

ORIGINAL ARTICLE

Laparoscopic cholecystectomy is more difficult after a previous endoscopic retrograde cholangiography

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Abstract

Background: Endoscopic retrograde cholangiography (ERCP) with endoscopic sphincterotomy (ES) followed by a laparoscopic cholecystectomy (LC) is generally accepted as the treatment of choice for patients with choledochocystolithiasis who are eligible for surgery. Previous studies have shown that LC after ES is associated with a high conversion rate. The aim of the present study was to assess the complexity of LC after ES compared with standard LC for symptomatic uncomplicated cholecystolithiasis.

Methods: The study population consisted of two patient cohorts: patients who had undergone a previous ERCP with ES for choledocholithiasis (PES) and patients with cholecystolithiasis who had no previous intervention prior to LC (NPES).

Results: The PES group consisted of 93 patients and the NPES group consisted of 83 consecutive patients. Patients in the PES group had higher risks for longer [more than 65 min, odds ratio (OR) = 4.21 (95% confidence interval (CI) 1.79–9.91)] and more complex [higher than 6 points, on a 0–10 scale, OR 3.12 (95% CI 1.43–6.81)] surgery. The conversion rate in the PES and NPES group (6.5% versus 2.4%, respectively) and the complication rate (12.9% versus 9.6%, respectively) were not significantly different.

Discussion: A laparoscopic cholecystectomy after ES is lengthier and more difficult than in uncomplicated cholelithiasis and should therefore be performed by an experienced surgeon.

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Introduction

Endoscopic retrograde cholangiography (ERCP) with endoscopic sphincterotomy (ES) is in most countries the treatment of choice in patients with combined choledochocystolithiasis. In patients with residual stones in the gallbladder, international guidelines advise performing a subsequent laparoscopic cholecystectomy (LC) in patients eligible for surgery, to prevent recurrent biliary symptoms.^{1–4} A recent randomized clinical trial showed that recurrent biliary events were avoided only if patients went on to have a LC within a short interval after ES. If LC was postponed for 6–8 weeks, a policy still followed in many centres, 36% of the patients develop recurrent biliary events in the intervening period.⁵

Previous studies have shown that LC after ES is more difficult than LC for uncomplicated cholelithiasis: the conversion rate after a previous ES has been reported to be as high as 8–55% versus lower than 5% in patients with uncomplicated disease.^{1–3,6–11} The aetiology is thought to be because of disruption of the sphincter of Oddi and subsequent bacterial colonization of the biliary tract leading to inflammation and subsequent scarring of the hepatoduodenal ligament hindering dissection of Calot's triangle.¹² This theory of reflux and bacterial colonization is strengthened by the finding that bile in patients who have undergone a sphincterotomy is colonized in approximately 60% of patients.^{12,13}

If indeed LC is more difficult after a previous ES it might be beneficial to have these patients operated on by an experienced laparoscopic surgeon to minimize the risk of conversion and subsequent morbidity.

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Therefore the aim of the present study was to assess the complexity of LC after ES in patients with combined choledocholithiasis, as compared with patients with uncomplicated gallstone disease, in relation to the experience of the surgical team.

Patients and methods

Patients

The study population consisted of two patient cohorts: patients who had undergone a previous ERCP with ES for choledocholithiasis and patients with cholecystolithiasis who had no previous intervention prior to LC.

Patients with a previous ES (PES) were derived from the previously reported multi-centre randomized clinical trial (LANS trial) analysing the effects of the timing of laparoscopic cholecystectomy after endoscopic sphincterotomy.⁵ Ninety-six patients were randomly allocated to either LC within 72 h after ES [early LC (ELC)] or 6 to 8 weeks after ES [delayed LC (DLC)]. No stent was placed during ERCP. The number of days between ES and LC (*the interval*) was counted from the last ERCP with ES (complete bile duct clearance) until the day of surgery. All patients were 18 years and older and had an ASA classification under IV. Analysis of these two groups showed no differences in patient- or procedure-related characteristics (conversion and complication rate, complexity and length of procedure). It was considered that these two groups were suitable for analysis as one group.

The group of patients without intervention before LC (NPES) consisted of a prospective, consecutive cohort of electively planned, laparoscopic cholecystectomies. These cholecystectomies were performed in three hospitals that had participated in the LANS trial.

