



Original Article

Could cholecystectomy be abandoned after removal of bile duct stones by endoscopic retrograde cholangio-pancreaticography?



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ABSTRACT

Background/objective: The current treatment for choledocholithiasis is endoscopic common bile duct clearance followed by cholecystectomy. However, few studies have investigated whether cholecystectomy is necessary after the endoscopic removal of bile duct stones. This study aimed to determine the rate of patients without symptoms during the follow-up period after endoscopic retrograde cholangiopancreatography (ERCP).

Materials and methods: We retrospectively analyzed data from patients with choledocholithiasis who underwent ERCP from a single centre. The patients were invited to the hospital for evaluation of symptoms during the follow-up period after ERCP. The primary outcome of this study was to determine the rate of patients with symptoms during the follow-up period after ERCP.

Results: A total of 286 patients with a median age of 57 (18–95) years old were included in the study. Of these, 195 patients (68%) remained asymptomatic during the follow-up period of 18 months (1–70) after endoscopic sphincterotomy without cholecystectomy. A total of 75 (50%) out of 151 patients who underwent cholecystectomy reported having symptoms after ERCP. In contrast, 119 (88%) out of 135 patients did not undergo cholecystectomy after the ERCP, remained asymptomatic during a median follow-up period of 43 months (11–70). The estimated 5-year asymptomatic rates of the patients after ERCP were 51% for the whole cohort (n = 286) according to Kaplan–Meier analysis.

Conclusion: Majority of patients with choledocholithiasis who did not undergo cholecystectomy after ERCP were asymptomatic during the follow-up period. Thus, cholecystectomy may be unnecessary after endoscopic sphincterotomy for bile duct stones within a midterm period.

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1. Introduction

Gallstones are a common health problem worldwide. Most gallstones are found in the gallbladder; but sometimes they pass through the cystic duct into the common bile duct and become bile duct stones, resulting in choledocholithiasis.¹ Endoscopic sphincterotomy (ES) is a safe and effective method for managing choledocholithiasis. In major centers, common bile duct clearance is successful in up to 97% of patients, with a procedure-related morbidity and mortality rates of 5.8% and 0.2%, respectively.² Patients who undergo ES for symptomatic common bile duct stones

are usually referred for cholecystectomy.³ Studies have analyzed the timing of the procedure after endoscopic retrograde cholangiopancreatography (ERCP),^{4,5} but rather than timing, cholecystectomy itself after ERCP remains controversial. It is unclear whether cholecystectomy itself is always necessary after endoscopic bile duct stone removal. In general, cholecystectomy after ERCP is very common in clinical practice. However, a few recent studies have showed that cholecystectomy after endoscopic bile duct stone removal could be unnecessary, particularly in patients who remained asymptomatic without cholecystectomy after ERCP or those who could not be operated on due to comorbidities. This study aimed to assess whether cholecystectomy may not be necessary after endoscopic bile duct stone removal.

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2. Material and methods

2.1. Patients

We retrospectively analyzed the records of patients who underwent ERCP in the Marmara University General Surgery Clinic between January 2012 and October 2015. We enrolled patients who met the following criteria¹: presence of common bile duct stones,² patients who underwent ERCP without prior cholecystectomy,³ the ERCP procedure attained complete clearance of common bile duct stones, and⁴ age older than 18 years at the initial ERCP. We excluded the following patients from the study¹: Patients who underwent cholecystectomy before the ERCP,² other biliary pathologies associated with common bile duct stones, and³ incomplete clearance of common bile duct stones. In our clinic, cholecystectomy is routinely recommended by the ERCP team for all patients after ERCP, except those who are unfit for surgery or very elderly patients.

Data regarding demographics, comorbidities, history of previous abdominal surgeries, ultrasound (USG) and magnetic resonance cholangiopancreatography (MRCP) findings before ERCP were retrospectively analyzed. The patients were invited to the hospital for evaluation of symptoms during the follow-up period after ERCP. The Research Ethics Committee approved the study, and all patients provided written informed consent before participating. The primary outcome of this study was to determine the rate of asymptomatic patients during the follow-up period after ERCP. Secondary outcomes included the assessment of factors which may be related to symptoms during follow-ups.

