distinct paradigms can be distinguished: one involving an endoscopical access to the peritoneum (EA-NOS or natural orifice surgery) and the other a more "surgeon-friendly" surgical access (SA-NOS). An analysis of the literature shows that the vast majority of human studies can be ascribed to SA surgery, whereas experimental research in animals and cadavers mostly involves EA surgery [42]. The former consists in gaining access through viscera (transgastric, colonic, rectal, vesical), with an operative endoscope that creates a controlled perforation which needs an endoscopical device to close it. It carries risks of infective contamination and the challenge of a failure of the parietal defect closure. Clinical case series are limited to few cases [43] (LE 4) in pilot and strictly controlled studies. They all used additional transabdominal mini-ports (hybrid NOTES), and a variable amount of the procedure is laparoscopically assisted (extraction of large specimens, closure of the gastrotomy). Preliminary results on morbidity in a prospective multicentric observational study counting 12 % of EA-NOS procedures (43 of 362 patients) [44] (LE4) demonstrate a 24 % complication rate, much higher than the transvaginal route (7 %). SA-NOS instead has developed relentlessly, especially the transvaginal route for NOTES-C. At the beginning of the experience, also the transumbilical surgery was considered part of the NOTES procedures as the incision was located in an embryological natural orifice (e-NOTES) [45]. The ease of creating and closing a surgical incision made in the posterior fornix of the vagina has facilitated the spread and the appeal of this operation, like European registry (EURO-NOTES) documents [46]. There is a single trial comparing transvaginal NOTES-C to LC with a third arm concerning a transumbilical cholecystectomy performed by means of hybrid NOTES (with the use of an endoscopic operative platform); results showed a success rate of 94 %, without differences in the rate of parietal complications at 1-year follow-up [47] (LE2). Postoperative pain, length of hospital stay, and time off from work were similar in the three groups. Surgical time was longer among cases in which a flexible endoscope was used (CL, 47.04 min; TV, 64.85 min; TU, 59.80 min).The largest prospective series of NOTES-C comes from the German registry [48] (LE4) on 551 patients, and the complication rate was 3.3 % with 4.7 % conversions to LA or open surgery. Intra- and postoperative complications accounted for 4 major complications requiring redo or additional surgery (bladder or intestinal perforations, bleedings, pelvic abscesses, and abdominal pain). Mean operative time was 62 min (20–211). Concerns were raised due to sexual complications (especially dyspareunia) after transvaginal approach, but observational studies have not proved it, and a prospective study on 106 female patients confirms a good quality of life after the operation [49] (LE4). When women were asked about their expectations after transvaginal hybrid NOTES, particularly young and nulliparous, women expressed concerns about sexual function and fertility [50, 51]. On the other hand, most studies addressing sexual function after transvaginal hysterectomy could not find a negative effect [52] (LE4); currently, the number of patients getting pregnant after

NOTES and particularly the number of patients seeking pregnancy after NOTES are much too small to draw any meaningful conclusions. Surveys have also proved a theoretical good acceptance of NOTES-C by 100 women [53], while 100 male partners don't justify the cosmetic benefit in front of the potential risks [54]. Reports on emergency surgery for acute cholecystitis are still sporadic [55] (LE4 on six patients). A new concept regards intralumenal surgery, in which endoscopic ultrasound-guided cholecystostomy performed via the duodenum appears promising in selected patients [46] (LE5). Future research should focus on larger randomized trials especially concerning transvaginal NOTES-C to assess safety issues. This probably is the branch of NOTES that will be the most rapidly diffused clinically in the near future while we await for a real benefit to be proved by future trials. All the other transvisceral approaches grouped in EA-NOS (transgastric, transcolonic, and transvesical) are limited by the need for significant technology improvements. Therefore, high-complexity surgical acts seem difficult to achieve under EA-NOS conditions in the near future. In this field, a consistent and continuous collaboration between industry and physicians in the area of robotics and magnetic instruments will play a substantial role in the takeoff of the technique. More research is also needed on training and learning curve. Prospective, randomized studies of large patient populations are necessary to assess the long-term results of NOTES procedures.

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Real Benefits of the Laparoscopic Approach

9

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9.1 Introduction

Classical outcome measures (mortality and complications) have to be considered to compare surgical treatments. As no significant differences between laparoscopic cholecystectomy (LC) and open cholecystectomy (OC) were found in classical outcome measures, it is justified to consider health-related quality of life (HRQoL) an important secondary outcome measure. Indeed quality of life (QoL), symptoms resolution, duration of convalescence, and patient satisfaction and well-being are at least as important as the classical outcomes from a patient's point of view.

Instruments for measuring HRQoL may be disease specific or generic:

(a) *Disease-specific instruments* are administrated in clinical trials to detect progressive changes after medical or surgical interventions and focus on improvements in symptoms and physical functioning.

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(b) *Generic health instruments* are designed for application to many diseases or interventions and are intended to obtain an overall evaluation of health outcomes.

The Gastrointestinal Quality of Life Index (GIQLI) is a self-reported, system-specific measure designed for use with people with different gastrointestinal disorders, and it has proved to be useful for outcome assessment after cholecystectomy. The 36 items (reflecting physical, emotional, and social function as well as typical gastrointestinal symptoms) are each scored on a 5-point scale (Likert) with higher scores denoting better QoL.

The Short-Form 36-Item Health Survey (SF-36) is a widely used generic quality-of-life measuring instrument that divides QoL into eight domains, including physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. Each subscale score is from 0 to 100, with 100 as the most optimal health status.

The Nottingham Health Profile (NHP) is another validated generic instrument to measure QoL, but it is not frequently used. This questionnaire is divided in two sections: the first one consists of 38 questions in 6 subareas, with each question assigned a weighted value; the sum of all weighted values in a given subarea adds up to 100 (energy level, pain, emotional reaction, sleep, social isolation, physical abilities); the second part investigates about 7 dimensions of the social life that could be affected by disease or treatment (work, looking after home, social life, home life, sex life, interest and hobbies, vacation).

In addition to those mentioned above, some authors have used other instruments such as: Visual Analogue Scale (VAS), Hospital Anxiety and Depression Scale (HADS), Body Image Questionnaire (BIQ), EuroQol-5D, Karnofsky Performance Scale (KPSS), Psychosocial Adjustment to Illness Scale (PAIS), and City of Hope QoL.

9.2 Methods

A systematic review based on a comprehensive literature research via *PubMed* and *The Cochrane Library* was done to evaluate the HRQoL.

The search details were (“cholecystectomy, laparoscopic”[*MeSH Terms*] *OR* (“cholecystectomy”[*All Fields*] *AND* “laparoscopic”[*All Fields*]) *OR* “laparoscopic cholecystectomy”[*All Fields*] *OR* (“laparoscopic”[*All Fields*] *AND* “cholecystectomy”[*All Fields*])) *AND* (“quality of life”[*MeSH Terms*] *OR* (“quality”[*All Fields*] *AND* “life”[*All Fields*]) *OR* “quality of life”[*All Fields*]) *AND* ((“1994/01/01”[*PDAT*]: “2012/12/31”[*PDAT*]) *AND English*[*lang*]).

A total of 147 citations were identified. The titles and abstracts of the retrieved citations were scanned to exclude all publications that were clearly not relevant to the guideline topic. Articles were considered relevant if they reported QoL outcomes using standardized or self-developed questionnaires. Full texts from selected abstracts were used based on specific criteria. Multiple publications of the same study were included only once. Pertinent studies from other references were also

Table 9.1 Selected studies and their level of evidence

N. 1	Evidence-based guidelines	
N. 1	Meta-analysis of retrospective case-control or case-series study	LoE 4
N. 7	Randomized controlled trial	N.2: LoE 3[a] N.5: LoE 2
N. 10	Nonrandomized prospective cohort/observational study	LoE 3
N. 8	Case-control study	LoE 4
N. 2	Case series	LE 4

[a]Evidence Level was downgraded from 2 to 3 because the study population is small

been selected. A total of 23 publications were examined for relevance; 6 further relevant publications were identified from citation of other references (Table 9.1).

Level of evidence of these selected papers was graded according to Oxford Centre for Evidence-Based Medicine 2011.

9.3 Considerations

An effective way to investigate the factors that may influence QoL outcomes after LC would be to measure the pre- and postsurgery satisfaction rate (QoL assessment is generally suggested at the 1st and 6th months after surgery) administrating SF-36 as generic instrument in conjunction with GIQLI as disease-specific instrument. If time and resources are limited, the GIQLI may be used alone because it incorporates all domains of a QoL assessment.

We pointed our attention to the QoL considering the following main topics:

(a) Effectiveness of LC
(b) Comparison to OC
(c) Comparison to small-incision laparotomic cholecystectomy (SC)
(d) Impact of iatrogenic bile duct injury (BDI)

9.3.1 QoL After LC: Is the Operation Effective?

From our systematic review of the literature, after exclusion of duplicates, we found only three prospective cohort studies concerning QoL after LC [1–3] [LE 3] (Table 9.2).

Finan et al. designed a study to determine gastrointestinal symptoms and QoL after cholecystectomy for better measurement of the change in QoL after surgery [1] [LoE 3]. This is a prospective cohort of consecutive patients with a small population (55 subjects) at a mean time to follow-up of 17.1 months; indeed only 64 % of patients involved in the study returned the filled questionnaire. In this study, SF-36 was employed along with a symptom survey that was designed to include both classic symptoms of biliary disease and other benign gastrointestinal (GI) diseases. Their results showed that LC significantly improved GI symptoms as well as QoL in subjects with symptomatic gallstone disease; nevertheless symptoms

Table 9.2 QoL after LC in 3 prospective nonrandomized study (410 patients)

Author	Test	Questionnaire delivered	Response rate (%)
Finan KR [LoE 3] [1]	SF-36 GISS (gastrointestinal symptom survey)	Median follow-up 17.1 months (range 2–32)	64
Lien HH [LoE 3] [2]	SF-36 GIQLI (Taiwan version)	12 months	100
Hon-Yi [LoE 3] [3]	SF-36 GIQLI (Chinese version)	3, 6, 12, and 24 months	72.5

associated with reflux (food or stomach contents in the throat, belching, feeling full after small meals, and pressure in the chest), irritable bowel syndrome (flatulence, constipation, and diarrhea), and chronic pain (pain all the time) did not show significant improvement. These results support the effectiveness of LC for elective biliary disease, with particular attention in regard to appropriate selection of patients, especially in terms of discrimination between biliary disease-related symptoms and other GI disorders.

Lien et al. reported the results of a prospective nonrandomized follow-up study on a cohort of 99 consecutive patients evaluated preoperatively and 12 months after surgery with SF-36 and GIQLI [2] [LoE 3]. The preoperative SF-36 scores from gallstone patients were significantly inferior to an age- and sex-matched control population; LC effectively reduced gastrointestinal symptoms, confirmed by the improvement in GIQLI total, physical well-being, mental well-being, gastrointestinal digestion, and defecation subscale scores; particularly patients with worse preoperative health condition are shown to benefit from greater QoL improvements following LC surgery. Yet some patients did not regain full GIQLI scores after surgery, deducing that some residual gastrointestinal discomfort remained 12 months after surgery.

Shy et al. reported the scores of SF-36 and GIQLI before surgery and then at 3, 6, 12, and 24 months after surgery in a prospective cohort study that includes 353 consecutive patients [3] [LoE 4]. Only 72.5 % of them returned the questionnaire after 24 months of follow-up, so the study consisted of 256 patients. All the LC patients had significantly improved GIQLI and SF-36 subscale scores at the 6-month follow-up survey. Interestingly most dimensions of the GIQLI and the SF-36 improved remarkably not only until the first year after surgery but also thereafter. In each GIQLI dimension, the fastest improvement occurred immediately after surgery and then reached a plateau after approximately 2 years. In particular, among eight SF-36 subscales, physical functioning, role physical, and role emotional showed the best improvement by the second year after surgery. HRQoL improvement after LC was inversely related to age, and according to Lien HH, the best predictors of postoperative HRQoL were preoperative functional status scores. The authors suggested that direct interventions to reduce role limitations due to physical and emotional problems may enhance physical functioning of patients after LC, increasing HRQoL in all dimensions.

We found only one paper in which the impact on QoL of a perioperative intervention after LC was investigated [4] [LoE 3]. The study was a randomized single-blinded trial, in which a population of 60 patients was followed up and analyzed. Those in the intervention group attended a standardized 45 min relaxation session with a health psychologist and were given relaxation exercise compact disk to take home; the control group did not have the intervention. Both groups had similar fatigue at baseline measured using the identity-consequence fatigue scale. The results of the trial demonstrated a reduction of fatigue on postoperative day 30 in the intervention group, allowing faster return to normal functions and activities.

From the above it could be deduced that:

- LC significantly improved either GI symptoms or QoL in subjects with symptomatic gallstone disease.
- Best results may be achieved by an appropriate selection of patients, in terms of discrimination between biliary disease-related symptoms and other GI disorders.
- Patients with worse preoperative health condition are shown to benefit from greater QoL improvements following LC surgery.
- Preoperative functional status scores are the best predictors of postoperative HRQoL.

9.3.2 QoL After LC Versus OC

EAES evidence-based guidelines on the evaluation of QoL after laparoscopic surgery published in 2004 focused on comparison of QoL after LC and OC [5]. Two randomized and eight nonrandomized trials were analyzed [6–15] [LoE 2]. The authors reported that LC improves QoL faster than OC and that long-term results after LC are slightly better or not different compared to OC. However, the authors included in the study publications that compare LC with classical OC together with publications that compare LC with SC. In particular there were no randomized controlled trials (RCT) in which QoL after LC was compared with QoL after classical OC: four prospective nonrandomized longitudinal studies and four retrospective case–control or population studies were cited in EAES guidelines about this topic [8–15] [LoE 3].

Sanabria et al., using an ad hoc questionnaire over an 8-week period after laparoscopic or open cholecystectomy, studied all patients who underwent elective cholecystectomy during three consecutive periods; there were 121 patients in each period [8] [LoE 4]. In the first period all patients underwent OC, in the second period 58 % underwent LC, and in the last period almost all patients underwent LC. A significantly shorter hospital stay and shorter recovery period in favor of LC was found, but at the final evaluation, the patients' answer did not differ between groups regarding their postoperative QoL.

Eypash et al. evaluated a cohort of 179 patients (21 OC versus 158 LC) with GIQLI and VAS score 2 and 6 weeks after surgery; QoL score was then compared with 70 healthy persons [9] [LoE 4]. LC resulted in immediate postoperative improvement of QoL; at both time points, there was a trend toward better QoL in the laparoscopic group.

Ludwig et al. used GIQLI in a prospective nonrandomized comparative study including 103 patients (29 OC and 74 LC) with 35 days of follow-up. The authors reported a quicker convalescence after LC with an earlier return to work [10] [LoE 3].

Plaisier et al. prospectively studied the course of QoL and gastrointestinal symptoms after laparoscopic and open cholecystectomy, demonstrating that LC improved QoL and symptomatology at an earlier stage than OC, yet the population of the study was very small including 31 patients only (14 LC and 17 OC) [11] [LoE 3].