Procedure

The laparoscopic cholecystectomy in both groups was carried out using a standard four-trocar technique. Antibiotic prophylaxis was not routinely administered. A pneumoperitoneum was established by insufflation of carbon dioxide gas up to an intra-abdominal pressure of 12 mmHg. The cystic artery and duct were clipped and transected only after the Critical View of Safety was established (which is routine procedure in the Netherlands). The gallbladder was then removed retrogradely. The cholecystectomies were performed by surgical residents and senior surgeons/consultants.

Outcome parameters

Complexity and length of the surgical procedure, conversion rate, post-operative complications and hospital stay were recorded for all patients. The complexity of LC was scored by the most experienced surgeon in the operating team on a 0–10 scale, with '0' (zero) being very easy and '10' very difficult. The scoring principle was the same as in the LANS trial.⁵ Operating time was defined as 'time between first incision and placement of last suture'.

Experience of operating and assisting/supervising the surgeon in performing laparoscopic cholecystectomies was noted in four categories: <20 cholecystectomies, 20–50, 50–200 and >200.

Conversion was done by a subcostal incision. The decision for conversion could only be taken by a senior surgeon/consultant. If conversion occurred the surgeon had to report the reason for conversion.

Complications were recorded during the hospital stay and at the outpatient clinic, which every patient visited after 2–4 weeks.

Sample size calculation

The analysis performed in the group with a previous ES from the LANS trial showed that the length of the surgical procedure was 60 min [standard deviation (SD) 22.7].⁵ In the sample size calculation a difference of 10 min in length of the surgical procedure was estimated. Using a power of 0.8 and an alpha of 0.05, a two-tailed sample size calculation revealed that per group 81 patients needed to be included.

Statistical analysis

Statistical analysis was performed with the use of the SPSS 18.0 software package for Windows (IBM Co., New York, NY, USA). Categorical data were compared by means of χ^2 analysis and Fisher's exact test when numbers were small. Comparison of continuous data was done with Student's *t*-test or Mann–Whitney *U*-test (non-parametric data). A *P*-value <0.05 was considered statistically significant.

The variables length and complexity of surgery were not normally distributed and therefore the variables were dichotomized. Cut points were defined for the length of surgery (≤ 65 and >65 min) and the complexity of surgery (≤ 6 points and >6 points). The relationship between the PES and NPES group and the length of LC was examined by means of multivariate logistic regression analyses. In the analysis adjustments for *potentially confounding variables* were performed. The relationship between the PES and NPES group and the complexity of LC was examined in the same way. Odds ratios (ORs) and 95% confidence intervals (CI) were calculated.

Results

Out of 96 randomized patients from the LANS trial, 93 patients (97%) actually underwent a cholecystectomy. Of these 93 patients, 47 (50.5%) were operated on early and 46 (49.5%) operations were delayed. These patients were included in the PES group. The NPES group consisted of 83 consecutive patients who underwent an elective cholecystectomy for uncomplicated gallstone disease.

Patient characteristics

Patient characteristics are listed in Table 1. There was no significant difference in age, gender or previous abdominal surgery between the PES and NPES groups. In the PES group, the median ERCP attempts was 1 (range 1–3). The median interval between

Table 1 Patient characteristics of patients undergoing a laparoscopic cholecystectomy

Patients	PES ^a (n = 93)	NPES ^b (n = 83)	P-value
Age, years			0.251
Mean (SD)	52.7 (17.3)	49.9 (14.5)	
Male, percentage	31.2%	30.1%	0.880
Previous abdominal surgery, percentage			0.058
No previous surgery	75.8%	63.4%	

Data are number. ES, endoscopic sphincterotomy; LC, laparoscopic cholecystectomy; NA, not available; SD, standard deviation.

^aLC after ES.

^bLC without previous ES.

Table 2 Procedural characteristics of patients undergoing a laparoscopic cholecystectomy and characteristics of the surgical team

	PES (n = 93)	NPES (n = 83)	P-value
Length of procedure (min)			
Median (range)	60 (25–120)	43 (15–135)	<0.001
Percentage > 65 min	37.0%	12.0%	<0.001
Level of complexity (0–10)			
Median (range)	5 (0–9)	3 (0–10)	0.002
Percentage > 6	35.6%	18.1%	0.01
Conversion	6 (6.5%)	2 (2.4%)	0.201
Gallbladder related	6 (6.5%)	1 (1.2%)	
Experience of the operating surgeon ^a			<0.001
<20	21 (22.6%)	8 (9.6%)	
20–50	22 (23.7%)	30 (36.1%)	
50–200	28 (30.1%)	11 (13.3%)	
>200	21 (22.6%)	34 (41%)	
Missing	1 (1.1%)	0	
Highest level of experience within the operating team ^a			<0.002
20–50	1 (1.1%)	2 (2.4%)	
50–200	37 (39.8%)	13 (15.7%)	
>200	55 (59.1%)	68 (81.9%)	

Data are number.