2.2. Statistical analysis

We performed statistical analyses using the Statistical Package for Social Sciences for Windows version 23 (SPSS Inc; Chicago, IL, USA). Two-tailed Chi-square or Fisher exact tests were used to compare categorical variables. Independent 2-sample t-test or Mann Whitney U-test was used to compare ordinal data. Symptom-free survival curves were created using the Kaplan–Meier product-limit method and compared using the log-rank test. Wilcoxon t and McNemar's tests were used to compare the pre- and post-procedure parameters of groups of patients. *P* values less than 0.05 were considered statistically significant.

3. Results

A total of 544 patients who underwent ERCP for choledocholithiasis between January 2012 and October 2015 in one center were analyzed. We excluded 26 patients from the study as follows: 15 patients with retained common bile duct stones, 4 patients with biliary stricture, 3 patients with pancreatic cancer, 2 patients with cirrhosis, and 2 patients with common bile duct cysts. We also excluded 151 patients with a previous history of cholecystectomy before ERCP and 81 patients who were lost to follow-up (Fig. 1). Finally, 286 patients were included in the study. Their median age was 57 years (18–95), and 164 patients (57%) were women. Among them, 151 patients (53%) underwent cholecystectomy after the ERCP, while 135 (47%) patients did not. Moreover, 195 (68%) patients remained asymptomatic during a median follow-up period of 18 months (1–70) after ERCP without cholecystectomy or up until cholecystectomy was eventually performed. The follow-up period of patients who underwent cholecystectomy was described as the time between the ERCP and the cholecystectomy. Among 151 patients who underwent cholecystectomy after the ERCP, 75 (50%) were asymptomatic during follow-up. On the other hand, among 135 patients who still had a gallbladder in situ after the ERCP, 119 (88%) remained asymptomatic during a median follow-up period of 43 months (11–70) (Table 1). The

estimated 5-year asymptomatic rates of patients after ERCP were 51% for the whole cohort according to the Kaplan–Meier analysis (Fig. 2). The estimated 5-year asymptomatic rate was significantly higher for those with a gallbladder in situ than that of those who underwent cholecystectomy (73% and 7% respectively, $p < 0.0001$, Tables 1 and 2) (Fig. 3). Recurrent bile duct stones were observed only in 4 (2%) patients after ES, and these were all in the gallbladder in situ group (Table 1). These recurrent bile duct stones were detected because the first 3 patients were symptomatic 29, 53, and 55 months after ERCP, respectively, while this was an incidental finding (by MRCP) after 62 months in the 4th patient. Table 2 shows the patients' demographics and a comparison of patients who underwent cholecystectomy with those who did not. The median age was significantly lower in patients who underwent cholecystectomy (44 years, 18–88) than in those who did not (67 years, 19–95) ($p < 0.0001$). The rate of comorbidities was significantly lower in the patients who underwent cholecystectomy (55 patients, 36%) than in those who did not (88 patients, 65%) ($p < 0.0001$) (Table 2). Cox analysis showed that no comorbidity, age less than 65, and the presence of gallbladder stones were all risk factors predicting future cholecystectomy after ERCP in this study (Table 3).

