Surgical treatment of choledochocystolithiasis
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CHAPTER 8

General summary and future perspectives
Chapter 8

GENERAL SUMMARY

The studies presented in this thesis focus on surgical aspect of patients with complicated gallstone disease, with an emphasis on choledochocystolithiasis. Studies presented in the first part of this thesis investigated the influence of timing of laparoscopic cholecystectomy after endoscopic sphincterotomy on preoperative, intraoperative and postoperative outcome. In the second part we evaluated the effect of subspecialization of surgeons on the outcome of laparoscopic cholecystectomy and analyzed literature on the surgical approach of bile duct stones and in particular, laparoscopic bile duct exploration.

| PART ONE |
After endoscopic sphincterotomy the conversion rate of a laparoscopic cholecystectomy is known to be higher compared to uncomplicated gallstone disease. Surgical dogmas favoured delayed surgery for a long time, hypothesizing that sphincterotomy induces inflammation and scarring of the hepatoduodenal ligament. In Chapter 2 we describe a randomized controlled trial on the timing of laparoscopic cholecystectomy after endoscopic sphincterotomy. Patients were randomized between early (<72 hours) or delayed (>6 to 8 weeks) laparoscopic cholecystectomy. The primary endpoint, a suspected difference in conversion rate, was not found; conversion rate was 4.3% in the early group and 8.7% in the delayed group. There was no difference in length or difficulty of surgery between both groups. There was no difference in complication rate between both groups. However, 36.2% of the patients in the delayed group suffered from biliary symptoms in the waiting period for cholecystectomy. In 20% of patients these were recurrent biliary complications (i.e. recurrent choledocholithiasis or acute cholecystitis), and 23.5% underwent emergency surgery. Based on these findings, we conclude that patients with symptomatic choledochocystolithiasis who will undergo endoscopic sphincterotomy, subsequent laparoscopic cholecystectomy should be performed within 72 hours. Early laparoscopic cholecystectomy is safe and might prevent the majority of biliary events in the conventional waiting-period following endoscopic sphincterotomy.

Chapter 3 focuses on the logistical and technical feasibility of early laparoscopic cholecystectomy after endoscopic sphincterotomy. After the clinical trial we performed, described in the previous chapter, we changed our policy and aimed to operate all patients as soon as possible after endoscopic sphincterotomy. The operative data of 98 consecutive patients operated in our hospital were analyzed if early laparoscopic cholecystectomy is feasible and safe. Of 98 patients, 74% was operated within 3 days, and 88% within 1 week after endoscopic sphincterotomy.
Conversion rate was 4.1%, surgical morbidity was 9.2% and overall morbidity 16.2%, data all comparable with the literature.

Secondly, we performed a survey amongst the Departments of Surgery of 83 Dutch hospitals. The survey showed that in nearly half (47%) of the hospitals there is no protocol on timing of laparoscopic cholecystectomy after endoscopic sphincterotomy for surgeons or residents. The percentage of patients operated upon within 2 weeks is also higher for hospitals with a protocol, than hospitals without; 27% versus 6% respectively. The majority of surgeons postpone laparoscopic cholecystectomy because of the fear of complications or for logistic reasons. The data from our hospital showed that early laparoscopic cholecystectomy is logistically feasible and safe to perform. Fear for more complications after early surgery is not justified. Together with the high rate of recurrent complaints during the conventional waiting period for delayed surgery, we believe early laparoscopic cholecystectomy should become accepted as the standard of care.