Similarly Chen et al. confirmed in their prospective nonrandomized trial, in which GIQLI was used preoperatively and then 2, 5,10, and 16 weeks after surgery, that LC can improve the QoL better and more rapidly than OC [12] [LoE 3]. Even for this paper the population of the study was small (51 patients).

Kane et al. retrospectively evaluated consecutive cases of elective cholecystectomy from 35 hospitals sending an ad hoc questionnaire about symptoms and functional status 6 months postoperatively [13] [LoE 4]. The questionnaire was returned in 76 % of cases; the population studied consisted of 2.481 patients: no difference in pain, symptoms, or general health was noted after LC or OC, but the mean time to return to work and to perform usual activities was significantly shorter for LC.

Topcu et al. performed a retrospective comparative study on 200 patients (100 LC and 100 OC) using the SF-36 questionnaire with a mean administration time of more than 40 months [14] [LE 4]. Both groups were comparable prior to surgery for demographic data, but no data about preoperative QoL were reported. The gastrointestinal clinical symptoms were similar in the two groups during the long-term follow-up evaluation, but LC was found to be significantly superior to OC with respect to the QoL over the long term. Authors reported a statistically significant difference in the scores of all eight domains of SF-36 in favor of LC; it would be understandable if the social aspect of QoL were impacted due to worse cosmesis after OC, but it is surprising that other aspects of QoL still showed significant differences as long as more than 3 years after the operation. Because preoperative QoL is not reported, these differences could simply reflect preexisting pretreatment differences; moreover, QoL data were not periodically collected, and the protracted period of more than 3 years that elapsed between the operation and the data collection casts more doubt on the reliability of the findings.

Quintana et al. conducted a prospective observational study of consecutive patients using GIQLI and SF-36 questionnaires [15] [LE 3]. 77.6 % patients (688 subjects) completed the questionnaires both before and 3 months after the intervention. HRQoL improvement at 3 months was relevant and similar for both surgical techniques, although the health transition perception was worse for those who underwent open surgery. Yet it must be noted that these results may depend by significant differences of the groups for sociodemographic and preoperative clinical variables. Patients who underwent OC had indeed symptomatic lithiasis with complications more frequently than those who underwent LC, mean age was older, and there were more patients with comorbidities and high surgical risk, measured by the ASA (American Society of Anesthesiologists) score, in the group treated with OC.

From our systematic review of the literature, we identified three papers comparing QoL after LC or OC: there are no randomized controlled trials [16–18] [LoE 3].

Velanovich et al. prospectively assessed the health status outcomes of 100 patients who underwent different types of laparoscopic and open procedures using SF-36 questionnaire before and 6 weeks after surgery [16] [LoE 3]. LC had better QoL outcomes than OC, but in the paper three other procedures are mixed with cholecystectomy, and the population who underwent cholecystectomy in the study is very small.

Hsueh et al. reported a large-scale prospective cohort study in which GQLI and SF-36 were used preoperatively and then 3 and 6 months after the procedure in 297 patients (38 OC and 259 LC) [17] [LoE 3]. They reported that HRQoL of patients who underwent cholecystectomy was significantly improved at 3rd and 6th months after surgery. At 3rd month postsurgery, HRQoL was significantly larger in LC than in OC patients. Additionally, after controlling for related variables, preoperative health status was significantly and positively associated with each subscale of the GQLI and SF-36 throughout the 6 months.

At last in the study of Matovic et al., 59 and 61 patients respectively treated with LC and OC were prospectively studied using GLQI before surgery and then at 2-, 5-, and 10-week intervals after surgery [18] [LE 3]. Patients' QoL at 2 and 5 weeks was significantly better in laparoscopic method group versus open method group in all four domains of GLQI, but after 10 weeks there were no differences in QoL total and domain score between two groups.

In conclusion, as a general agreement, postoperative QoL depends on preoperative clinical status: patients with worse preoperative health condition may benefit from better QoL improvements following LC surgery. There are no RCT or high-evidence-level studies that compare QoL after LC or OC. Based on the studies available, even though LC improves QoL faster than open surgery, long-term results are only slightly better or show no difference compared to OC (Table 9.3); at the

Table 9.3 QoL: LC versus OC data from E.A.E.S. Evidence-based guidelines 2004 (4,096 patients) and 3 prospective non-randomized studies (447 patients)

		QoL results		
Author	Test	Questionnaire delivered	Short term	Long term
EAES Evidence-based guidelines [5]	2 SF-36 4 GIQLI 3 ad hoc questionnaire 1 VAS		LC > OC	LC ≥ OC
Velanovich [EL 3] [16]	SF-36	6 and 9 weeks	LC > OC	–
Hsueh et al. [EL 3] [17]	SF-36 GIQLI	3 and 6 months	LC > OC	LC ≥ OC
Matovic et al. [EL 3] [18]	GIQLI	2, 5, and 10 weeks	LC > OC	LC = OC

same time, these data should be considered as a mean and might be limited to study design (e.g., small sample size, biased and confounding variables, low response rate to questionnaires).

9.3.3 QoL After Laparoscopic Versus SC

SC or minilaparotomic cholecystectomy is a surgical procedure performed through a subcostal incision shorter than 8 cm.

Barkun et al. studied 35 and 23 patients prospectively randomized in the LC and SC groups, respectively, and used GIQLI in addition to NHP and VAS to assess QoL [6] [LoE 3]. No blinding was used. Cumulative totals of both GIQLI and NHP data were used instead of using subscales. Changes in one dimension might be offset by changes in other dimensions. Both questionnaires have more than one dimension; subscales indeed provide the advantage of additional information on several dimensions. As a rather small number of patients were included (the trial was stopped preliminary), no subscales were assessed, and no considerations were given to the construct or divergent validity of both questionnaires. The authors reported that LC patients improved more quickly than did SC patients.

McMahon et al. compared health status in 151 and 148 LC and SC patients, respectively, using the SF-36 health survey questionnaire and the “Hospital Anxiety and Depression Scale” (HADS) [7] [LoE 2]. Generation of the allocation sequence in their trial was unclear and no blinding was used. They found that patients recovering from LC enjoyed significantly better health 1 and 4 weeks after the operation compared with those recovering from SC, but no significant difference was found at 12 weeks. Moreover, LC patients were more satisfied with the appearance of their scar. The absence of preoperatively baseline measurements makes conclusions about postoperative data uncertain; moreover, they used in SC group a subcostal incision up to 10 cm long.

Squirrell et al. used the NHP in 100 patients (50 in each group) preoperatively and 3 weeks and 6 months postoperatively [19] [LoE 2]. At no time there was a significant difference between the two groups. The study used a rather small sample size and unfortunately without a disease-specific questionnaire, but only one generic questionnaire.

Nilsson et al. randomized 726 patients in two groups: LC (364 patients) and SC (362 patients) [20] [LoE 2]. The total population of consecutive patients of this study was of 1,719 subjects: 993 patients were not randomized (227 patients not eligible, 472 patients were excluded by surgeon in charge, and 244 patients choose not to participate), representing an important bias of this large trial. EuroQol-5D and VAS questionnaires were used to assess QoL. EuroQoL-5D questionnaire consists of five questions with three response alternatives concerning patient mobility, self-care, activity, pain or discomfort, and mood. One week postoperatively, there were small but statistically significative differences favoring LC compared with SC in four EuroQol-5D dimensions (mobility, self-care, main activity, pain/discomfort) and in “self-reported health status today compared with the status the previous 12 months,” whereas patients in two groups did not differ with respect to mood and self-estimated well-being according to the EuroQol-5D VAS. After 1 month and 1 year, there were no differences between the two groups in any EuroQol-5D dimension. At the end, direct and indirect costs due to loss of production were calculated in this study: total costs between LC and SC did not differ with high-volume surgery (>100 procedures per year) and using disposable laparoscopic instruments, whereas LC was more expensive in low-volume surgery (<50 procedures per years) and using disposable instruments.

Harju et al. randomized 157 not consecutive patients between LC and SC treatment [21] [LoE 2]. Patients were reevaluated 4 weeks after surgery using the SF-36 QoL questionnaire. In the LC group role functioning/physical score was slightly but significantly better than in the SC group, but in the other SF-36 dimensions (physical functioning, role functioning/emotional, energy, emotional well-being, social functioning, bodily pain, general health), there were no statistically significant difference between the two groups.

Kues et al. used SF-36, GIQLI, and Body Image Questionnaire (BIQ) delivered preoperatively, the first day after surgery and at outpatient follow-up at 2-, 6-, and 12-week intervals, to a total of 257 patients randomized between LC and SC [22] [LoE 2]. No significant differences between both operative techniques concerning health status were reported with the exception of perceived health change in SF-36 that was significantly different in favor of laparoscopic procedure at 2 and 6 weeks postoperatively, but not at 3 months follow-up. This difference in perceived health change was not reflected in an earlier return to work. Interestingly subgroups analysis showed significant differences immediately after surgery and in long-term follow-up in pain perception; physical, social, and mental functioning; and body image comparing minimal invasive procedures (both laparoscopic and small incision) and procedure converted to the classical OC.

In conclusion when LC is compared with SC, the perception of health immediately after surgery is slightly better for patients treated with laparoscopic procedure, but the gain in HRQoL is small and of very limited duration; moreover, it does not reflect in an earlier return to work (Table 9.4). Conversion of minimally invasive cholecystectomy in classical open procedure affects short-term and long-term QoL.

9.3.4 Impact of Iatrogenic BDI on QoL

The occurrence of a BDI has a significant impact on QoL. From the systematic review of the literature, 7 publications were found about this topic (1 meta-analysis including 831 patients from 6 retrospective case-control or case-series study) [23–29] [LoE 4]. Long-term results are conflicting (Table 9.5). In the first three publications, a detrimental effect of BDI in long-term follow-up has been reported in both mental and physical aspects [23–25] [LoE 4]. Boerma et al. studied 241 patients affected by bile duct injury in the course of LC, 70 % of whom were treated endoscopically or radiographically [23] [LE 4]. The follow-up ranged from about 3 years to 9 years. Authors demonstrated that scores on the 8 domains of the SF-36 of patients with BDI were significantly different from those of patients with uncomplicated LC and Dutch population norms.

Table 9.4 QoL after laparoscopic versus SC in 6 randomized controlled trials (1,597 patients)

Author	Test	QoL results		
		Questionnaire delivered	Short term	Long term
[a]Barkun et al. [LE 3] [6]	NHP GIQLI VAS	10 days, 1 month, 3 months	LC ≥ SC	LC = SC
McMahon et al. [LE 2] [7]	SF-36 HADS	1, 4, and 12 weeks	LC > SC	LC = SC
Squirrell et al. [LE 2] [19]	SF-36	3 week, 6 month	LC = SC	LC = SC
Nilsson et al. [LE 2] [20]	EuroQol-5D	1 week, 1 month, 1 year	LC > SC	LC = SC
Harju et al. [LE 2] [21]	SF-36	4 weeks	LC = SC	–
Keus et al. [LoE 2] [22]	SF-36 GIQLI BIQ	1 day, 2, 6, and 12 weeks	LC = SC	LC = SC

[a]Evidence Level was downgraded from 2 to 3 because the study population is small

Table 9.5 Impact of BDI on QoL in 831 patients enrolled in 5 case-control study and 1 case series

Author	Test	Follow-up (median—months)	QoL results Complicated (C) versus uncomplicated (UnC)
Boerma et al. [LE 4] [23]	SF-36	70	C < UnC
Moore et al. [LE 4] [24]	SF-36 KPSS PAIS	62	C < UnC
de Reuver et al. [LE 4] [25]	SF-36 GIQLI	66/132	C < UnC
Melton et al. [LE 4] [26]	City of Hope QoL	59	C ≤ UnC
Sarmiento et al. [LE 4] [27]	SF-36	100	C = UnC
Hogan et al. [LE 4] [28]	SF-36	152	C = UnC

Similarly Moore et al. in a study including 86 patients with bile duct injury during LC reported at an average of 5 years of follow-up lower scores on the Karnofsky Performance Scale and all SF-36 measures of HRQoL, when compared with patients who underwent uncomplicated LC [24] [LoE 4]. When the authors categorized patients into those with less than 5 years of follow-up and those with 5 years or more of follow-up, their findings were similar. While physical functioning in both groups remained relatively constant despite the length of follow-up, their mental functioning worsened with duration of follow-up. Less than one fourth of these patients reported filing lawsuits. There were no significant demographic or clinical differences between those who reported filing a lawsuit and those who did not. However, patients who did file a lawsuit reported significantly greater impairment in HRQoL. Despite long-term physical and psychosocial impairment, the majority of the patients with BDI were able to return to work. However, they returned to work almost 3 months later on average than patients who underwent uncomplicated LC.

de Reuvers et al. reported in a cohort of 278 patients with BDI a score significantly worse than the healthy population norms in seven of the eight QoL domains [25] [LE 4]. The longitudinal assessment after another 5.5 years of follow-up did not show improvement in QoL. Nineteen percent of the patients ($n = 53$) filed a malpractice claim after BDI. These patients reported better QoL when the claim was resolved in their favor than when the claim was rejected.

On the opposite three other publications documented a detrimental effect of BDI in long-term follow-up only in mental, but not in physical, aspect [26–28].

Melton et al. examined QoL in 89 patients with BDI, all of whom underwent surgical repair [26]. They used the City of Hope Medical Center Quality of Life Survey, which comprises three domains: physical, psychological, and social. Authors reported that patients with BDI had physical and social QoL similar to that of patients undergoing uncomplicated LC, but greater impairment in psychological QoL. In addition, they found that legal activity was associated with worse outcomes. However, the QoL instrument used in that study was developed for and validated in cancer patients only.

Sarmiento et al. studied 59 consecutive patients undergoing surgical reconstruction of the biliary tract after the injury induced by LC (mean follow-up of 8.4 years) using SF-36 questionnaires [27] [LE 4]. All eight dimensions evaluated in the SF-36 questionnaire were similar for patients undergoing biliary reconstruction, their matched controls, and national norms.

Even in the paper reported by Hogan et al., the QoL of surviving patients following BDI compares favorably to that after uncomplicated LC [28] [LoE 4]. Authors compared 78 patients treated for BDI with an age- and sex-matched control cohort of 62 patients undergoing to uneventful LC. SF-36 was used to assess the QoL, with a median follow-up of 12 years. Such comparison has revealed that seven of eight examined variables were statistically similar to those of the control group (physical functioning, role physical, bodily pain, general health perceptions, vitality and social functioning, and mental health index). Mean role emotional scores were slightly worse in the BDI group. Subgroup analysis by method of intervention for BDI did not demonstrate significant differences.