4. Discussion

We included 286 patients in this study, of which 195 (68%) remained asymptomatic during a median follow-up period of 18 months (1–70) after ERCP without cholecystectomy or up until cholecystectomy was performed. Furthermore, among 151 patients who underwent cholecystectomy after the ERCP, 75 (50%) remained asymptomatic during follow-up. Currently, cholecystectomy is routinely performed after ERCP to avoid the recurrence of symptoms (6). However, few studies have assessed the need of cholecystectomy after ERCP, and thus the issue remains controversial. This study tackled this issue by presenting data from a single center with high volume of patients. Previous studies have evaluated the need of surgery in elderly patients who could not undergo cholecystectomy due to comorbidities.^{7–11} However, we evaluated all patients after ERCP regardless of age and comorbidities. Most of the late cholecystectomies in this study are due to patient preference, unavailability of our medical institution due to heavy patient load, or the recommendation of surgeons to wait further after ERCP. ES and ductal clearance of the stones followed by cholecystectomy is currently the most common treatment for choledocholithiasis.^{6,12} However, this approach is still controversial since few studies have shown that cholecystectomy is not absolutely necessary after ES. Furthermore, this issue is not extensively discussed in existing literature. While the majority of authors recommend routine cholecystectomy for all patients after ES,¹³ others recommend only for patients with gallstones.¹⁰ The authors who recommend cholecystectomy believe that cholecystectomy after ES can reduce the recurrence of biliary complications,⁸ but other authors disagree with this.¹⁴ Previous reports claim that cholecystectomy may not be performed for elderly patients who underwent ES for choledocholithiasis and not fit for surgery.^{15,16} However, in this study there was 39 young (<50 years old) patients still had a gallbladder in situ after ES. In this study, we found that 88% of patients that did not undergo cholecystectomy remained asymptomatic during the long follow-up period of 43 months (11–70). On the other hand, a randomized controlled study by Boerma et al. found that approximately 47% of patients developed at least 1 biliary symptom during a median of 30 months (15–67) following ERCP without cholecystectomy, but this rate was only 2% in cholecystectomy group.¹⁰ In our study, 32% of patients developed at least 1 biliary symptom during a median of 18 (1–70) months following ERCP without cholecystectomy. We think that this relatively lower rate of

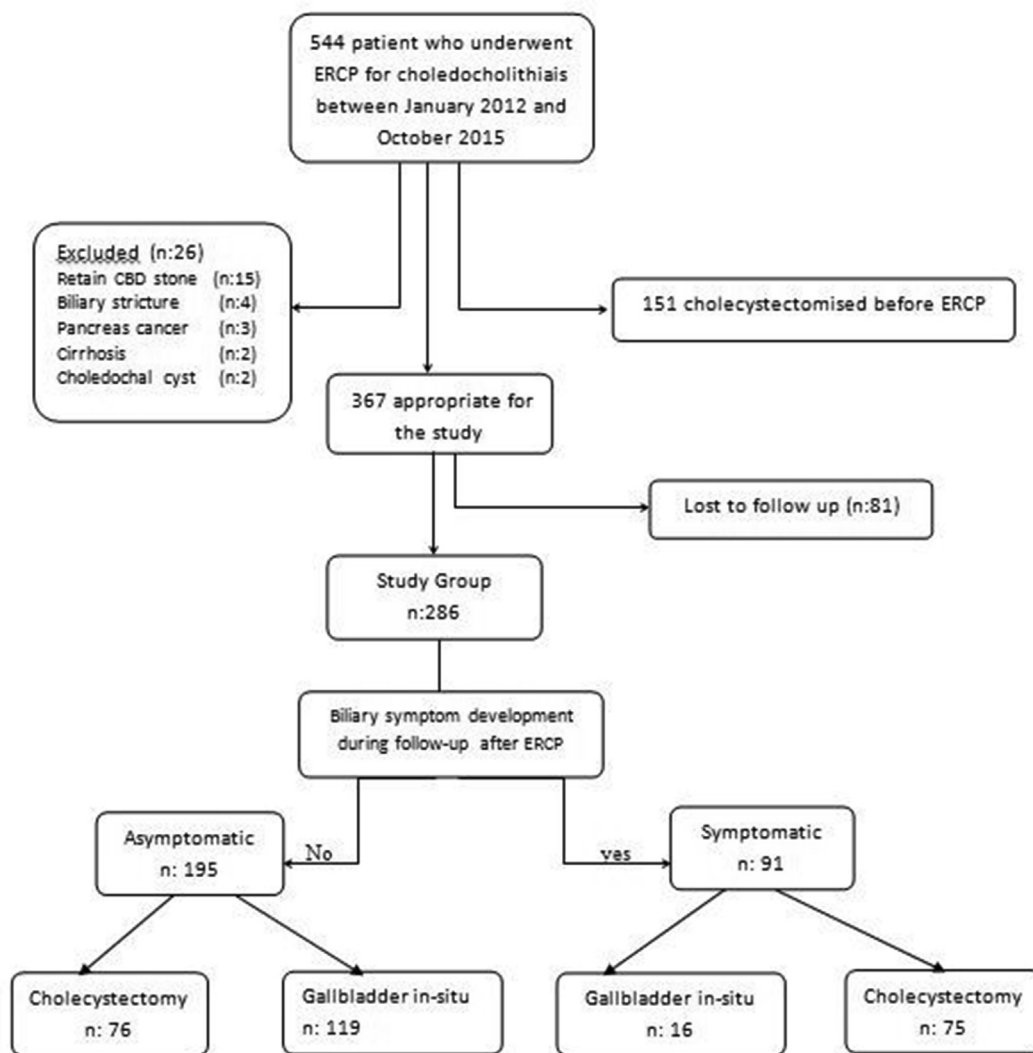


Fig. 1. Flowchart of patients.