As mentioned before, studies have shown that there seems to be a higher conversion rate after endoscopic sphincterotomy. For long, this has been the only measurement of complexity of the post-endoscopic sphincterotomy cholecystectomy. In Chapter 4 we aimed to objectify the complexity by comparing laparoscopic cholecystectomy in patients with combined choledochocystolithiasis with patients with uncomplicated gallstone disease. Our data showed that patients who had undergone endoscopic sphincterotomy are subject to a more difficult and lengthier operative procedure, and a longer postoperative hospital stay. Median difference in length of procedure was 17 minutes; 60 minutes for the post-endoscopic sphincterotomy group vs 43 minutes for the uncomplicated group. Postoperative hospital stay was 2 vs 1 day respectively. This difference in length and complexity of surgery remained significant when corrected for a difference in experience of the operating teams. Even though morbidity and conversion rate were comparable, we believe it seems to be justified to have a skilled laparoscopic (hepatopancreatobilary) surgeon perform the cholecystectomy in patients who underwent an endoscopic sphincterotomy.

It has been shown previously that endoscopic sphincterotomy leads to bacterial colonization of the common bile duct. In Chapter 5 we analyzed bile samples of 64 post-sphincterotomy patients, taken during laparoscopic cholecystectomy to investigate if the presence of bactobilia influences peri- and postoperative outcomes. Almost two thirds of the bile samples were infected (62.5%), with up to 4 different micro-organisms per sample. Patient’s age and time between endoscopic sphincterotomy and laparoscopic cholecystectomy were independent predictors for having bactobilia (p=0.001 and p=0.039.
respectively). We did not find a relationship between the presence of bactobilia and operating difficulty, length of surgery, complications or conversion rate. The study was underpowered for detecting differences in biliary or infectious complication rates, and could therefore not provide strong recommendations on the need for prophylactic antibiotics preoperatively.

| PART TWO |

In Chapter 6 we analyzed 1509 patients undergoing laparoscopic cholecystectomy for uncomplicated and complicated gallstone disease. Our aim was to evaluate the impact of surgical subspecialization on outcome of surgery. In 220 patients with acute cholecystitis who underwent emergency surgery, we found that nonlaparoscopic surgeons (<50 laparoscopic procedures annually) had a more than 4 fold higher conversion rate compared to laparoscopic-oriented surgeons (15.6 vs 3.6%, p=0.003). In elective surgery, there was no difference between the both groups of surgeons in conversion rate or operating time. As studies showed before, conversion is generally associated with increased postoperative pain, pulmonary complications and a longer recovery to normal activities. In case of acute cholecystitis, we strongly believe surgery should be performed by a laparoscopic (HPB) surgeon to prevent exposing patients to unnecessary risks. Postponing the operation to the following day has to be considered if expertise is not available during duty-hours.

With the increase in laparoscopic skill worldwide, laparoscopic common bile duct exploration has gained popularity in some countries the past few years. There is however still controversy of the advantages of the single-stage management, and in particular the transductal approach. A systematic review of studies comparing single-stage and two-stage management of choledochocystolithiasis was performed in Chapter 7. A literature search yielded 8 eligible randomized studies. The studies were subjected to a critical appraisal but methodological and statistical heterogeneity precluded a meaningful meta-analysis. In the single-stage group we specifically divided transcystic and transductal stone extraction, unlike any other earlier published review. The review showed that stone clearance is comparable between the 3 treatment modalities. However, transductal stone extraction has increased morbidity rates compared to transcystic and endoscopic stone extraction; especially bile leakage (11% vs 1.7% vs 1% respectively). Transcystic stone extraction seems to be the treatment of choice, in particular if intraoperative cholangiography is already performed routinely. Intra- or postoperative ERCP might be the viable second option when the former technique fails. However, most important is that
treatment of common bile duct stones should be based on available expertise. Transductal approach should be performed only by very experienced surgeons.