A recent meta-analysis included all the six publications cited above [29] [LoE 4]. Because the HRQoL surveys differed among reports, BDI and uncomplicated LC groups' HRQoL scores were expressed as effect sizes (ES) in relation to a common, general population, standard. A negative ES indicated a reduced HRQoL, with a substantive reduction defined as an $ES \leq -0.50$. Weighted logistic regression tested the effects of BDI (versus LC) and follow-up time on whether physical and mental HRQoL were substantively reduced. The analytic database has comprised 90 ES computations representing 831 patients and 11 unique study groups (6 BDI and 5 LC). After controlling for follow-up time ($P \leq 0.001$), BDI patients were more likely to have reduced long-term mental [odds ratio (OR) = 38.42, 95 % confidence interval (CI) = 19.14–77.10; $P < 0.001$] but not physical ($P = 0.993$) HRQoL compared with LC patients.

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10 Laparoscopic Cholecystectomy in Day Surgery

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10.1 Introduction

Laparoscopic cholecystectomy (LC) has now become the "gold standard" treatment for symptomatic gallstone disease. Thanks to its advantages (i.e., smaller scars, reduced postoperative pain), patients enjoyed a shorter hospital stay and consequently, many healthcare providers have started to explore the feasibility of offering LC as a day-case procedure, and in 1990 some authors had already reported the first experiences of ambulatory surgery [1, 2].

When LC was first introduced, patients were admitted 1 day prior to their operation and stayed for 1–2 days postoperatively. With improvements in surgical and anesthetic technique, the concept of same-day admission (SDA) was introduced in 2001, thereby shortening the length of stay (LOS) by 1 day.

Day-surgery setting allows to combine patients' satisfaction to cost-saving policies that seems to be more and more important for a modern hospital management. Minimally invasive surgery seems to be the ideal surgical approach for day-case

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Table 10.1 Practice/clinical guidelines published on January 2010 by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)

1. Search date: July, 2009
2. Search terms: "laparoscopic cholecystectomy hospital discharge"
3. Limits: English language, humans, and published within the last 5 years
4. Results: 58 articles, abstracts reviewed, 8 chosen as pertinent
Levels of evidence I – Evidence from properly conducted randomized, controlled trials II – Evidence from controlled trials without randomization or cohort or case-control studies or multiple time series, dramatic uncontrolled experiments III – Descriptive case series, opinions of expert panels
Scale used for recommendation grading Grade A – Based on high-level (level I or II), well-performed studies with uniform interpretation and conclusions by the expert panel Grade B – Based on high-level, well-performed studies with varying interpretation and conclusions by the expert panel Grade C – Based on lower-level evidence (level II or less) with inconsistent findings and/or varying interpretations or conclusions by the expert panel

procedures since reducing trauma to a minimal level allows patients to return quickly to a normal life with minimal nursing assistance.

Early experience of day-case laparoscopic cholecystectomy produced very high overnight admission rates of up to 44 % [3], but more recent studies have shown more acceptable overnight unplanned admission rates of less than 10 % [4–7]. It can be argued that this is far in excess of the 2–3 % normally accepted for intermediate day-case procedures, but if overall day-surgery rates are to achieve the hoped for 75 %, as targeted in the US National Health plan [8], then this higher unplanned admission rate for more major procedures is acceptable, at least initially, in most units. The reduction in overnight admission rates to less than 10 % is due to rigorous patient selection, accepting only well-motivated patients, and attention to detailed anesthetic and surgical technique.

SAGES guidelines [9] for the clinical application of laparoscopic biliary tract surgery—Practice/Clinical Guidelines published on January 2010 by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)—analyzed length of stay after LC, and modality of data extraction from PubMed, levels of evidence, and grade of recommendations of this study are reported in Table 10.1.

These guidelines stated the following conclusions:

- Patients undergoing uncomplicated laparoscopic cholecystectomy for symptomatic cholelithiasis may be discharged home on the day of surgery [10]. (*Level II*, *Grade B*)
- Control of postoperative pain, nausea, and vomiting is important to successful same-day discharge [11], and admission rates despite planned same-day discharge are reported to be 1–39 %; patients older than age 50 may be at increased risk for admission [11–17]. (*Level II*, *Grade B*)

- Readmission rates range from 0 to 8 %; common causes for readmission after same-day discharge include pain, intra-abdominal fluid collections, bile leaks, and bile duct stones [10, 12]. (*Level II*, *Grade B*)
- Time to discharge after surgery for patients with acute cholecystitis and bile duct stones or in patients converted to an open procedure should be determined on an individual basis. (*Level III*, *Grade A*)

10.2 Methods

Moving from these conclusions, we thought to analyze the available data in PubMed and to restrict the research just on specific papers concerning day-case or ambulatory LC within the last 20 years with the following queries:

1. Search date: March 2013.
2. Search terms:
   "laparoscopic cholecystectomy
   laparoscopic cholecystectomy and hospital discharge
   laparoscopic cholecystectomy and day case
   laparoscopic cholecystectomy and ambulatory procedures
   laparoscopic cholecystectomy and hospital discharge and day case and ambulatory procedures"
3. Results:
   laparoscopic cholecystectomy – 5,490 articles
   laparoscopic cholecystectomy and hospital discharge – 138 articles
   laparoscopic cholecystectomy and day case – 175 articles
   laparoscopic cholecystectomy and ambulatory procedures – 137 articles
   laparoscopic cholecystectomy and hospital discharge and day case and ambulatory procedures – 15 articles

All articles published in English were initially collected. From this huge pull of papers, the randomized clinical trials, multicenter studies, practice guidelines, systematic reviews and meta-analyses, and Cochrane Reviews were included for a deeper examination of their abstracts. Finally, we selected 35 papers for the most accurate and extensive research of the methods, the results, and the conclusive statements (Table 10.2).

The level of evidence of these selected papers was graded according to Oxford Centre for Evidence-Based Medicine 2011.

Table 10.2 Selected studies and their level of evidence

N. 4	Meta-analysis and review of clinical trials [10, 18–20]	LoE 1
N. 5	Randomized controlled trial [21–25]	LoE 2
N. 12	Nonrandomized prospective cohort/observational study [12, 14–17, 26–32]	LoE 3
N. 12	Retrospective case series [11, 33–43]	LoE 4
N. 2	Questionnaire survey [44, 45]	LoE 5

10.3 Discussion

During the years after the initial experiences, the surgeons have become more and more confident to suggest ever faster discharges. Ambulatory LC (ALC) has automatically been the next step in patients' management. Nowadays day-case LC (DLC) has been adopted with different rates and it is not fully accepted by all surgeons. The main question concerns whether the DLC might be feasible for all or just for selected cases. So some aspects deserve to be deepened. First of all it is useful to point out our attention on its definition, safety in terms of surgical results, readmissions, eventual selective criteria for patients, the costs, patients' satisfaction, and return to normal activities.

The day surgery is a model of care that allows to diversify the flow of surgical patients, allowing, in over half the cases, the discharge on the same day of admission or no later than the morning of the next day. First of all, we must pay attention to the definition of day surgery, because at the international level, different terms are used, such as ambulatory surgery, day surgery, day case, same-day surgery, 1-day surgery, office-based ambulatory surgery, and office-based surgery, with considerable difficulties of interpretation. The term ambulatory surgery must be considered synonymous with day surgery, day case, and/or same-day surgery and it should not include an overnight stay, which is expected in cases of extended recovery. The ambulatory/day surgery, with or without an overnight stay, must also be distinguished from office-based ambulatory surgery, or office-based surgery, namely, the ability to perform surgery or diagnostic procedures and/or treatment in the clinics, also placed away from shelter facilities.

The proportion of ambulatory management generally increases with experience [36] [LoE 4].

In some cases the hospital stay lasts until the day after the LC and the admission overnight after the operation can be due to different surgical, social, or logistic reasons [32] [LoE 3]: surgeon preference, operation late in the afternoon [40] [LoE 4], medical problems (i.e., nausea and vomiting, pain, urinary retention, intraoperative pneumothorax) [19, 40, 42, 43] [LoE1], doubt about reimbursement by insurance companies or psychological [43] [LoE 4], age (elderly patients showed a tendency to like to stay in the hospital rather than being a day case) [37] [LoE 4], medical observation, patient's preference [40, 42] [LoE 4], and conversion to laparotomy [17] [LoE 3].

There are no significant differences between DLC and overnight lap cholecystectomy (ONLC) as regards to morbidity, prolongation of hospital stay, readmission rates, pain, quality of life, patient satisfaction, and return to normal activity and work [18] [LoE 1].

In the majority of papers, good results have been reported.

DLC is safe because its morbidity and mortality rates are low. Complications and mortality rates vary, respectively, from 0 to 11.6 % [12, 17, 21, 24, 36, 37, 41–43] [LoE 2] and from 0 to 0.13 % (0.08 in ALC and 0.5 % in ONLC) [27, 37] [LoE 3]. The overall conversion rate varies from 0 to 2 % [31, 32] [LoE 3]. Prolonged hospital stay and readmission are connected with minor and more easily controlled complications or social reasons [10] [LoE 1] and are a valid indicator of safety.

Some patients later can require admission to the inpatient department for conversion to the open procedure or relaparoscopy [12, 18, 19, 32, 34, 38] [LoE 1], but the readmission rate is low (0–10 %) [12, 16, 17, 22, 24, 27, 28, 33, 36, 37, 40, 42, 43] [LoE 2] and less frequent after ALC than in ONLC [27] [LoE 3].

It is common opinion that DLC is indicated for selected cases and the selection may concern medical and logistic criteria.

Some *exclusion criteria* may be considered advisable: common bile duct stones [10, 32, 43] [LoE 1], acute cholecystitis [10, 38, 43] [LoE1], pancreatitis [10, 43] [LoE1], patients' age [11, 12, 16, 29, 32] [LoE 3], and intraoperative complications [11] [LoE 4].

In different experiences some *inclusion criteria* have been adopted and they concern:

(a) *Medical aspects*: absence of symptomatic cholelithiasis [34] [LoE 4] or low risk for concomitant presence of bile duct stones [34] [LoE 4], preoperative workout (abdominal US, liver function tests, and routine preoperative tests) [10] [LoE 1], absence of other diseases [18, 19] [LoE 1], surgical risk measured by the ASA (American Society of Anesthesiologists) score [10] [LoE 1] (grade < II [12, 16, 32–34, 40, 43] [LoE 3] or < III [38] [LoE 4]), and body mass index (BMI) [10, 32, 34, 40] [LoE 1].

(b) *Logistic aspects*: operation performed in the morning [32, 33] [LoE3], social aspect [10] [LoE 1], informed consent [38] [LoE 4], living in easy reach of the hospital [18, 19, 34] [LoE 1] (within 50 km [32] [LoE 4] or 100 km of the hospital [40] [LoE 4] or 1 h traveling time [12] [LoE 3]), willing to make their own arrangements for a return to hospital in case of problems [12] [LoE 3], and availability of a responsible carer [16, 18, 19, 34, 40, 43] [LoE 1].

(c) *Surgeon's expertnesses*: in the centers in which the trainees are involved in day DLC, there are no significant differences in terms of number of complications, patient outcomes, prolonged stay, and readmission [10] [LoE 1]. Many procedures (62 %) can be also performed by trainees in DLC, with statistically significant difference in operating time between consultants (41 min) and trainees (47 min) ($p = 0.001$), but clinical outcome or patient satisfaction is the same [30] [LoE 3].

    The adoption of new devices might be important such as the use of the harmonic scalpel that is associated with a low complication rate and a high-same-day discharge rate when carried out as DLC [35] [LoE 4]. Sensible scheduling of operations and avoiding the use of drains may decrease unplanned admissions following DLC [40] [LoE 4].

(d) *Geographic differences*: DLC is found to be safe and effective in developed countries, but it has not been well accepted all over of the world probably because of the lack of infrastructures, established norms, and published reports [28] [LoE 3], but for selected groups of patients DLC can be safely done with good patient satisfaction even in undeveloped countries [34] [LoE 4].

    Some authors pointed out the importance of anesthesia and postoperative control of pain, nausea, and vomiting as strongly needed elements to allow patients' early discharge:

1. *Choice of anesthesia*
   Bessa et al. [22] [LoE 2] compared the surgical outcome of DLC performed with the patient under spinal anesthesia (SA-DLC) with that performed with the patients under general anesthesia (GA-DLC) in the management of symptomatic uncomplicated gallstone disease with four (4.4 %) anesthetic conversions due to intolerable right shoulder pain. In the SA-DLC group, all patients were discharged on the same day. Overnight stay was required in eight patients (8.9 %) in the GA-DLC group ($p < .001$). The cause of overnight stay was nausea and vomiting in four patients (4.4 %), inadequate pain control in three patients (3.3 %), and unexplained hypotension in one patient (1.1 %).
2. *Pain management*
   Recent randomized trials showed the efficacy of transversus abdominis plane (TAP) block in providing postoperative analgesia after abdominal surgery. A TAP block may reduce pain while coughing and at rest for the first 24 postoperative hours, opioid consumption, and opioid side effects in patients undergoing LC. In DLC TAP block may have some beneficial effect in reducing pain, but this effect is probably rather small. Petersen et al. [21] [LoE 2] reported that the median morphine consumption (0–2 h postoperatively) was 7.5 mg (interquartile range, 5–10 mg) in the placebo group compared with 5 mg (interquartile range, 0–5 mg) in the TAP group ($p < 0.001$). The odds ratio of a random patient in group TAP having less morphine consumption than a random patient in group placebo was p (group TAP < group placebo) = 0.26 (confidence interval, 0.15, 0.37) where 0.5 represents no difference between groups. Total ketobemidone consumption, levels of nausea and sedation, number of patients vomiting, or consumption of ondansetron were similar between the groups.

   An adequate control of pain is an essential component in DLC service and it is possible at home after LC [10] [LoE 1].

   The duration of hospitalization after LC is mainly determined by temporary side effects such as pain, comparing remifentanil, a short-acting opioid, and sufentanil, a longer-acting opioid, on their ability to reduce these postoperative effects and facilitate LC in day-case surgery. Damen et al. [23] [LoE 2] did not find major relevant differences between remifentanil and sufentanil on the quality of recovery after DLC in a randomized blinded trial. Post-discharge pain may be controlled and the 2-day supply of diclofenac and co-codamol could also be extended as 65 % of patients had moderate to severe pain [14] [LoE 3].
3. *Postoperative nausea and vomiting* (*POVN*) *prevention or avoidance*
   Jawaheer et al. [35] [LoE 4] reported that the induction of anesthesia might be changed to total intravenous anesthesia, using propofol (target 4–6 μg/mL) and remifentanil (target 3–5 ng/mL) and using the gaseous anesthetic sevoflurane eliminated with the aim of reducing the risk of PONV.

Adequate control of nausea or vomiting is an essential component in DLC and it is possible at home [10] [LoE 1].

Postoperative nausea and vomiting are common in patients receiving a morphine-based PCA and in those with higher antiemetic requirement (10/25 in PCA and 7/41 non-PCA groups; $p<0.05$) [26] [LoE 3].

The incidence of PONV post-discharge suggests that adding an antiemetic to our take-home analgesic packs may improve patient comfort [14] [LoE 3].

At the end, economic and social aspects deserve particular attention and they might be very attractive to increase the diffusion of DLC.

LC provides a reduction in *hospital costs* approximately to 41 % [43] [LoE 4].