Table 1
Outcomes during follow-up after ERCP (n = 286).

	All patients (n = 286)	Patients who underwent cholecystectomy (n = 151)	Patients with gallbladder in situ (n = 135)
Patients described complaints on follow-up after ERCP	91 (32%)	75 (50%)	16 (12%)
Biliary colic	80 (27%)	67 (42%)	13 (10%)
Acute cholecystitis	13 (5%)	13 (9%)	0 (0%)
Recurrent bile duct stone	4 (2%)	0 (0%)	4 (3%)
Jaundice	2 (1%)	2 (1%)	0 (0%)
Pancreatitis	0 (0%)	0 (0%)	0 (0%)
Cholangitis	2 (1%)	1 (1%)	1 (1%)
estimated 5-year asymptomatic rates after ERCP (%)	71%	7%	73%
Follow-up (median)	18(1–70) months	2 (1–64) months	43 (11–70) months

symptoms in our study is because we included patients without gallbladder stones in our study, but Boerma et al. only studied patients with gallbladder stones. In a cohort study by Schreurs et al.⁹ 27% of patients who did not undergo cholecystectomy developed biliary symptoms during a median follow-up of 74 (1–145) months, while this rate was found to be 7.6% in the cholecystectomy group. However, recent studies have shown no significant difference in the rate of recurrent choledocholithiasis and

cholangitis ERCP with and without cholecystectomy.^{9,17} In this study, only 1% and 3% of patients developed cholangitis and recurrent choledocholithiasis respectively following ERCP without cholecystectomy. In long-term follow-up studies after ES, the rates of recurrent choledocholithiasis range from 3.2% to 22.3%, while the rates of late biliary complications range from 5.8% to 22%.⁷ Similarly, in this study, recurrent common bile duct stones developed in 3% of patients, while cholangitis was observed in only 1%.

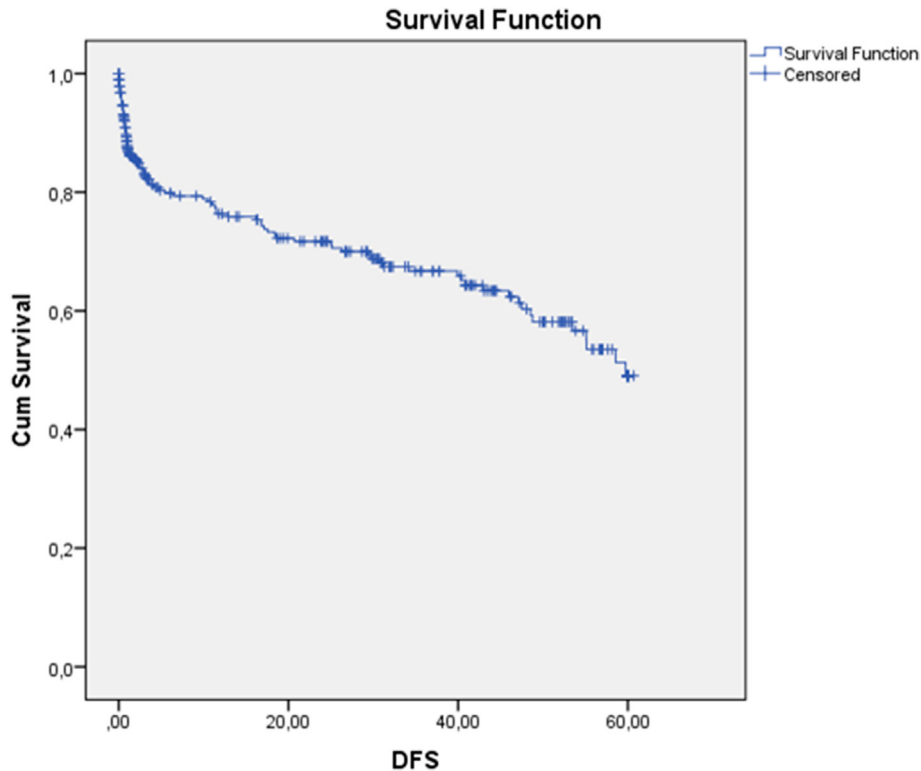


Fig. 2. The estimated 5-year asymptomatic rates of the whole cohort according to Kaplan–Meier analysis.