^aExperience measured in the number of performed laparoscopic cholecystectomies.

ES and LC was 2 days (range 0–533) for the ELC group and 45 days (4–363) for the DLC group.

Complexity and length of procedure, conversion rate and characteristics of the surgical team

Procedural characteristics are listed in Table 2. The median length of LC was 17 min longer for the PES group compared with the NPES group ($P < 0.001$). The median complexity of the LC was

Table 3 Morbidity, mortality and hospital stay

	PES (n = 93)	NPES (n = 83)	P-value
Morbidity	12 (12.9%)	8 (9.6%)	0.499
Mortality	0	1	0.291
Hospital stay			
Post-operative days			
Median (range)	2 (1–16)	1 (0–99)	<0.001
Discharged after 2 days	73.6%	90.4%	

Data are number.

Table 4 Multivariate linear regression analysis on the influence of the length of surgery

Predictor	PES versus NPES	95% confidence interval	P-value
Length of surgery	4.45	2.03 9.78	<0.001
Length of surgery ^a	4.21	1.79 9.91	0.001
Complexity of surgery	2.83	1.37 5.82	0.005
Complexity of surgery ^a	3.12	1.43 6.81	0.004

^aAdjustments for previous abdominal surgery, experience of the operating surgeon and the highest level of experience in the operating team.

scored 2 points higher in the PES group ($P = 0.002$). There were six conversions in the PES group (6.5%), all related to the dissection of the gallbladder: two for biliodigestive fistulae in combination with an unclear anatomy, three because of an unclear anatomy and one owing to hilar infiltrate. The conversions were in none of the patients related to previous abdominal surgery. In the NPES group there were 2 conversions (2.4%), with only one being related to dissection of the gallbladder (bleeding in the hilar region which deprived surgeons of a clear view); the second conversion was because of an intestinal perforation because of trocar introduction.

The conversion rate was not dependent on the experience of the surgeon.

Analysis of the surgical team

Eighty per cent of the operations in the PES group were performed by a two-person team versus 68.7% in the NPES group ($P = 0.068$). In the PES group, 22.8% of the operating surgeons had performed >200 LC's versus 41% in the NPES group ($P < 0.001$). The differences between the PES and NPES group for the highest level of experience within the operating team was for >200 LCs, respectively, 59.1% versus 81.9% ($P < 0.002$).

Morbidity, mortality and hospital stay

Complications occurred in 12 patients from the PES group (12.9%) and in 8 patients in NPES group (9.6%) ($P = 0.497$) (Table 3). There were more cystic stump leakages in patients who had undergone an ES (4 versus 1 patient, $P = 0.218$). In 4 of these

patients the highest level of experience of the surgical team was >200 LC's. There was no difference in experience with the other complications.

Iatrogenic bowel injury occurred in 2 patients in the NPES group, leading to a laparotomy in one patient and conversion in the other. The latter eventually died of multi-organ failure after a second laparotomy for abdominal sepsis.

The median post-operative hospital stay was significantly longer for patients in the PES group ($P < 0.001$).

Conversion of LC to an open cholecystectomy was associated with the occurrence of post-operative complications. Of 8 patients who underwent conversion, 4 developed a complication versus 16 of 168 non-converted patients ($P < 0.001$).

Differences between the PES and NPES group

In the PES group, higher risks were observed for the *length and complexity of surgery*. The unadjusted risk of surgery that lasted more than 65 min in the PES versus the NPES group was 4.45 (95% CI 2.03–9.78) (Table 4). Entering *previous abdominal surgery, experience of the operating surgeon* and *highest level of experience in the operating team* as potentially confounding variables into the multiple logistic regression model, the risk remained almost unchanged at 4.21 (95% CI 1.79–9.91).