The mean direct medical cost per patient in DLC (3,085 € or 768 £) was lower than that in the ONLC (3,394 € or 1,430 £) [24, 30] [LoE 2].

DLC has acceptable discharge rate and level of patient satisfaction [10] [LoE 1].

In many experiences patients' satisfaction may be complete in 95.3 % of cases, related to a correct preoperative information [43] [LoE 4], and in the majority of research it goes from 80 to 97 % [11, 15, 28, 30–32, 34, 43] [LoE 3].

It is very important that patients feel themselves safe at home. For this reason, surgeons and/or nurses have to maintain a clinical control after patients' discharge. Different manners and timing have been planned to contact patients at home. Someone considers it useful to call by telephone in the same day of surgery [17] [LoE 3] or the day subsequent to surgery. Briggs et al. [10] [LoE 1] have suggested that recovery may be monitored by telephone questionnaire on days 2, 5, and 14, including complications, satisfaction, and general practitioner consultation.

There is no clear agreement regarding the duration of the total period of monitoring [45]. [LoE 4] in a questionnaire survey reported a postoperative surveillance planned in the outpatient unit 8–10 days after LC. Majority of patients are followed up after first and sixth week [34, 38] [LoE 4], while for some authors it should last within the first month after surgery in 93.9 % of cases and within the first year in 86.7 % of patients [17] [LoE 3].

Patients are generally able to resume their usual daily activities within 2 weeks after surgery [16] [LoE 3], and more than 90 % of patients resumes their normal job or activities after 1 week [34] [LoE 4].

Wasowicz et al. [25] [LoE 2] reported the use of an accelerometer and standardized encouragement accelerated recovery in women in contrast with men, and women in the intervention group did show a faster recovery of daily physical activity as compared to the control group ($p=0.02$). Although there was no significant difference in postoperative VAS scores for pain and nausea between both groups, patients in the intervention group experienced pain less often as a limiting factor ($p=0.006$).

In conclusion, DLC seems to be a safe and effective intervention in selected patients (with no or minimal systemic disease and within easy reach of the hospital) with symptomatic gallstones.

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11 Laparoscopic Cholecystectomy: Training, Learning Curve, and Definition of Expert

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Since the first laparoscopic cholecystectomy was performed, more than 20 years ago, literature validated the procedure as gold standard. Nevertheless, it continues an important discussion about methods to perform the procedure and about the best way to teach the procedure to surgical trainee. Three questions remain unanswered today that are the subjects of a heated debate: Which is the ideal learning method for a surgical trainee? What is the surgical learning curve? What is the definition of expert in laparoscopic cholecystectomy?

11.1 Training

Laparoscopic surgery is different from open surgery because of:

(a) Increased need for hand-eye coordination to perform tasks looking at a screen to compensate for not being able to operate under direct vision.
(b) Increased need for manual dexterity to compensate for the use of long instruments, which can amplify any error in movement.

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(c) Fulcrum effect of the body wall: When the surgeon moves his hand to the patient's right, the operating end of the instrument moves to the patient's left on the monitor.
(d) The need for handling tissues carefully (to compensate for the lack of sensation of touch using hands).
(e) The lack of 3-dimensional images.

How to teach laparoscopic surgery to residents in a safe and efficient way is the topic of many debates, conventions, and research projects. Surgical training has traditionally been one of apprenticeship, where the surgical trainee learns to perform surgery under the supervision of a trained surgeon. Different procedures have different learning curves. Surgeons experienced in one procedure may not be experienced in another, and results improve with experience in an individual procedure. An increasing number of surgical procedures are being done laparoscopically. This includes laparoscopic cholecystectomy, laparoscopic anti-reflux procedures, laparoscopic hysterectomy, and laparoscopic nephrectomy. Learning should be gradual. For example, laparoscopic intracorporeal suturing and knot tying are considered some of the most technically demanding minimally invasive skill to acquire. Proficiency in these skills is a requirement for surgeons to perform advanced laparoscopy. Studies have demonstrated that technical aptitude in open suturing and knot tying is not transferable to the laparoscopic technique. Compounding the difficulty inherent in learning this advanced laparoscopic skill are the diminished operative opportunities for surgical residents resulting from work-hour restrictions and the ethical concerns related to trainees learning novel skills on patients. As a consequence of these pressures and the technical demands of minimally invasive surgery, alternative ex vivo training methods have been developed [1] (LoE1b). The different methods of laparoscopic surgical training include live animal training, human and animal cadaver training, training using box trainer (video trainer), and virtual reality training (training using computer simulation). Video trainer is currently being used for laparoscopic training in various courses run by the Royal College of Surgeons of England and has been shown to be better than standard training. Virtual reality training has been reported to improve the learning outcomes in different surgical procedures [2–6] (LoE4). It also offers an ethical way of assessing the competency of a surgeon in performing a procedure without a risk to the patient. There are other reports that suggest that virtual reality training alone is inferior to traditional training for certain procedures [7] (LoE3b). Virtual reality training has been mainly used for development of component skills (such as diathermy, clipping, suturing) and not training in the entire procedure (such as laparoscopic cholecystectomy). As opposed to the limited variability of data available during a flight on which a pilot requires to be trained using a custom-designed simulator, anatomical variations are common throughout the human body, and skills acquired on a single computer simulation program may not be applicable in patients. Although the price of the simulators can vary depending upon the learning outcome, traditional training is not without costs. The operating time increases significantly for junior surgeons compared to senior surgeons, and the average costs of this increased operating time is about 12,000 US dollars per year per resident during the period 1993–1997 [8] (LoE1a).

The complication rate is also higher for junior surgeons compared to senior surgeons [9] (LoE2a), [10] (LoE3a). Thus, the cost of the virtual reality training system has to be balanced against the cost of increased operating time and complication rates during traditional surgical training. The Cochrane Review [11] (LoE1) included 23 trials with 612 participants, comparing virtual reality training versus other forms of training including video trainer training, no training, or standard laparoscopic training in surgical trainees with little or no prior laparoscopic experience. Also include trials comparing different methods of virtual reality training. Four trials compared virtual reality versus video trainer training. Twelve trials compared virtual reality versus no training or standard laparoscopic training. Four trials compared virtual reality, video trainer training and no training, or standard laparoscopic training. Three trials compared different methods of virtual reality training. Most of the trials were of high risk of bias. In trainees without prior surgical experience, virtual reality training decreased the time taken to complete a task, increased accuracy, and decreased errors compared with no training; virtual reality group was more accurate than video trainer training group. In the participants with limited laparoscopic experience, virtual reality training reduces operating time and error better than standard in the laparoscopic training group; composite operative performance score was better in the virtual reality group than in the video trainer group. The conclusion is that the virtual reality training can supplement standard laparoscopic surgical training of apprenticeship and is at least as effective as video trainer training in supplementing standard laparoscopic training. Newer studies [12] (LoE3) have evaluated the benefits of haptics in VR laparoscopic surgery training. Randomly, 33 laparoscopic novice students were placed in one of three groups: control, haptics trained, and nonhaptics trained. The number of attempts required to reach proficiency did not differ between the haptics- and nonhaptics-trained groups. The haptics and nonhaptics groups exhibited no difference in performance. Both training groups outperformed the control group in number of movements as well as path length of the left instrument. In addition, the nonhaptics group outperformed the control group in total time. The conclusion in that haptics does not improve the efficiency or effectiveness of LapMentor II VR laparoscopic surgery training; the limited benefit and the significant cost suggest that haptics should not be included routinely in VR laparoscopic surgery training. Van Det et al. [13] (LoE1) have proposed a new training method called INtraoperative Video-Enhanced Surgical Training (INVEST) and have compared it with the traditional master-apprentice model (MAM). The conclusions are that INVEST significantly enhanced skill development during the early learning curve for laparoscopic cholecystectomy, but a balanced training program commences with essential basic skills training on VR and/or AR simulators. Elements of procedures should be practiced in box trainers with cadaveric models. Ideally, but is difficult in Europe, trainees should attend courses that use live animal model or human cadavers to perform specific procedures on healthy organs before they go to the operating theater to perform their first procedures on real patients with INVEST. A number of governing bodies and surgical societies have published guidelines that outline standards for training for postgraduate surgeons for skill acquisition in minimal access surgery, but these recommendations are based more on common sense and clinical experience than rigorous evidence.

Continued research is needed to determine the threshold for safe performance of this and other procedures, the most effective training methods to ensure competence, and strategies to minimize patient harm, while proceduralists gain the experience they need to be competent and to train others.

The training of surgeons is a subject of broad concern to health professionals, patients, government officials, and the public alike. Reports of medical error within the healthcare and public domains have driven the need to define objective and valid measures of competence before credentialing of surgeons for independent practice. The medical community is thus obliged to develop and maintain new training paradigms that can deliver competent practitioners without undue harm to patients during the acquisition of these skills [14] (LoE3).

Training of future surgeons is a mission of vital importance to society.

In conclusion, we believe that the most important element in training a specific surgical procedure remains the hands-on training on a real patient with an experienced surgeon at the trainee's side. Virtual reality training can supplement standard laparoscopic surgical training of apprenticeship and is as effective as video trainer training in supplementing standard laparoscopic training.

11.2 Learning Curve

The learning curve was first described by psychologist Hermann Ebbinghaus in 1885 and elaborated by psychologist Arthur Bills in 1934. The concept of the learning curve is an abstract and concrete concept at the same time. The world of politics, finance, business, and enterprise must deal daily with this concept, but what is the definition of "learning curve"? In many dictionaries, it is defined as an idea that describes how new skills or knowledge can be quickly acquired initially, but subsequent learning becomes much slower. At first, a minimal investment of resources yields significant results, but the payback from continuing effort is smaller.

The difficulties of interpretation and application of this concept are the same also in the surgical world. The theme of the learning curve in laparoscopic cholecystectomy (LC) is intimately connected with the training. The strategy search on PubMed regarding the learning curve overlaps almost completely with the search about training in LC. The need to evaluate a learning curve arises from this consideration that the training has a cost, the learning curve; no training has a higher cost, complications. All studies reported clinical outcomes, most commonly bile duct injury. EAES guidelines [15] (LoE5) indicate that a minimum of 20–35 LC are necessary for a surgical trainee to be able to use laparoscopic techniques safely. Moore and Bennett [16] (LoE3) analyze bile duct injuries (BDI) in 8,839 cholecystectomy from 55 surgeons. Fifteen BDI (by 13 surgeons) resulted with 90 % of the injuries occurring within the first 30 cases performed by an individual surgeon, and, at the multivariate analyses, the only significant factor associated with an adverse outcome was the surgeon's experience with the procedure. A regression model predicted that a surgeon had a 1.7 % chances of BDI occurring in the first cases and 0.17 % chances of BDI at the 50th case. The rapidity of learning LC was not significantly related to physician age, number of surgeons in the practice, or whether the hospital setting was academic or private practice. The results of a learning curve for LC are consistent with those reported for other surgical procedures, such as coronary artery bypass grafts, abdominal aortic aneurysm repair, and hip surgery. The functional form of the learning curve relationship for LC is of the low-threshold type whereby good outcomes are predicted to occur after 10–20 cases. Usually, the first ten cases were done with close supervision. More stringent policies requiring supervision of greater than 15 cases are predicted to have smaller effects on decreasing the expected number of BDI. Gigot et al. [17] (LoE2a) reported the incidence of bile duct injury was 1.3 % when the surgeon had performed fewer than 50 cases and 0.35 % afterward ($p<0.001$). However, bile duct injuries still occurred with surgeons who had performed >100 case. Koulas et al. [18] (LoE2a) analyze 1,370 LC performed by trainees (33 %) and by consultants (67 %). They showed that supervised LC performed by trainees does not increase surgical morbidity and does not compromise surgical outcome. The grade of the operating surgeon has not predictive value for complications. Fahrner et al. [19] (LoE2c) show that, provided adequate training, supervision, and patient selection, surgical residents are able to perform LC with results comparable to those of experienced surgeons. The only statistically significant difference was the operative time (attending surgeons AS < resident surgeons RS).

We can conclude that the learning curve should be performed initially in only carefully selected patients under the supervision of an experienced surgeon. Virtual or standard laparoscopic training can significantly increase the skills and reduce the learning curve in LC.

11.3 Definition of "Expert"

A thorough analysis of all the literature, does not allow us to give the definition of surgeon "expert" in laparoscopic cholecystectomy. Most of the articles examined show that the results of the experts are better than those of surgeons who have not completed their learning curve, but no one specifies what is meant for "expert surgeon," and only a few specifies a minimum number of procedures required to define the "expert surgeon." Aggarval et al. [20] (LoE3) developing a virtual reality training curriculum for laparoscopic cholecystectomy divide surgeons in three groups: inexperienced, those who have performed fewer than ten laparoscopic cholecystectomies, intermediate, those who have performed between 20 and 50 cholecystectomies, and experienced, those who have performed more than 100 cholecystectomies. Schijven et al. [21] (LoE2b) evaluating the experience on simulators consider expert surgeons having performed over 100 laparoscopic cholecystectomies and novice surgeons having not performed previous laparoscopic cholecystectomies. Dagash et al. [22] (LoE1a) have tried to quantify the learning curve in laparoscopic surgery. After a systematic review of the evidence, the authors analyzed seven common laparoscopic procedures (cholecystectomy, fundoplication, colectomy, herniorrhaphy, splenectomy, appendectomy, and pyloromyotomy) and conclude that the number of procedures required to reach proficiency in laparoscopic surgery has not been defined clearly. These findings are important for training, ethical, and medicolegal issues. The word *proficient* is synonymous with *expert* in most dictionaries. In the surgical context, proficiency refers to expert, independent execution of treatment (operation). Surgical proficiency is best modeled by a zone rather than a sharp threshold, since surgeons bring different levels of innate abilities to the task (average, above average, below average) [23] (LoE2c). In this model, the proficiency zone represents what society expects of fully trained surgeons: an outcome that varies from one surgeon to another within very narrow limits defined by the upper and lower thresholds. For any given operation, there will be some surgeons who perform at the top end (at the upper threshold of the proficiency zone), the performance of the majority of surgeons for the same operations will be within the zone (acceptable standards of care), but none should be below the lower threshold [24] (LoE5). The various published reports on "learning curves" for specific operations based exclusively on incidence of iatrogenic injuries and morbidity rates and reaching conclusions/recommendations on the "x" number of operations required for acquisition of proficiency in the execution of an operation lack both science and validity. The truth is that the proficiency-gain curve is specific to the individual as it is to the intervention. We can never of course abolish surgical error completely, but we can reduce it to the as-low-as-reasonably-possible region.

We believe that the number of procedures required to reach proficiency in laparoscopic surgery cannot be defined. The expert as defined by the skills and experience cannot be numerically validated. The expert could be defined as the harmonious balance between experience, technical skills, and predispositions of the individual surgeon. However, the definition of "expert" cannot be separated from the concept hospital volume (HV) and surgeon volume (SV).