Table 2

Patients' characteristics and comparison between patients who underwent cholecystectomy and those who did not.

	All patients n = 286	Cholecystectomy after ERCP n = 151	Gallbladder In situ group n = 135	P value
Age (median in years)	57 (18–95)	49 (18–88)	67 (19–95)	<0.0001
Gender				0.09
Female	164 (57%)	96 (64%)	68 (50%)	
Male	122 (43%)	55 (36%)	67 (50%)	
Percentage of patients with comorbidities	142 (50%)	54 (36%)	88 (65%)	<0.0001
HT	81 (28%)	32 (21%)	49 (36%)	0.004
DM	48 (17%)	17 (11%)	31 (23%)	0.008
CAD/CHF	41 (14%)	10 (7%)	31 (23%)	<0.0001
COPD	19 (7%)	7(5%)	12 (9%)	0.13
CRF	3 (1%)	0 (0%)	3(2%)	0.1
Laparotomy	62 (22%)	39 (26%)	23 (17%)	0.1
Complaints related to choledocholithiasis				
Pain	197 (69%)	101 (67%)	96 (71%)	0.9
Nausea-vomiting	34 (12%)	20 (13%)	14 (10%)	0.2
Jaundice	51 (18%)	29(19%)	22 (16%)	0.2
Cholecystitis	4 (1%)	1 (0.7%)	3(2%)	0.6
Cholangitis	14 (5%)	4 (3%)	10 (7%)	0.1
Pancreatitis	29 (10%)	14 (9%)	15 (11%)	0.9
estimated 5-year asymptomatic time after ERCP (mean ± sd, months)	31 ± 2	15 ± 2	58 ± 1	<0.0001

HT: Hypertension.

DM: Diabetes mellitus.

CAD/CHF:Coronary artery disease/Chronic heart failure.

COPD: Chronic obstructive pulmonary disease.

CRF: Chronic renal failure

sd:standart deviation.

Pancreatitis did not occur during follow-up in any case without cholecystectomy, including the patients who experienced acute pancreatitis before ERCP. A previous study Lau et al. showed that pancreatitis did not occur within 36 months of follow-up after ERCP without cholecystectomy.⁸ This was thought to be because sphincterotomy decreased the risk of pancreatic canal obstruction

and biliary reflux. Some studies have shown that patients with gallbladder stones need cholecystectomy after ERCP.^{18–20} However, Kwon SK et.al¹¹ found no significant difference between patients with and without gallbladder stones in terms of recurrent biliary symptoms after ERCP, and this also held true for our study. Therefore, some authors believe that cholecystectomy is unnecessary for