FUTURE PERSPECTIVES

The treatment of combined choledochocystolithiasis is bipartite; removal of the stones in the bile duct and a (laparoscopic) cholecystectomy to prevent recurrent biliary complications. Multiple modalities are available to obtain these goals. Endoscopic sphincterotomy followed by laparoscopic cholecystectomy is currently still the treatment of choice in many (western) countries. We discussed the issue of timing of both procedures involved in Chapter 2 & 3 and concluded that early laparoscopic cholecystectomy after endoscopic sphincterotomy is safe, feasible and improves outcome. Other studies have been published the past few years confirming the advantages of early laparoscopic cholecystectomy after clearance of the bile duct stones by ERCP.\cite{1-4} The health benefits of early laparoscopic cholecystectomy will as shown outweigh the organizational intricacies, and surgeons should change their working attitude concerning this relative acute approach as we did in the past concerning the timing of the laparoscopic cholecystectomy in acute cholecystitis. Another important aspect in the treatment of patients with complicated gallstone disease is the shift towards a more specialized surgeon in line with the volume and outcome discussion in many different areas of surgery. In Chapter 4 & 6 we showed that laparoscopic cholecystectomy for complicated gallstone disease (including patients suffering from acute cholecystitis and choledocholithiasis) is more complex and has a higher conversion rate, especially when performed by non-laparoscopic oriented surgeons. In the future, complicated gallstone disease should preferably or probably solely be operated by a laparoscopic skilled HPB-surgeon. Surgeons dealing with complicated gallstone disease should also (further) dedicate themselves in performing intraoperative cholangiography as the first step for visualisation of bile duct stones and consequently being prepared for the single-stage (transcystic) laparoscopic treatment. Transcystic or transductal stone extraction combined with a cholecystectomy as a single-stage procedure seems to be the near future because of a decreased interventional burden for the patient, shorter hospital stay and lower costs. Also, with increasing numbers of bariatric procedures for morbid obesity being performed annually it’s likely that more patients with a change in local anatomy (i.e. gastric bypass) will present with symptomatic gallstone disease and bile duct stones.\cite{5,6} These patients are difficultly accessible for endoscopic stone clearance and preferably treated with laparoscopic bile duct clearance. In an attempt to further reduce the still
general accepted practice of diagnostic ERCP for suspected bile duct stones in combination with symptomatic gallstone disease, treatment of patients with suspected choledochocystolithiasis should start with the laparoscopic approach by performing an intraoperative cholangiography. If no stones are found, laparoscopic cholecystectomy is performed (including prevention or early diagnosis of bile duct injury). The potential risk of complications by diagnostic ERCP in patients with bile duct stones is excluded. If bile duct stones are found, the procedure should be followed by transcystic stone extraction and cholecystectomy. If transcystic stone extraction fails, transductal approach might be attempted as a next step. However the transductal technique, as showed in Chapter 7, has a higher complication rate compared to the transcystic route, and should only be performed when expertise is available. Another option for failed transcystic stone extraction is placing a guidewire through the cystic duct, common bile duct and via the papilla into the duodenum to facilitate intraoperative endoscopic sphincterotomy as the currently well accepted rendezvous procedure. A recent meta-analysis by Gurusamy et al. showed reduced morbidity, shorter hospital stay and reduced costs compared to preoperative endoscopic sphincterotomy, even excluding morbidity of negative diagnostic ERCP’s.\footnote{7} We believe this new approach needs further evaluation in future studies. One should realize that intraoperative endoscopic sphincterotomy requires the availability of endoscopists and their equipment in the operating theatre. This is in line with the new concept of the development of operating theatres for the multidisciplinary intervention approach of patients. This has been shown already in (cardio-)vascular surgery, including vascular surgeons, intervention radiologist, cardiologist and cardiothoracic surgeons. Performing intraoperative cholangiography has another advantage; it allows visualization of the biliary tree, lowering the risk of bile duct injuries during the cholecystectomy or early diagnosis of a potential bile duct injury as shown in a recent meta-analysis\footnote{8}. It is also important as the first step in development of the skills to perform a transcystic approach of bile duct stones removal. Therefore intraoperative cholangiography during laparoscopic cholecystectomy for (un-)complicated gallstone disease should be included in the armamentarium of gastrointestinal surgeons confronted with the treatment of combined choledochocystolithiasis.
REFERENCES