Those who call themselves experts should be careful to this regard: learned individuals have always warned us [25] (LoE5): "The greatest enemy of knowledge is not ignorance, it is the illusion of knowledge" (Stephen Hawking); "An expert is a man who has stopped thinking: he knows!" (Frank Lloyd Wright). Some general principles are fairly simple, but their translation to practical application might be very difficult. This is exactly what St. Thomas Aquinas claimed.

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The Expert Opinion: An International Audit

12

Alessandro Carrara, Ferdinando Agresta, Luigi Ricciardelli, Michele Motter, and Gianmarco Ghezzi

12.1 Introduction

A central thesis of EBM is the putative superiority of scientific evidence over opinion. In the scale of the evidence published by the Oxford Centre for EBM [1] expert opinion falls in the last place with a level of five. The truth is that both evidence and opinion are important and have their limitations. Scientific evidence is absent for much of medicine and, when available, is often lacking of validity, misleading, or misinterpreted. On the other hand the beliefs to which experts subscribe, often in the face of conflicting data, can be based on misconceptions and personal recollections that misrepresent population norms. Problems with expert opinion, as well as described by Woolf, include the "selective use of evidence (inadvertently or consciously ignoring studies suggesting another view), biases about magnitudes of effect and appropriateness that stem from personal experience (e.g. how one was trained, a notably bad outcome in a past patient), flawed assumptions about the frequency or natural history of diseases, and external influences (e.g. professional norms, business pressures, patient expectations, medico-legal concerns)" [2]. Nevertheless expert opinion plays an important role in all practice guidelines since these are usually developed by the use of systematic, interactive methods, which

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rely on a panel of experts. In the lack of evidence, panels of experts differ on the extent to which they are willing to make recommendations based on opinion. On the other hand, when evidence is available, its strength, generalizability, and applicability are assessed by subjective judgments. Duty of the panel is to be explicit when opinion is used so that readers well understand the basis for the recommendations.

As clearly explained in the individual chapters of this book, the scientific evidence is sufficiently strong to produce statements with a high grade of recommendations in many of the discussed topics. However, the scientific evidence is not always slavishly followed in clinical practice. In a recent national audit carried out on hospital discharge records in Italy, the diffusion of laparoscopic cholecystectomy as standard treatment of cholelithiasis was shown to be not uniform throughout the nation, with a range that varies from 0.5 to 98 % in different hospitals. Even the time of hospital stay varied from 2 to 8 days showing an noticeable discrepancy in the surgical practice of surgeons from different towns. As it is clear, surgical practice is not only guided by the latest scientific evidences, but often strongly influenced by limitations related to local health system and by the opinion of the single surgeon. To confirm this, the experience of international surgeons from different continents shows an extremely heterogeneous attitude with respect to the treatment of acute cholecystitis [3–8]. For these reasons, we found attractive the idea of involving experts from countries of every continent requesting their views on the most discussed topics in the literature regarding the surgical treatment of gallbladder stones.

12.2 Expert Selection

A literature research was performed on PubMed using "laparoscopic cholecystectomy" as MeSH terms from 2002 to 2012. All relevant articles concerning at least one of the ten topics of the present work were considered in our review. A particular preference went to those authors who wrote more than one article about the subject and who had published on journals with high impact factor. A second selection was then performed on geographical criteria to get a pool of experts from nations of every continent. Finally 169 authors were selected as experts, and a questionnaire of 20 multiple-choice questions was mailed to them. The participation rate was 11.3 % with 19 responses received. Countries of origin of all authors who have joined our audit are shown in Fig. 12.1.

12.3 Expert's Opinion

The authors' responses were collected and analyzed; a pie chart was produced for each topic expressing the percentage of adhesion of the experts to the multiple-choice answers. Finally a statement expressing the answer shared by the majority of experts was drawn up. Again, it should be emphasized that limitations in resources, and local health system policies often oblige the surgeon to constrained choices independently from their convictions, so that the reported answers (Fig. 12.2) are

Fig. 12.1 Countries of origin of the authors who have joined our audits

expression of the expert's personal opinion and do not represent their current surgical practice. Comparing the responses of experts with statements issued from the present work, an evident alignment on many of the topics does emerge. Nevertheless regarding some issues, a discrepancy of views is evident. Among these is the management of cholelithiasis in pregnancy, where international experts favor a conservative attitude as much as possible conversely to current evidence which supports an early elective laparoscopic cholecystectomy regardless of trimester of pregnancy.

Even the number of trocars to use routinely in the laparoscopic cholecystectomy is a matter of discussion. Sixty-nine percent of international experts prefer four accesses differing from what emerges from the scientific literature (three-port technique has similar outcomes than conventional four-port technique – grade of recommendation strong). Finally, the use of abdominal drainage after laparoscopic cholecystectomy: scientific evidences strongly recommend not to place it; however, only 26 % of international experts is in line with this attitude.

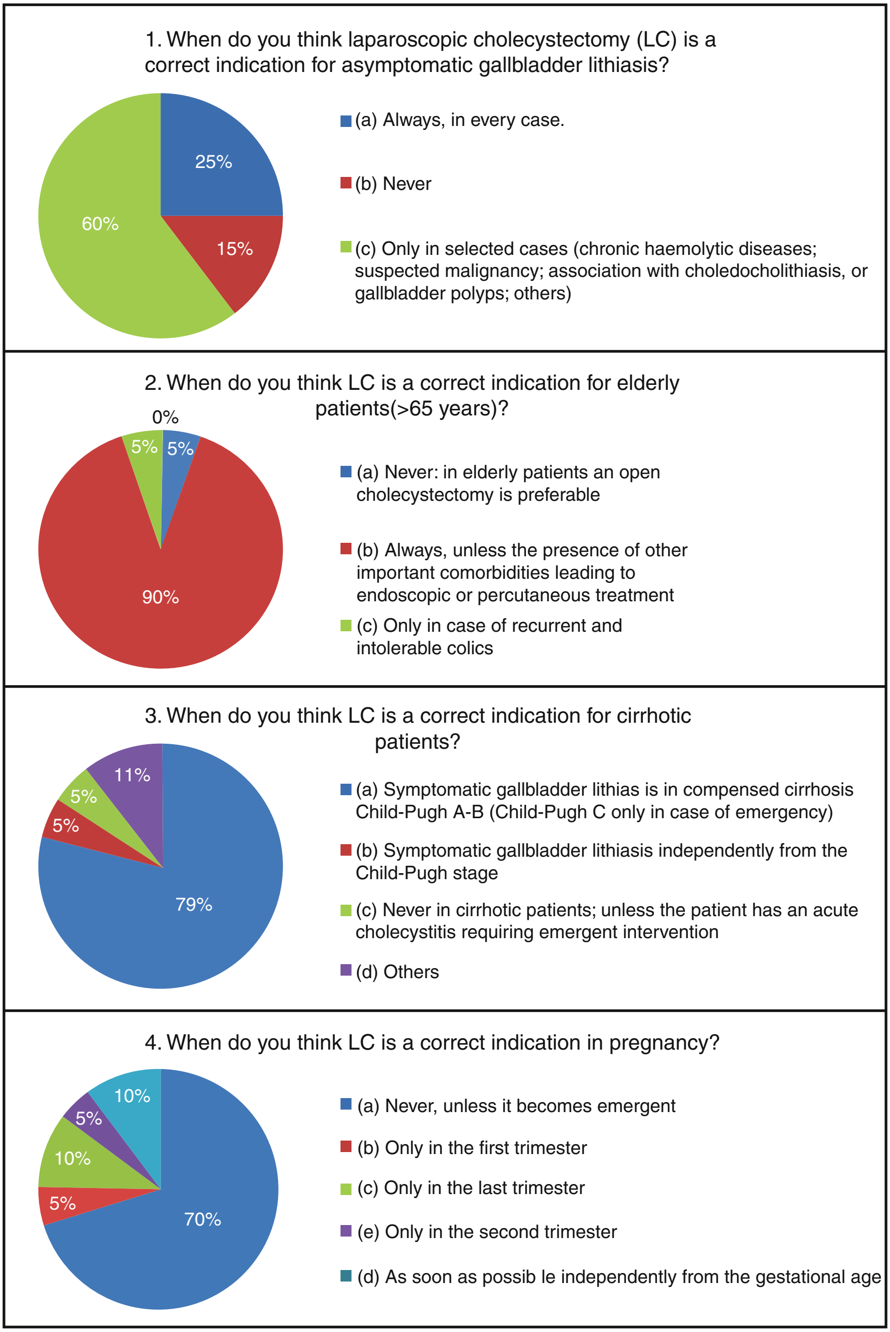
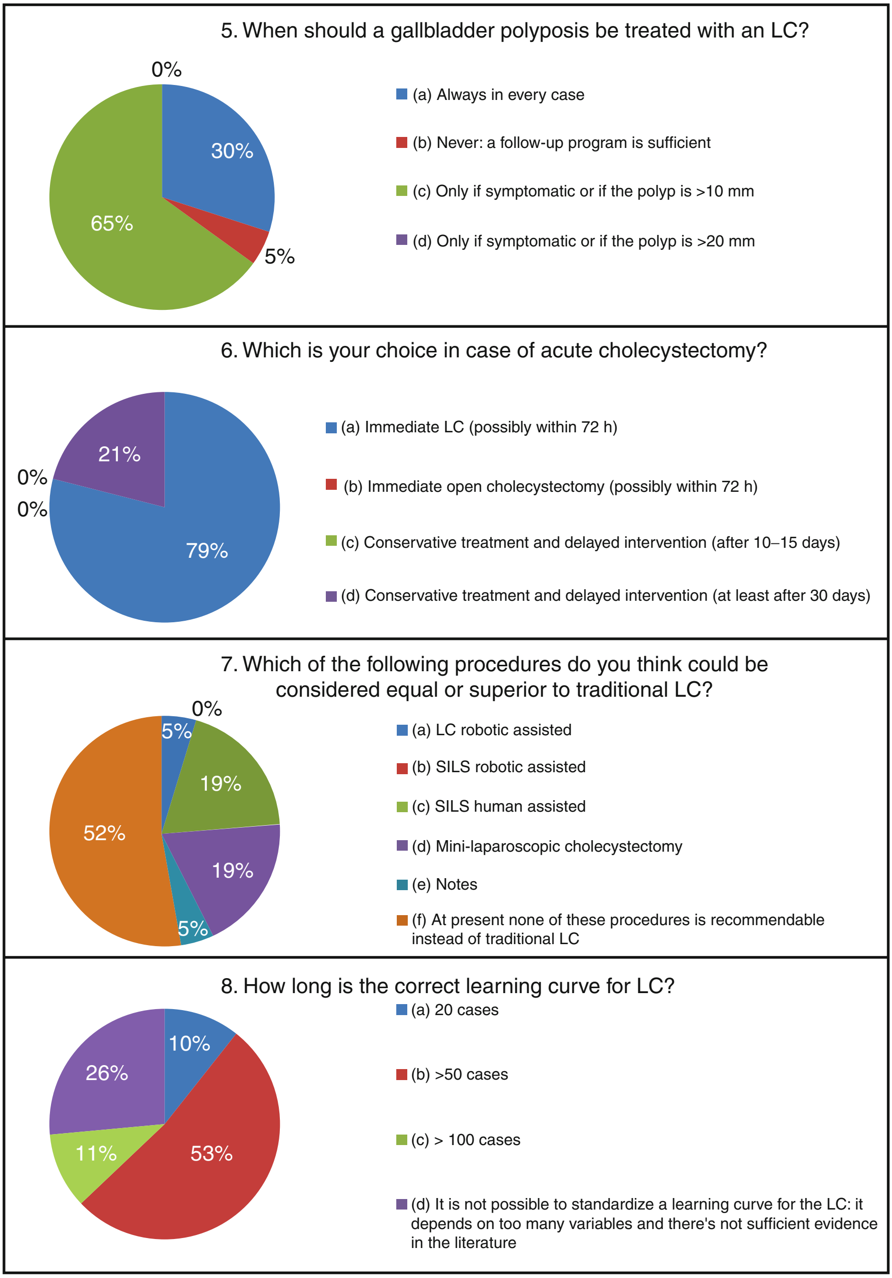


Fig. 12.2 Cumulative answers of the 19 authors to the 20 multiple-choice questions



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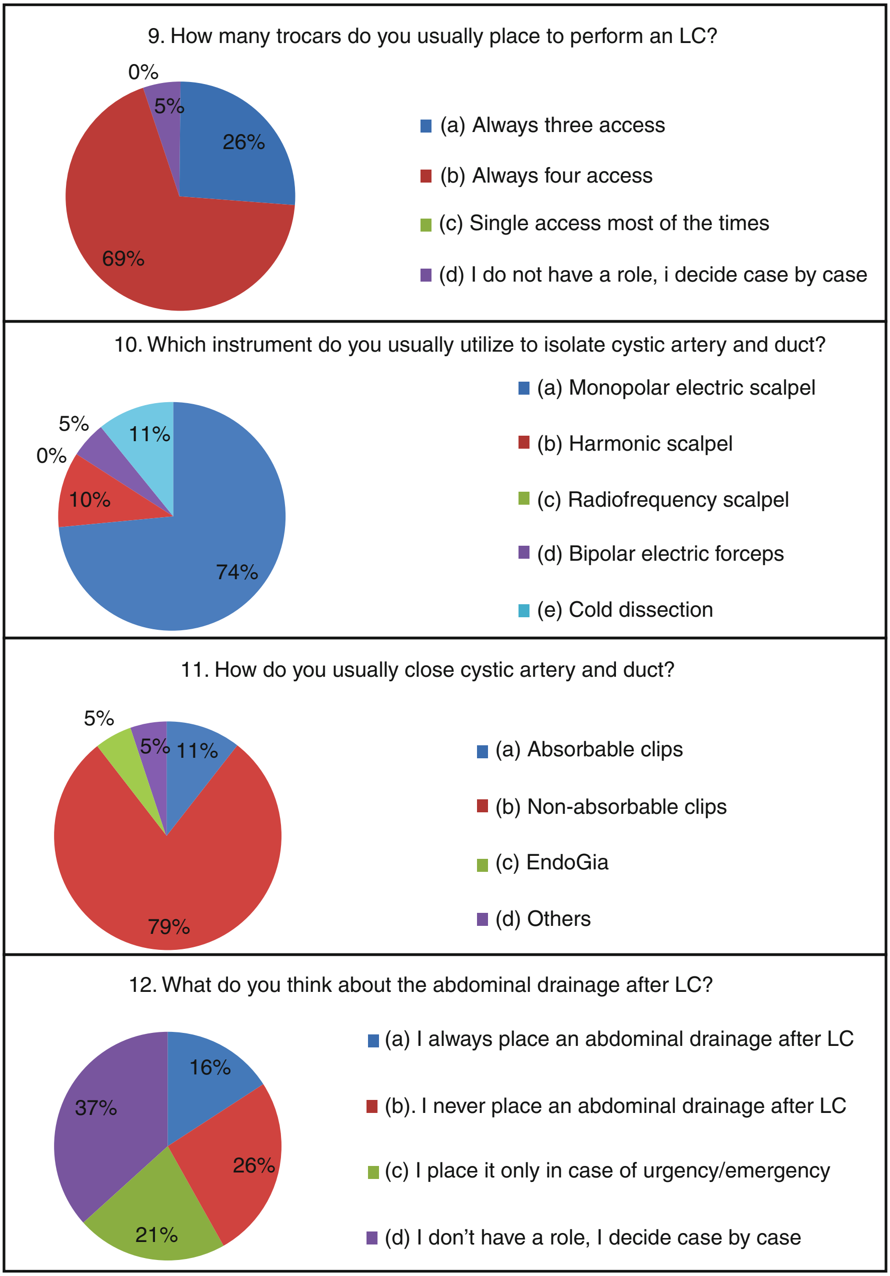