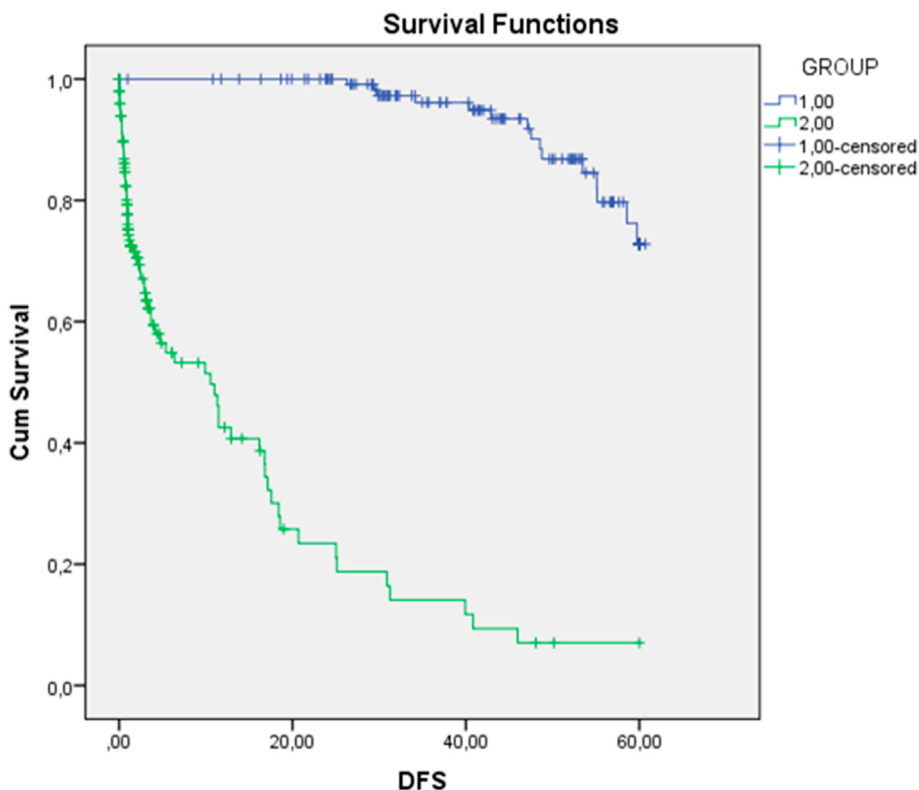


Fig. 3. The 5-year symptom-free rate was significantly higher in those who underwent ERCP without cholecystectomy (Group 1) compared to those with cholecystectomy (Group 2).

Table 3
Cox analysis for risk factors predicting future cholecystectomy after ERCP.

Risk factors predicting future cholecystectomy	Wald	df	Sig.	Exp(B)	95,0% CI for Exp(B)	
					Lower	Upper
No comorbidity	8,272	1	,004	1,730	1,191	2,513
History of cholecystitis	,744	2	,689			
History of pancreatitis	2,369	2	,306			
Gallbladder stone	7,727	2	,021			
Age<65	13,760	1	,000	2,205	1,452	3,347

elderly patients after ES and common bile duct clearance, including those with gallbladder stones. Others believe that cholecystectomy is necessary after ERCP in cases with a history of cholecystitis, cholangitis, or pancreatitis.^{7,21} Among 286 patients, acute cholecystitis was described in only 13 (5%) of patients, all of which underwent ERCP with cholecystectomy (Table 1). Acute acalculous cholecystitis is defined as an acute inflammation of the gallbladder in the absence of gallstones. Patients are usually critically ill, with atherosclerotic heart disease, recent trauma, burn injury, surgery, or hemodynamic instability.²² No cases of acute acalculous cholecystitis was described in this cohort. However, this may be observed in the future with patients who did not undergo cholecystectomy and are still under follow-up, particularly those who are hospitalized for other serious illnesses, such as trauma, burns, or major surgery. Fig. 3 illustrates that the 5-year symptom-free rate was significantly higher in patients who underwent ERCP without cholecystectomy. This result is expected since symptomatic patients will seek consult and therefore undergo cholecystectomy. Based on the results of this study, cholecystectomy is recommended for patients who remain symptomatic after ERCP, while this can be forgone in asymptomatic patients.

This study also has several limitations, such as the retrospective design, relatively high number of patients lost to follow-up, lack of data regarding previous ERCP procedures, and the lack of a subgroup analysis.

5. Conclusion

This study showed that majority of patients with choledocholithiasis who underwent ERCP without cholecystectomy remained asymptomatic during a midterm period of follow-up. Thus, cholecystectomy may be unnecessary after endoscopic sphincterotomy for bile duct stones within a midterm period.

Authors' contributions

Sakir Karpuz: literature search, figures, study design, data collection, data analysis, data interpretation, writing.
Wafi Attaallah: literature search, figures, study design, data collection, data analysis, data interpretation, writing.