The risk of surgery with a complexity of 7 or more points was also higher in the PES group than in the NPES group (unadjusted OR = 2.83, 95% CI 1.37–5.82). After adjustments for previous abdominal surgery, experience of the operating surgeon and the highest level of experience in the operating team the OR was 3.12 (95% CI 1.43–6.91).

Discussion

This is the first prospective cohort study comparing the complexity of LC after ES with LC for uncomplicated gallstone disease. Data showed that patients who have undergone an ERCP with ES for choledochocystolithiasis are subject to a more difficult laparoscopic cholecystectomy, both in operating time and the complexity of the operative procedure as indicated by the surgical team, compared with patients with uncomplicated gallstone disease. It was also apparent that a higher incidence of cystic stump leakage was present in patients who had undergone an ERCP. This difference was not significant, probably as a result of the small numbers, and was not related to the surgeons' experience. Literature on cystic duct leakage after LC has shown an increased prevalence after an emergency cholecystectomy; however, this relationship has not yet been described after ES.¹⁴ One of the well-known causes of cystic duct leakage is a wide cystic duct. It is understandable that after an episode of choledocholithiasis the cystic duct can be oedematous and clips can be hard to place or easily slip off. When suspicion arises it might be wise to use endoloops or suture ligation.

The post-operative hospital stay was also longer in the PES group.

Previous retrospective studies have demonstrated a higher complication and conversion rate of LC after ES,^{6–9} and this study demonstrates that indeed surgeons qualify this procedure as more difficult and lengthier than a LC for uncomplicated cholelithiasis. There was a difference in surgical experience between both groups. This was probably because of the elective character of one, and the (semi-) emergency character of the other group.⁵ But even after adjustments for level of experience, the risk of prolonged and more difficult surgery remains higher in the PES group.

This finding that LC after ERCP is more difficult is in accordance with previous retrospective studies that demonstrated a higher complication and conversion rate of LC after ES. A possible explanation might be the destruction of Oddi's sphincter, leading to bacterial colonization of the common bile duct, inflammation and scarring of the hepatoduodenal ligament. The theory of reflux and bacterial colonization is strengthened by previous studies showing that the bile in patients who have undergone a sphincterotomy is infected in approximately 60% of patients.^{12,13}

In this study there was a six-fold higher gallbladder-related conversion rate of LC after ERCP compared with LC for uncomplicated cholelithiasis. Even although this difference fails to reach statistical significance, it does show a strong trend ($P = 0.055$). Also, conversion was associated with a significantly higher complication rate compared with a laparoscopically completed cholecystectomy. This is in accordance with other studies showing that conversion of a laparoscopic to an open cholecystectomy is associated with increased post-operative pain, pulmonary complications, longer hospital stay and a slower recovery to normal daily activities.^{10,15} Although this higher complication rate may partly be explained by selection bias, i.e. that conversion to an open cholecystectomy indicates more advanced disease. We do believe that conversion must never be an issue when dealing with a difficult LC, as the consequences of bile duct, or other, injuries are very severe. However, a conversion should be avoided as a result of a lack of (laparoscopic) experience of the operating surgeon. In a study of 4139 cholecystectomies by Boddy *et al.*, the authors clearly found fewer conversions and fewer complications if the LC was performed by a surgeon with a specialist interest in upper gastroenterology or hepatopancreaticobiliary surgery.¹⁶

This has also been suggested by Kortram *et al.*, who had found that non-laparoscopic surgeons (i.e. performing <50 laparoscopic procedures annually) have a significantly higher conversion rate when dealing with acute cholecystitis (3.6% versus 15.6%).¹⁷ In this study, the conversion rate was not related to surgeons' experience in LC. Probably the few conversions that occurred combined with the mixed background of this study group make it statistically difficult to show a difference. However, more and more evidence is being presented that complicated cholelithiasis (i.e. cholecystitis and choledocholithiasis) is the terrain of a laparoscopic-skilled hepato-pancreatic-biliary surgeon and we believe the operating room planning should be made more efficient according to this dogma.

Conclusion

A laparoscopic cholecystectomy after ERCP with ES for combined choledochocystolithiasis is a significantly more difficult and prolonged procedure than in uncomplicated gallstone disease with a longer post-operative hospital stay.

Although a higher amount of conversions or complications could not be shown, it does seem justified to have a laparoscopically skilled surgeon perform the laparoscopic cholecystectomy after an endoscopic sphincterotomy.

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Conflicts of interest

None declared.

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