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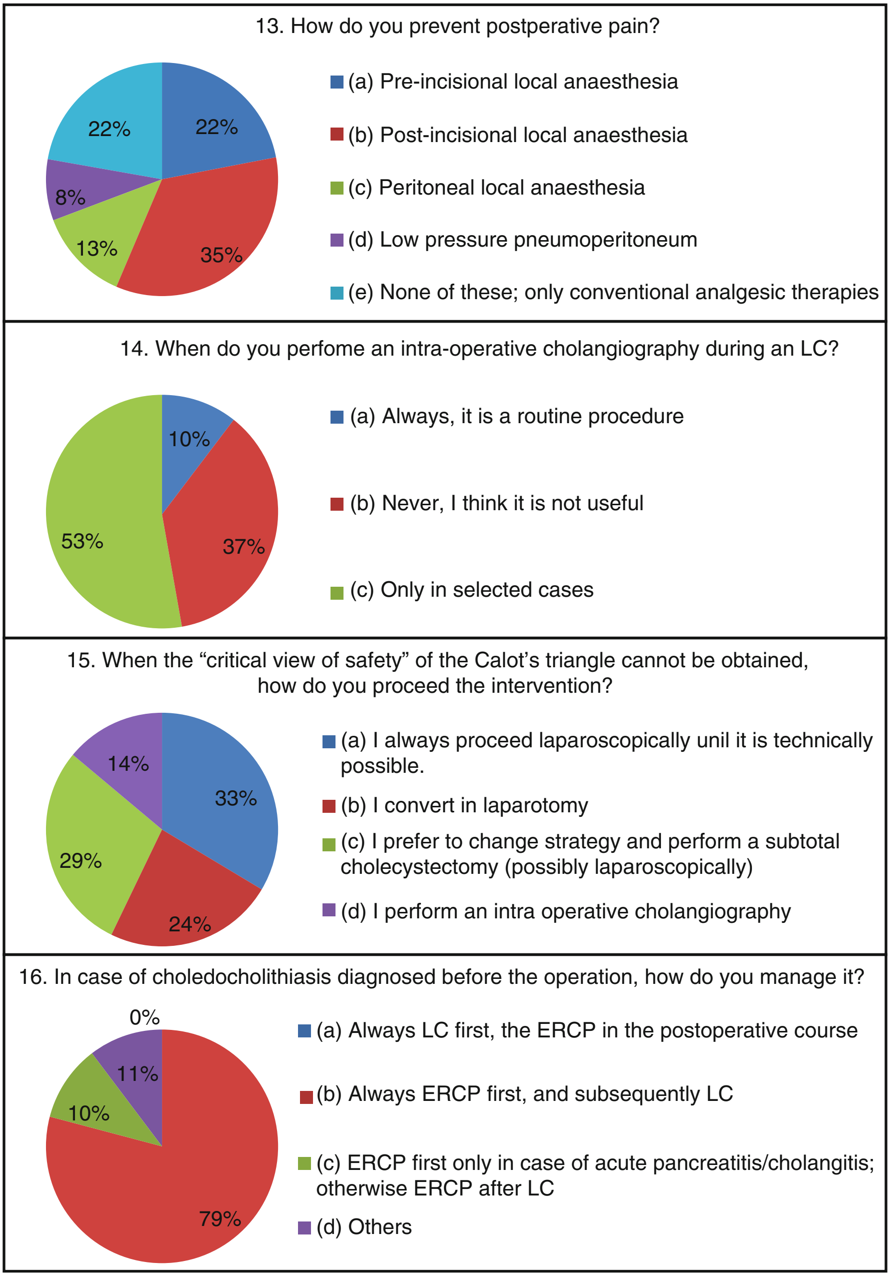

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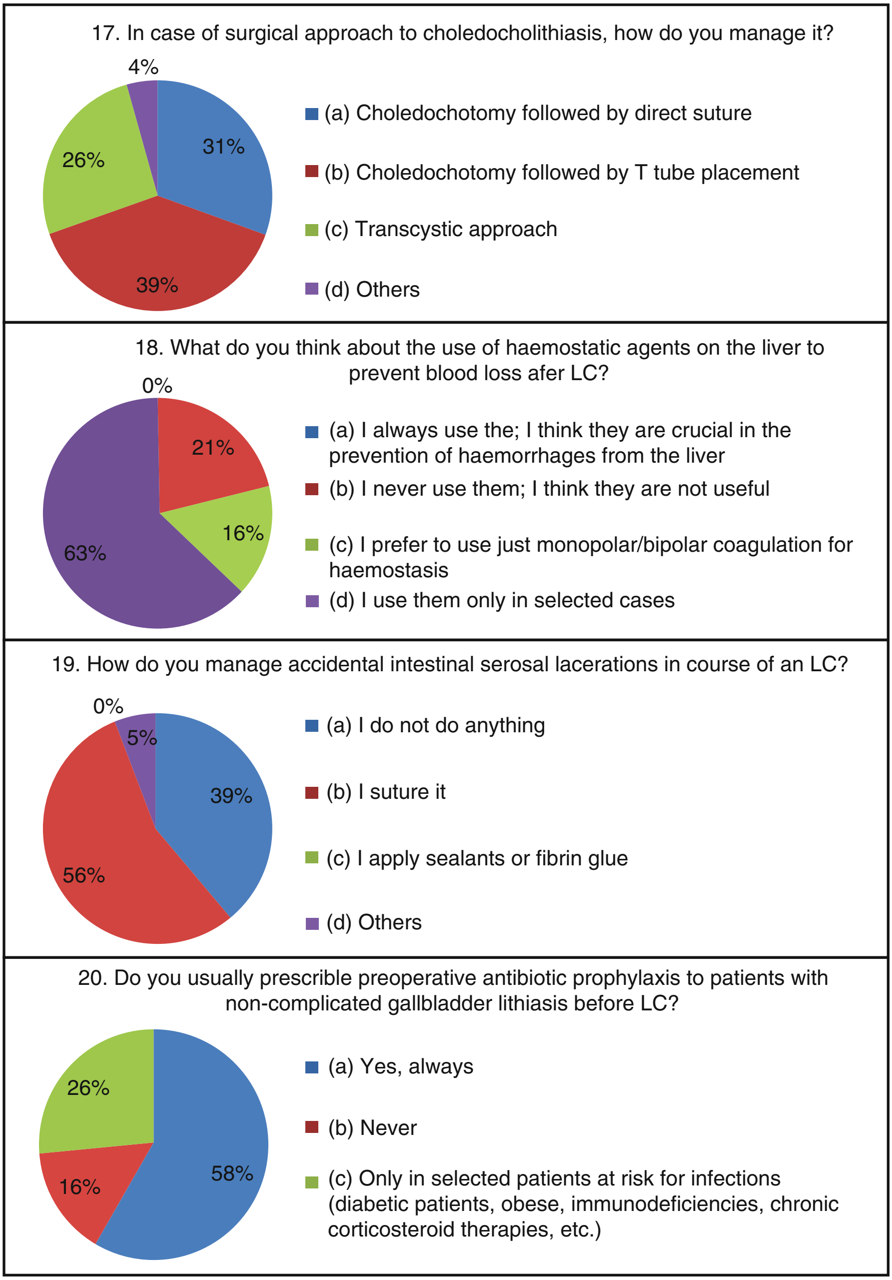

Fig. 12.2 (continued)

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13 Establishing Pneumoperitoneum: What Is the Safest Technique for Pneumoperitoneum?

Gian Luca Baiocchi, Daniela Prando, Davide Piccolo, Francesco Brandara, Luigi Ciccoritti, Federico Gheza, and Ferdinando Agresta

13.1 How to Access the Peritoneal Cavity and How to Create the Pneumoperitoneum

The emergence of laparoscopy, which is currently widespread throughout the world as the technique of choice for many surgical procedures, was closely associated to the issues of pneumoperitoneum establishment and first access to the abdomen whereby the camera should be inserted. This step is a must for any laparoscopic surgery, and all surgeons who have dedicated themselves to the development of minimally invasive culture and procedures have devoted much effort and attention to the detection of a technique for pneumoperitoneum joining together speed, simplicity, safety, and low complication rate.

The techniques for optical trocar insertion can be divided into open and closed techniques; the latter in turn are divided into techniques with and without preliminary creation of pneumoperitoneum. Numerous variants, characterized by minute

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detail, have been provided. In this chapter, the SILS has not been analyzed: owing to the size of the door and to the peculiarities related to instrument management, this technique deserves a separate discussion.

13.1.1 Open Laparoscopy (OL) or "Minilaparotomy"

This is the technique originally described in 1971 by Hasson [1] and foresees the insertion of the camera trocar upon visual recognition of the intraperitoneal structures through a small laparotomy, eventually thanks to an S-shaped retractor. The visualization of the abdominal contents is considered a fundamental step in this technique. The access is usually umbilical and envisages the sequential opening of skin, subcutaneous tissue, linea alba, and peritoneum and the digital inspection of the inner surface of the peritoneal cavity.

The main advantage of this technique is that it minimizes the risk of preperitoneal insufflation and then gas embolism; other advantages include a high likelihood of success and a reduced probability of causing vascular and visceral lesions, even if this is not totally set at zero (two cases of aortic injury and multiple cases of small bowel injury [2, 3] have been reported); moreover, by OL it is easy to close the access site plan by plan, which could theoretically reduce the incidence of incisional hernia. The disadvantages are mainly related to the need to carry out an incision larger than in other techniques, with consequences on aesthetic and postoperative symptoms, and a greater chance of suffering from gas leakage during surgery. From a theoretical point of view, the greater size of the access and most trephination of tissues may lead to a higher rate of parietal infection.

Hasson himself in 2000 published a historical series of 5,284 patients over 29 years, bringing a total of 27 (0.5 %) complications related to the first access (comprising for the most part minor wound infections and minor hematomas [4]). In the following years, some small technical variations have been proposed, not altering the substance of the foregoing [5, 6].

13.1.2 Veress Needle Laparoscopy (VN) or Closed Laparoscopy After Creation of Pneumoperitoneum

The classical alternative to the open technique provides for the blindly creation of pneumoperitoneum through abdominal puncture with a Veress needle (an approximately 2 mm hollow needle with an obturator that retracts when it engages firm tissue such as fascia [7]) and subsequent, still blind, insertion of the first trocar for the camera, counting on the fact that the pneumoperitoneum has distanced the vascular and visceral contents of the abdomen from the abdominal wall. Many surgeons prefer still using Veress needle in the left upper quadrant instead of the umbilical scar, and in any case this is the place indicated in the presence of previous midline laparotomy. Many tricks have been reported in the literature, with the aim to reduce injuries by VN [8, 9]: the use of a sharp Veress needle, patient lying level and in flat position, timing of trocar placement based on pressure rather than gas volume, and very high-pressure pneumoperitoneum, up to 25 mmHg.

This method has been classically used, especially in the gynecological field, more than the open laparoscopy, since it is considered less traumatic and more respectful of the principles of minimal invasiveness. However, disadvantages are well known, even from a theoretical point of view, as not only does this technique entail an increased risk of serious vascular and visceral injury but also the same can remain unrecognized. In an outdated French study, focused on vascular lesions, it was shown that more than ¾ of them had been caused by the VN [10].

Even the VN technique has recently received some proposals for amendments, with the aim to reduce the risk of vascular and visceral lesions while maintaining the highest minimal invasiveness; the most reported modification of the VN technique is represented by the STEP system (Inner Dyne, Sunnyvale, California, USA): after introduction of the classical VN, the needle is removed, and the outer sleeve, which remained in place, is used as a guide for a series of dilations through which a port up to 12 mm diameter may be obtained [11].

13.1.3 Direct Trocar Insertion (DTI), Direct Entry Technique, or Closed Laparoscopy Without Creation of Pneumoperitoneum

An alternative to the two classical techniques above described, called DTI, has developed in recent years and has taken more and more space among the surgeons dealing with laparoscopy [12]. This technique provides, with many variations, a small skin incision and the insertion of the first trocar without having preliminarily induced pneumoperitoneum. Some authors suggest lifting the skin at the time of the introduction of the trocar [13] and others to lift the fascia, and many surgeons use this technique with a disposable shielded trocar. After visual check that the tip of the trocar has crossed the peritoneum, gas insufflation may start. After the procedure, it is generally not necessary to close the parietal defect.

The advantages of this technique are a smaller incision and a rate of gas leakage lower than the OL, while the time of obtaining pneumoperitoneum and the probability of gas insufflation in the abdominal wall are lower compared to VN. The disadvantages are a success rate lower than the OL and a risk of vascular and visceral injury greater than the OL (but less than the VN). The rate of parietal infection may be less than in OL and similar to VN. Obviously, for the fact of being a closed technique, the DTI is not ideal in patients with a history of peritonitis or with scars from previous abdominal operations.

Recent developments in medical technology have focused more on the DTI than on the other techniques; in particular, trocars shaped to apply a radial force and trocar housing the camera at the same time of the entrance through the abdominal wall (the so-called optical trocar) have been developed.

13.2 Complications in Establishing Pneumoperitoneum: Classification and Definition of Outcomes

Possible complications of the first access for laparoscopy can be classified into major and minor and intraoperative and postoperative (early and late). There is no unanimous agreement on this classification, particularly with regard to the judgment about the severity of a complication. Strictly speaking, a complication should be considered major if it leads to a change in normal operative and postoperative procedure (i.e., significant lengthening of the intervention time, blood transfusions, conversion to laparotomy, longer length of stay, ICU course, and mortality). Cochrane review classifies the complications as follows: major complications are mortality, vascular injury, visceral injury, gas embolism, solid organ injury, and failed entry (unable to access the peritoneal cavity); minor complications are extraperitoneal insufflation and trocar site bleeding [14].