Declaration of competing interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. Tazuma S. Gallstone disease: epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic). *Best Pract Res Clin Gastroenterol.* 2006;20:1075–1083.
2. Cotton PB, Geenen JE, Sherman S, et al. Endoscopic sphincterotomy for stones by experts is safe, even in younger patients with normal ducts. *Ann Surg.* 1998;227:201–204.
3. Bostanci EB, Ercan M, Ozer I, Teke Z, Parlak E, Akoglu M. Timing of elective laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreatography with sphincterotomy: a prospective observational study of 308 patients. *Langenbeck's Arch Surg.* 2010;395:661–666.
4. Salman B, Yilmaz U, Kerem M, et al. The timing of laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreatography in cholelithiasis coexisting with choledocholithiasis. *J Hepato-Biliary-Pancreatic Surg.* 2009;16:832–836.
5. Schiphorst AH, Besselink MG, Boerma D, et al. Timing of cholecystectomy after endoscopic sphincterotomy for common bile duct stones. *Surg Endosc.* 2008;22:2046–2050.
6. Pham TH, Hunter JG. Gallbladder and the extrahepatic biliary system. In: *Schwartz's Principles of Surgery.* Brunicaudi FC; 2015:1309–1340.
7. Kageoka M, Watanabe F, Maruyama Y, et al. Long-term prognosis of patients after endoscopic sphincterotomy for choledocholithiasis. *Dig Endosc.* 2009;21:170–175.
8. Lau JY, Leow CK, Fung TM, et al. Cholecystectomy or gallbladder in situ after endoscopic sphincterotomy and bile duct stone removal in Chinese patients. *Gastroenterology.* 2006;130:96–103.
9. Schreurs WH, Vles WJ, Stuijbergen WH, Oostvogel HJ. Endoscopic management of common bile duct stones leaving the gallbladder in situ. A cohort study with long-term follow-up. *Dig Surg.* 2004;21:60–64.
10. Boerma D, Rauws EA, Keulemans YC, et al. Wait-and-see policy or laparoscopic cholecystectomy after endoscopic sphincterotomy for bile-duct stones: a randomised trial. *Lancet.* 2002;360:761–765.
11. Kwon SK, Lee BS, Kim NJ, et al. Is cholecystectomy necessary after ERCP for bile duct stones in patients with gallbladder in situ? *Kor J Intern Med.* 2001;16:254–259.
12. Jackson PG, Evans SRT. Biliary system. In: *Sabiston Textbook of Surgery.* C. Townsend Elsevier; 2017:1494–1496.
13. Hansell DT, Millar MA, Murray WR, Gray GR, Gillespie G. Endoscopic sphincterotomy for bile duct stones in patients with intact gallbladders. *Br J Surg.* 1989;76:856–858.
14. Lai KH, Lin LF, Lo GH, et al. Does cholecystectomy after endoscopic sphincterotomy prevent the recurrence of biliary complications? *Gastrointest Endosc.* 1999;49:483–487.
15. Martin DF, Tweedle DE. Endoscopic management of common duct stones without cholecystectomy. *Br J Surg.* 1987;74:209–211.
16. Neoptolemos JP, Carr-Locke DL, Fraser I, Fossard DP. The management of common bile duct calculi by endoscopic sphincterotomy in patients with gallbladders in situ. *Br J Surg.* 1984;71:69–71.
17. Yasui T, Takahata S, Kono H, et al. Is cholecystectomy necessary after endoscopic treatment of bile duct stones in patients older than 80 years of age? *J Gastroenterol.* 2012;47:65–70.
18. Hammarstrom LE, Holmin T, Stridbeck H. Endoscopic treatment of bile duct calculi in patients with gallbladder in situ: long-term outcome and factors. *Scand J Gastroenterol.* 1996;31:294–301.
19. Kullman E, Borch K, Dahlin LG, Liedberg G. Long-term follow-up of patients with gallbladder in situ after endoscopic sphincterotomy for choledocholithiasis. *Eur J Surg.* 1991;157:131–135.
20. Sharma BC, Agarwal DK, Baijal SS, Negi TS, Choudhuri G, Saraswat VA. Effect of endoscopic sphincterotomy on gall bladder bile lithogenicity and motility. *Cut.* 1998;42:288–292.
21. Himel HS. Role of endoscopic sphincterotomy alone in patients with choledocholithiasis and cholelithiasis. *Canadian J Surg.* 1996;39:225–228.
22. Owen CC, Jain R. Acute acalculous cholecystitis. *Curr Treat Options Gastroenterol.* 2005 Apr;8(2):99–104.