In more detail:

1. The major vascular complications consist in damage of the great retroperitoneal vessels. Unfortunately, some cases were recorded, although anecdotal, of patients who died of VN accidental injuries of the iliac and cava veins, because the time between the placement of the needle and the introduction of the camera is sometimes more than a few minutes and in this time a significant amount of blood may leak from this kind of vascular tear.
2. The major visceral complications consist in the creation of a full-thickness tear in the wall of an intestinal loop, stomach, or colon. The puncture with VN rarely entails severe damage; it has been shown that a visceral hole made from a needle, although large, can repair itself after needle extraction, due to the overlapping of different layers by which the visceral wall is composed; the injury to a viscus done by the first trocar inserted with closed technique is more serious, owing to the size of the trocar itself. Visceral lesions made by OL have normally less consequences, as they are caused by failure in recognizing the structure that is going to be opened, which is exchanged for the parietal peritoneum and is instead the bowel serosa. Indeed, the most important aspect of the gastroenteric damage is the timing of recognition, which is usually immediate with OL and DTI coupled with optical trocar, while by classical DTI and VN it cannot be recognized. The rare cases of death due to abdominal sepsis from iatrogenic fistula were due to lack of intraoperative recognition of the lesion and then to the delayed treatment of peritonitis, especially when at the end of the procedure an abdominal drain is not left in place.
3. Another organ that can be damaged during the first access for laparoscopy is the bladder; obviously, the lack of bladder catheter and very low incision are risk factors for this eventuality. Sometimes the bladder is completely passed away, so even intraoperatively the lesion cannot be recognized. The late consequences are less severe than those mentioned above; the simple and often prolonged maintenance of the bladder catheter allows for the bladder healing.
4. Injury of solid organs (liver, spleen, kidney) and of the omentum is reported less frequently and is almost always quickly recognized for bleeding; their

intraoperative treatment, though it may sometimes require laparotomy, is normally easy.

5. Minor vascular complications consist of parietal vessel lesion, the most frequent of which are represented by the injury to the epigastric vessels and, more laterally, to circumflex iliac vessels. Often during surgery, trocar buffers bleeding, which, however, continues after the trocar avulsion; bleeding in the abdomen in the postoperative period is a rather frequent event, which may require blood transfusions, angiographic treatment, or reintervention .
6. If the Veress needle is not positioned correctly beyond the parietal peritoneum, the insufflation of gas in the preperitoneal space can lead to troublesome subcutaneous emphysema and in rare cases even to gas embolism, of which some fatal cases were reported. Both the DTI and OL techniques virtually set at zero the risk of this complication.
7. The Veress needle may otherwise be located within the omentum, and inflation may continue in this structure, resulting in the creation of intra-abdominal air collections that can partially hinder the operation. The same can happen, even with DTI and OL, with the round ligament, which is a frequent site of pneumatosis by insufflation.
8. The unsuccessful establishment of pneumoperitoneum is a classical and frequent complication of the VN, which is significantly lowered by DTI and virtually cleared by OL.
9. The most frequent early postoperative complication is represented by the infection and the hematoma at the entry point of the port. Some risk factors related to the patient (diabetes, obesity, immunosuppression) and to the technique (OL brings a greater risk than DTI and VN; multiple repositioning of the trocar carries a higher risk) have been identified; obviously, the main risk factor is constituted by the presence of an intraperitoneal contamination, associated to a not protected extraction of the surgical specimen from the wall.
10. A dreaded late complication is the port-site incisional hernia, which entails the need for a second operation, in most cases with placement of a mesh. This occurrence is more frequent with port placed by OL through large fascial incisions and for cases in which the parietal defect is not sutured at the end of the intervention.

Overall, the incidence of complications related to the placement of the first trocar and the induction of pneumoperitoneum is extremely low, but many authors have pointed out that even an incidence proportionally negligible, compared to the extremely high number of procedures performed every day throughout the world, assumes an epidemiological importance; for instance, more than 250 major injuries/year would be expected in the UK alone [8]. Obviously, this considerably limits the possibility of addressing this topic with the principles of evidence-based medicine: in a study by Garry, it was estimated that to reduce the incidence of intestinal injury from 0.3 to 0.2 %, it would have been required 828,204 patients [15].

The incidence of injury to the great vessels is about 0.09 % and injury to the bowel is about 0.18 % [14]. However, in other studies, the relationship between these two events seems reversed: out of the 629 lesions described in the Medical

Device Reports to the FDA between 1993 and 1996, 65 % were vascular and 29 % visceral lesions [16]. Other series reported an incidence of vascular lesions varying from 0.04 % [17] to 0.14 % [18] and 0.18 % [19] in retrospective evaluations of 103,852, 2,201, and 14,243 laparoscopic procedures, respectively; visceral lesions in the same series ranged from 0.06 to 0.4 %.

The incidence of minor parietal complications is rather higher, although data are significantly different in published series, probably in relation to a different definition of these complication: Lal, for example, in 2004 reported 6.49 % of minor umbilical sepsis and 2.91 % of periumbilical hematoma in 755 laparoscopies performed with OL [20], but then in a later paper by the same group, including 6,000 cases, wound infections had fallen to 0.9 %; the port-site hernia rate in this second series was 0.4 % [21].

13.3 Analysis of the Literature

The first laparoscopic access and the creation of the pneumoperitoneum are one of the surgical areas of investigation in which in recent years evidence-based medicine principles have been most frequently applied; however, while in the 1990s and 2000s several prospective studies were conducted, sometimes randomized and blinded, in recent times systematic reviews and meta-analysis have prevailed. The reason for this lies in the fact that the low incidence of complications necessitates the examination of an extremely large sample, the collection of which in a single center or in a single series is difficult.

13.3.1 Retrospective Studies

In the 1990s and 2000s, several authors have retrospectively revisited their experience; most of them finally suggest, based on clinical results and probably also on their own belief, that OL is safer than closed laparoscopy (EL 4) [22, 23].

13.3.2 RCT

A substantial amount of studies has compared OL with VN [24–28], concluding that OL is safer and faster (EL 2), with the exception of one study [28]; however, this series is focused only on the setting of polytrauma and shows that VN was faster (but not safer). Moreover, the average time for the creation of the pneumoperitoneum by OL in this paper was more than 7 min (while VN was 2.7 min), much higher than reported in most other series. Some studies provide evidence that OL reduces the rate of failed entry with respect to VN.

One study compared OL with DTI [25], however in a subgroup of patients (this was not the only comparison in this study), and another study [29] compared OL with DTI with optical trocar (direct vision); none of these studies demonstrated a significant advantage of one of the two techniques (EL 2).

Several prospective studies have compared VN and DTI [25, 27, 30–33]; another paper compared VN and DTI with optical trocar [34]. Generally speaking, the majority of these studies pointed out that DTI allows a significantly lower incidence of failed entry (LoE 2), extraperitoneal insufflation (LoE 2), and omental injury (LoE 2), while no one could document a significant reduction in major adverse events neither of wound infections (LoE 2).

Finally, other randomized trials have compared standard trocars with radially expanding trocars (STEP), showing that the latter significantly reduce the incidence of bleeding from the port (LoE 2) [35], lifting and not lifting the abdominal wall before Veress needle insertion (LoE 2) [36], carbon dioxide gas insufflation with gasless laparoscopy (LoE 2) [37], a closed technique versus a parallel technique of Veress needle insertion (LoE 2) [38], and cutting versus blunt trocar (LoE 2) [39].

13.3.3 Multicentric Surveys and Systematic Reviews

Already in 1997, a first literature review, mainly based on retrospective series—in which the risk of underreporting is high—examined 489,335 cases of VN and 12,444 cases of OL: the rate of visceral injury was found to be 0.083 % with a mortality of 2.5 %, and the rate of vascular injury was 0.075 % with a mortality of 0.8 % in the VN group, while in the OL group the incidence of visceral injury was 0.048 % with no mortality, and there was no reported incidence of vascular injury [40]. The conclusion was that OL was the safer technique (LoE 3).

Another review mainly based on observational studies was published in 2002 [41]; even in this paper, it is hypothesized that, at least from the point of view of vascular complications, the OL would seem to be safer (LoE 3).

In 2003, a systematic review conducted by Merlin and Coll. [42], including prospective studies of open versus closed (VN + DTI) laparoscopy, indicated for OL a trend toward a reduced risk of major complications, of access-site herniation, of minor complications (by 57 %), and of conversions to laparotomy (LoE 3).

The meta-analysis published by Larobina and Coll in 2005 [43] included 760,890 cases of closed laparoscopy (336 major vascular injuries, a mean rate of 0.044 %, 1 injury per 2,272 cases) and 22,465 cases of OL (0 vascular injuries, $P = 0.003$). Visceral injuries occurred more frequently in closed laparoscopy (515 cases, mean rate 0.07) than in open laparoscopies (11 cases, mean rate 0.05; $P = 0{:}18$) (LoE 2).

In 2009, 2 important studies appeared: Azevedo [44] published his meta-analysis of 38 articles including overall 696,502 laparoscopies with VN, in which 1,575 injuries were reported (12.23 %), 126 (8 %) of which involved blood vessels or hollow viscera (0.018 % of all laparoscopies). Again in 2009, another meta-analysis was published [45], including 31 studies, in which OL was considered safest in 17 studies (54.84 %) and the closed approach safest in only 3 (9.68 %). Both papers concluded that OL is safer than VN (LoE 2).

13.3.4 Cochrane

The issue we are dealing with in this chapter has been the subject of a preliminary assessment by the Cochrane in 2008 [46] and of a revaluation in 2012 [14]. The latter is part of the editorial group, Cochrane Menstrual Disorders and Subfertility, and contains a comprehensive assessment of randomized trials comparing one technique with another until February 2011. In total, the authors selected 28 randomized controlled trials, which have as their object 4,860 patients; 14 types of comparisons have been reported in these studies. From an extremely thorough evaluation, it appears that none of the published studies were of high quality, for a series of bias, the most important of which was the lack of statistical power calculation. Several other methodological limitations characterize some of the papers: the absence of clear and homogenous exclusion criteria, the lack of information about the learning curve of the operators, the undefined preliminary outcomes, and the unclear method of randomization; moreover, intention to treat analysis was employed in only 3, and source of funding was declared in only two trials.

And indeed from this systematic review, no significant difference between the various techniques is revealed in the incidence of major complications (LoE 1). The failure to place the optical trocar into the peritoneal cavity was instead significantly less frequent with OL and DTI than with VN (OR 0.12, 95 % CI 0.02–0.92, and OR 0.21, 95 % Cl 0.14–0.31, respectively) (LoE 1). Extraperitoneal insufflation (OR 0.18, 95 % Cl 0.13–0.26) and omental injury (OR 0.28, 95 % CI 0.14–0.55) were less frequent with the DTI than with the VN (LoE 1).

13.4 Discussion and Final Remarks

From a historical perspective, considering with how fast and disruptive force laparoscopy has emerged as a standard approach for numerous surgical procedures, it was inevitable that the first step of this approach to the peritoneal cavity was one of those most subject to critical evaluation. All surgeons in their training phase have classically addressed the formative steps of access to the abdominal cavity by laparotomy; there is no doubt that, with the exception of the "hostile abdomen" due to the presence of multiple and diffuse entero-parietal adhesions, this procedure is easier to run than the creation of the pneumoperitoneum and the introduction of the camera. The complications of these technical steps, as far as rare, can be really dramatic, affecting the benefits that the mini-invasive technique certainly delivers.

For all these reasons, the scientific analysis of the best technique to start a laparoscopy is of considerable and widespread interest. And yet this is an area where there is reluctance by experienced surgeons to accept the dictates of evidence-based medicine: a 2007 survey between the English gynecologist experts in minimally invasive surgery [47] showed that more than one-third of them were unwilling to change practice (EL 3). The main reason for this lies in the fact that, as previously stated, there is no good-quality scientific evidence in favor of a technique or another.

However, some data appears reasonably clear. The ideal technique should be both effective, safe, and ultimately fast. Well, even if there are no data that identify any of the available techniques to be certainly superior to the other in these terms, it seems that what is logical and what was reported as statistically significant in the overall match at least does not belie.

What is logical:

1. That OL has a higher success rate than DTI and VN
2. That OL is safer (with regard to the major complications) than DTI and DTI is safer than VN
3. That DTI is faster than OL and VN

What emerges as significant from the available studies:

1. That OL and DTI have a higher success rate than VN
2. That OL and DTI are safer (with regard to major complications) than VN
3. That DTI is faster than OL and VN

The above would seem to point toward the use of DTI as the elective access for laparoscopy; however, safeguarding, as is obvious, the freedom of every surgeon to use the technique that is most convenient to him, that he knows best, and that in his own experience has created fewer problems for patients he operated.

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14 Anesthetic Management for Laparoscopic Cholecystectomy

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14.1 Introduction

Laparoscopic cholecystectomy (LC) is the treatment of choice for routine gallbladder removal and is one of the most commonly performed abdominal procedures in the Western world [1].

Benefits of laparoscopic procedures include reduced postoperative pain, quicker recovery times, earlier return to normal activities, shorter hospital stays resulting in overall reduction in medical costs, less intraoperative bleeding, fewer postoperative pulmonary complications and postoperative wound infections, and better postoperative respiratory function and cosmetic results [2]. Furthermore, there may be less internal scarring.

All these advantages represent only one side of the same coin: they should be balanced with potential adverse effects caused by pneumoperitoneum.

The physiological effects of intra-abdominal CO_2 insufflation combined with the variations of patient positioning and with the effects of anesthetics can have a major impact on cardiorespiratory function.

Thus it is crucial for both the surgeon and the anesthesiologist to understand the physiological consequences of laparoscopy and to work in cooperation to achieve a good surgical outcome.

LC is most routinely performed with general anesthesia, but spinal or epidural block alone or together with a light general anesthesia has been used.

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14.2 Pathophysiological Effects of Pneumoperitoneum During Laparoscopic Cholecystectomy

14.2.1 Cardiovascular System: Hemodynamic Effects of Pneumoperitoneum

The creation of pneumoperitoneum is the essential component for LC. It is obtained by insufflation of 2.5–5.0 L of carbon dioxide into the peritoneal cavity to permit adequate visualization of the abdominal viscera. The normal intra-abdominal pressure (IAP) is 5 mmHg or less [3], but pneumoperitoneum increases it to 12–15 mmHg. IAP above 10 mmHg is clinically significant, and above 15 mmHg can result in an abdominal compartment syndrome, which affects multiple organ systems. Increased IAP associated with pneumoperitoneum compresses venous capacitance vessels, causing an initial increase in preload and cardiac output, but later preload decreases significantly. Afterload is raised by the compression of the arterial vasculature resulting in a marked increase in systemic vascular resistance (SVR) while causing a decrease in cardiac output (CO). This change in SVR is generally greater than the reduction in CO, maintaining or even increasing blood pressure [4]. The extent of the cardiovascular changes depends on the interaction of several factors including the IAP attained, the volume of CO_2 absorbed, patient's intravascular volume, patient positioning (head-up tilt position), ventilatory technique, neurohumoral response, surgical conditions, and anesthetic agents used. The increase of SVR is caused by the release of catecholamines and vasopressin and by the activation of the renin-angiotensin system as well [5].

The decrease in CO is due to reduced venous return from compression of the inferior vena cava and from increased resistance in the venous circulation. CO typically decreases from 10 to 30 %. However, despite a decrease in intracardiac blood volume, intracardiac filling pressures may be elevated due to pressure transmitted across the diaphragm to the heart. There are analogous effects in the pulmonary circulation that manifest themselves as an increase in pulmonary vascular resistance (PVR) and a decrease in CO to the lungs.

The patient with normal cardiovascular function tolerates these hemodynamic changes well, and even if CO decreases, organ perfusion is maintained [6]. However, patients with cardiovascular disease or hypovolemia may be at increased risk and require particular attention to volume loading, positioning, and insufflation pressures [7]. Since the increased IAP during pneumoperitoneum is the main cause responsible for alteration of cardiac function, literature suggests a moderate to low IAP (<12 mmHg) to limit these effects [8]. On the other hand at IAP levels greater than 15, venous return decreases leading to decreased CO and hypotension [9].

14.2.2 Cardiovascular System: Hemodynamic Changes Due to Patient Position

In the reverse Trendelenburg position (head up) there are marked effects on the cardiovascular system because a decrease in venous return may lead to a fall in CO and mean arterial pressure. Young and healthy people can compensate it by increasing the heart rate and vascular resistances, but in the elderly patients with ischemic heart disease or cerebrovascular disease a severe hypotension may lead to myocardial or cerebral ischemia. These changes are amplified if these patients are hypovolemic. This may be the case of patients undergoing an urgent LC for acute cholecystitis presenting dehydration for prolonged vomiting.

Bradyarrhythmias, atrioventricular dissociation, nodal rhythm or even asystole can occur during insertion of the Veress needle and the trocar or during the insufflation of the abdomen that causes a sudden stretching of the peritoneum and a related profound increase in vagal tone [10] inducing a cardiovascular collapse even in healthy patients. Increased concentration of CO_2 and catecholamines can cause tachyarrhythmias.

14.2.3 Respiratory Effects

The increased IAP displaces the diaphragm upward causing the reduction in lung volumes and a preferential ventilation of nondependent parts of the lung resulting in ventilation-perfusion (V/Q) mismatch.

The thoraco-pulmonary compliance and the functional residual capacity are decreased while there is an increase in peak airway pressure [11]. The reduced thoraco-pulmonary compliance together with the elevated airway pressures may cause pneumothorax and pneumomediastinum particularly in patients with pulmonary disease [12].

14.2.4 Other Effects

An elevated IAP causes an increase in intracranial pressure (ICP) by reducing cerebral venous drainage as a consequence of the higher intrathoracic pressure. The hypercapnia due to the absorption of CO_2 from the peritoneal cavity may further raise the ICP, cerebral blood flow, and intraocular pressure. Blood flow to the kidneys, liver and gastrointestinal mucosa is reduced only when the IAP is increased over 20 mmHg. At this level renal cortical and medullary blood flow is reduced together with an associated reduction in glomerular filtration rate, urinary output, and creatinine clearance [6].

Increased IAP reduces femoral venous blood flow. This is due to the increased pressure on the inferior vena cava and iliac veins. Portal blood flow may be reduced as well leading to a transient elevation of liver enzymes.

14.3 Anesthetic Management

14.3.1 Preoperative Assessment

A careful preoperative assessment should be carried out before a laparoscopic procedure. It consists of a detailed history and a physical examination of the cardiovascular and respiratory systems associated with a thorough airway evaluation.

The preoperative laboratory evaluation depends more on patient's status than on the procedure itself. Patients with cardiac or pulmonary diseases should be carefully assessed and may require additional investigations. Relative contraindications include severe ischemic heart disease, increased intracranial pressure, uncorrected severe hypovolemia, and patients with known right-to-left cardiac shunt.

Premedication is usually not necessary except in anxious patients.

14.3.2 Patient Monitoring

Standard intraoperative monitoring includes noninvasive blood pressure, electrocardiogram, pulse oximetry, airway pressure, and end-tidal CO_2 ($ETCO_2$). Monitors of the neuromuscular junction provide the measure of adequate muscle relaxation: train of four (TOF) might be routinely used. Invasive hemodynamic monitoring may be appropriate in patients with severe cardiorespiratory diseases [13]. Ventilatory monitoring of tidal volume, FiO_2, and airway pressures is essential to detect the respiratory effects caused by the pneumoperitoneum.

$ETCO_2$ concentration monitoring is mandatory during a laparoscopic procedure because CO_2 is absorbed transperitoneally. Its elevation must be reduced, increasing the ventilation. In healthy patients the $ETCO_2$ is correlated to the $PaCO_2$, but in patients with compromised cardiopulmonary function, the gradient increases to become unpredictable, and only a direct arterial blood gas analysis can reveal a hypercarbia. A sudden fall of $ETCO_2$ can be caused by a severe hypotension or air embolism.

If a total intravenous anesthesia (TIVA) is preferred, the use of a bispectral index (BIS) can help to reduce the occurrence of awareness.

14.3.3 Anesthetic Techniques

Both general and regional anesthetic techniques have been performed for LC. General anesthesia with endotracheal intubation is certainly the most commonly used. Balanced anesthesia and TIVA are equally performed: short-acting inhalational agents such as sevoflurane or desflurane or ultrashort-acting opioids such as remifentanil are usually preferred, as many LC are done on an outpatient basis. Target controlled infusion (TCI), an evolution of TIVA in which a plasma or a site-effect drug concentration of propofol and remifentanil or other opioids can be achieved and maintained by using a pharmacokinetic model included in the infusion pump, is particularly useful in this setting because it allows a better control of the anesthesia level and hence of the patient's awakening at the end of the operation too.

The use of N_2O during laparoscopic procedures remains controversial because it has been reported to increase the incidence of postoperative nausea and vomiting (PONV), and a recent study confirmed this correlation [14].

Whatever technique is chosen, at induction of anesthesia, intravenous administration of atropine prevents vagally mediated bradyarrhythmias that can occur during the institution of pneumoperitoneum.

Since 2002, several clinical studies have investigated the use of supraglottic airway devices (SADs) in laparoscopic procedures [15, 16]. In the LC general anesthesia without tracheal intubation can now be performed suitably and effectively with second-generation gastric access SADs like the ProSeal™ and the Supreme™ laryngeal mask airway (LMA) [15–17]. Data from larger cohort are needed to determine whether any of the newer SADs (i.e., the i-gel®) offer the same advantages [18, 19]. Second-generation SADs improve pharyngeal seal and allow a passage of a gastric tube (12, 14, 16 Fr) to deflate the stomach. In such a way gastric content reflux is prevented, surgical view is improved, and at the same time gastric injury on trocar insertion is avoided. Usually the drain tube is left in situ until the surgeon has checked the stomach: if it is deflated, the drain tube should be removed. If left inside, the drain tube can cause obstruction, preventing a possible reflux from the stomach.

The main concern that prevents the diffusion of SADs in laparoscopy is the risk of gastroesophageal reflux that the high IAP produced by the pneumoperitoneum might increase. This is not the case, however, because the elevated IAP increases the lower esophageal sphincter tone [20]; moreover, the reverse Trendelenburg position adopted for LC makes the regurgitation of gastric content more difficult, and finally if it does happen, the drain tube allows venting of the stomach content.

The use of SADs results in less hemodynamic and hormonal activation, less postoperative cough, and less postoperative nausea and vomiting (PONV); shortens the recovery time; and decreases early- and late-onset sore throats [21, 22].

Neuromuscular block is achieved using short-acting agents such as cisatracurium or agents that can be antagonized immediately and completely such as rocuronium.

However, the need for muscle relaxant during laparoscopy is still controversial: for example, in patients undergoing laparoscopic gynecological surgery, the use of ProSeal LMA™ and SLIPA™ was as effective as the use of tracheal tube; they did not require muscle relaxants and gave fewer side effects [21]. Yet other authors suggest that neuromuscular blocking agents give a better surgical view and allow to decrease the IAP from 12 to 8 mmHg, and in this way postoperative pain is lowered [23]. This deep neuromuscular block must be maintained until a few minutes before the end of the operation. Hence, the time for the reverse of this block is very short. Only sugammadex can reverse the neuromuscular block immediately and completely, thus allowing a safe and quick discharge of the patient from the operating room. Unfortunately this drug is expensive and for this reason it is not largely available in Italy. On the other hand, the "curare-free" TCI anesthesia allows a quick discharge of the patient to the ward.

During LC pressure-controlled ventilation (PCV) mode seems to work better than volume-controlled ventilation (VCV) mode, because the peak inspiratory pressures are lower. PCV limits a further increase of the already elevated airway pressures due to pneumoperitoneum. This protection is especially important in patients with chronic obstructive pulmonary disease and in patients with a history of spontaneous pneumothorax or bullous emphysema [24].

Epidural anesthesia and spinal anesthesia have been safely used albeit in a smaller proportion. Spinal anesthesia has been used as segmental anesthesia, performed at T_{10}, using a small dosage of a local anesthetic plus a small dosage of an opioid [25] or as a lumbar spinal anesthesia using larger doses of the same drugs [26]. With the first option the risk of cord damage albeit rare may become devastating, while with the second approach, the larger dosages of local anesthetics may worsen the hemodynamics and increase the postoperative urinary retention rate. Anyway, spinal anesthesia gives a better control of postoperative pain [25, 26].

Patients involved in these studies were carefully selected: they were healthy and young, have a body mass index less than 30, and were scheduled for elective surgery. Spinal anesthesia requires a cooperative patient, low IAP to reduce pain and ventilation disturbances, gentle surgical technique, and a supportive operating room staff. Perhaps for these reasons spinal anesthesia has been less used, except for high-risk patients in whom general anesthesia was contraindicated.

Thoracic epidural anesthesia is also efficacious and might be applicable for LC. However, the extensive sensory block (T_4 through L_5) and the shoulder pain secondary to diaphragmatic irritation may lead to patient discomfort [27].

14.3.4 Complications

LC may cause some complications and the anesthesiologist has to be aware and ready to deal with these problems.

Vascular injuries within the peritoneum are usually apparent immediately, while retroperitoneal hematomas are often insidious to diagnose.

CO_2 pneumothorax is a rare complication of laparoscopy. It can occur spontaneously from insufflated CO_2 tracking into the thorax through a tear in the visceral peritoneum or congenital diaphragmatic defects. It can be diagnosed by a sudden decrease in oxygenation, an increase in $ETCO_2$ and in airway pressures, tachycardia, and decreased arterial blood pressure. Treatment includes deflation of the abdomen and supportive treatment. CO_2 is rapidly absorbed, but in patients with severe hemodynamic compromise, placement of a thoracic drainage may be necessary. In severe cases there can be profound hypotension and cardiac arrest.

CO_2 subcutaneous emphysema is the most common respiratory complication during laparoscopy and occurs as a complication of accidental extraperitoneal insufflation of CO_2. It increases the area for CO_2 diffusion, which can result in significant hypercarbia and respiratory acidosis. The hypercarbia is managed by increasing ventilation.

Venous embolism, although rare, is the most dangerous and potentially lethal complication of laparoscopy. Its severity depends on the volume of CO_2 injected, rate of injection, and patient position. Profound hypotension, arrhythmias, or asystole can occur as a result of a "gas lock" in the vena cava or right ventricle that interrupts circulation. Initially an increase in $ETCO_2$ is observed, but an acute decrease follows if a profound hypotension develops. The major cause of gas embolism is intravascular insufflation of gas from misplacement of the Veress needle or trocar, directly either into a vessel or into a parenchymal organ. Therapy includes immediate deflation of pneumoperitoneum, hyperventilation with 100 % O_2, and placement of the patient in steep head-down and left lateral decubitus to limit the amount of gas progression through the right ventricle outflow track. A central line may be required to aspirate gas from the right ventricle.

Owing to its high solubility in blood and rapid absorption, there are generally few risks with CO_2 embolism if compared with air venous embolism.

Endobronchial intubation may be caused by a cephalad displacement of the diaphragm during pneumoperitoneum and the related cephalad displacement of the carina.

14.3.5 Postoperative Period

Recovery after LC is usually rapid and most patients may be discharged from hospital the same day or the next day. However, although LC results in substantially less severe discomfort compared with the open surgery, postoperative pain (POP) can still be considerable. Pain can result in increased postoperative morbidity and delayed hospital discharge, issues that have health economic implications as LC can often be performed on a day surgery setting [28]. Local anesthetic infiltration at the trocar sites significantly reduces POP [29]; it is safe and cost-effective and currently is routinely performed. Wound infiltration with local anesthetics is more effective if performed at the beginning of the operation [30]. Usually long-acting local anesthetics such as ropivacaine or levobupivacaine are chosen, and it is important that they are administered not only subcutaneously but also into the subfascial layers.

Another strategy to reduce POP is the intraperitoneal nebulization of local anesthetics. Literature shows conflicting results [31]. While a recent well-designed study seems to rehabilitate this procedure [32], showing that ropivacaine nebulization before or after LC reduced POP, another systematic review does not recommend routine usage of intraperitoneal instillation after LC [33]. LC-specific evidence shows that this route of administration has a significant benefit in the early postoperative period (4–6 h), but not beyond [34].

Transversus abdominis plane (TAP) block can be another option to decrease pain in the early postoperative period [35]; however, TAP block works only for the first 6–8 postoperative hours and is time-consuming, and the amount of local anesthetics needed to perform TAP block bilaterally precludes the possibility of using local anesthetics at the trocar sites without exceeding the toxic limit. Finally no study has documented the superiority of TAP block versus the faster and safer infiltration at the trocar sites.

In LC pain is complex in nature and is a conglomerate of three different components: somatic pain (originating from incision sites), visceral pain (originating from the gallbladder bed), and shoulder pain (originating from diaphragmatic irritation) [36]. As a result, the therapy might be multimodal. Pain is particularly intense during the first 48 postoperative hours: regular use of nonsteroidal anti-inflammatory drugs (NSAIDs) or cyclooxygenase-2 (COX-2) inhibitors and paracetamol is effective for pain relief, but the treatment should be started preoperatively or at the induction of anesthesia and continued for 3–4 days [37]. There are no specific data to support prophylactic use of opioids after LC, even though their use may be justified for patients with severe pain as rescue medications [34]. The use of dexamethasone 8 mg given 90 min before LC halved pain and reduced opioids requirements in a randomized trial [38]. In another recent paper, the same dose of steroid given 60 min before the induction provoked less nausea, pain, and requirements for analgesics [39]. There is significant evidence of a benefit for dexamethasone in LC without significant evidence of risk [34].

Shoulder tip postoperative pain may be reduced by employing a lower pressure during the procedure and if the surgeon expels as much gas from the peritoneal cavity as possible [40].

PONV remains an important concern because it is a common complication after LC. PONV can be very distressing, and patients rank vomiting as the number one complication they want to avoid [41]. PONV may also worsen pain and prolong hospital admission. There are many ways to prevent or to limit it. Firstly, propofol-based anesthesia reduces PONV compared to inhalational anesthetics [42]; secondly, an effective pain treatment decreases PONV; thirdly, the opioid-sparing effect obtained with the multimodal analgesia reduces their side effects and, among them, PONV. Prophylactic dexamethasone decreases the incidence of PONV in this setting, and higher doses (8–16 mg) are more effective than lower doses; the best timing for administration remains uncertain [43]. PONV, prophylactic use of droperidol, prophylactic or therapeutic use of 5-HT3 antagonists, and a good perioperative hydration all contribute to reduce PONV.

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