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Is cholecystectomy necessary after endoscopic treatment of bile duct stones in patients older than 80 years of age?

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Author contributions

T.Y. and S.T. interpreted data. T.Y wrote the manuscript. T.Y., H.K, Y.N., Y.M., K.T. and Y.S. collected and assembled the data. S.T., O.T., M.N. and M.T. supervised the project. M.T. made the final approval of the article.

Take-home Message

Patients with cholecystocholedocholithiasis are generally referred to cholecystectomy after endoscopic sphincterotomy and common bile duct clearance. But there is no clear guiding principle in very elderly patients. In this study cholecystectomy decreased biliary events and mortality in young patients, but not in very elderly patients (>/= 80 years). Cholecystecomy after ES for CBDS should not be recommended in very elderly patients.

Acronyms

CBD; common bile duct, CBDS; CBD stone

Keywords: endoscopic sphincterotomy, choledocholithiasis, cholecystolithiasis, elderly, cholecystectomy

Abstract

Background: Patients with cholecystocholedocholithiasis are generally referred to cholecystectomy after endoscopic sphincterotomy (ES) and common bile duct clearance. However, we often have a conflict whether cholecystectomy is necessary in very elderly patients with comorbid diseases.

Objective: To assess whether cholecystectomy in elderly patients is justified after ES.

Design: Multicenter retrospective study.

Setting: Department of Surgery and Oncology, Kyushu University and its affiliated hospitals.

Patients: Patients with cholecystocholedocholithiasis who underwent ES and stone extraction and were followed-up for more than 10 years were retrospectively reviewed.

Main outcome measurements: We divided these patients into two groups; elderly group (equal to or more than 80 years old) and young group (less than 80 years old) and compared late biliary complications and mortality.

Results: The 5-year cumulative incidence of overall biliary complications was significantly lower in cholecystectomized patients than in patients with gallbladder in situ in young group (6.1% vs. 15.6%, p=0.0037), but not different in elderly group (8.3% vs. 7.4%, p=0.92). When each complication was evaluated separately, the rate of

recurrent common bile duct stones (CBDS) was not different, but that of acute cholecystitis was significantly lower in elderly group than in young group (4.1% vs. 16.0%, p=0.011).

Conclusions: In very elderly patients the incidence of acute cholecystitis is low even when the gallbladder is preserved after endoscopic treatment of CBDS, with a similar risk of CBDS recurrence and a lower risk of acute cholecystitis. Thus it may not be necessary to recommend cholecystecomy after ES for CBDS in very elderly patients.

INTRODUCTION

Endoscopic sphincterotomy (ES) first reported in 1974 has gained wide acceptance as a safe and effective treatment for common bile duct stones (CBDS) with continuous progress in the techniques. On the other hand, laparoscopic cholecystectomy (LC) introduced in 1987 has been recognized as a standard procedure for cholecystolithiasis due to its advantages over open cholecystectomy[1]. The indication for cholecystectomy after ES and common bile duct clearance is frequently debated. We previously reported that an acalculous gallbladder preserved after ES did not cause major complications[2], and thus preserving an acalculous gallbladder after ES has become a standard practice[3]. In patients with cholecystocholedocholithiasis, however, untreated gallbladder stones are generally thought to be a risk of biliary complications after ES like acute cholecystitis or migration into the CBD; therefore, some authors recommend cholecystectomy because of the high risk of recurrent biliary symptoms[3-6]. In two recent prospective studies cholecystectomy after ES was justified, because patients with gallbladder in situ had late biliary complications more frequently than cholecystomized patients [7, 8]. On the other hand, some retrospective studies suggested that routine prophylactic cholecystectomy is not essential after ES, because the risk of developing biliary symptoms was equal to that of the normal population with silent stones [9-11]. Thus,

it is still controversial whether a calculous gallbladder should be removed after ES and bile duct clearance. Furthermore, we often have a conflict whether cholecystectomy is necessary in very elderly patients with comorbid diseases. In several studies cholecystectomy after ES in very elderly patient is not recommended, but there is no clear guiding principle [8]. In this study we assessed whether cholecystectomy after ES in elderly patient is justified from the viewpoint of long term follow-up data more than 10 years after ES.

PATIENTS AND METHODS

From 1974 to May, 2008, 1728 patients underwent ES for removal of CBD stones in Department of Surgery and Oncology, Kyushu University, Fukuoka, Japan and its affiliated hospitals. Long term follow-up data more than ten years were obtained from 1060 patients. Patient with history of hepatolithiasis, biliary tract surgery or malignant diseases were excluded. Three hundred and twenty-seven patients with cholecystocholedocholithiasis were found in this study population. We divided these patients into two groups; elderly group (equal to or more than 80 years old; 77 patients) and young group (less than 80 years old; 250 patients).

Follow-up data were obtained from outpatient records, by mail, telephone call, and /

or interview, or by ERCP when indicated. All patients were asked about the presence or absence of abdominal pain, fever, jaundice and the time of the occurrence of these symptoms if any. Data on patients who died during the follow-up were included in the analysis, because we thought that it was important to analyze whether their death was related to ES and/or any biliary disease.

Data are expressed as the mean ± SD or median with range. Categorical parameters were compared using the χ^2 or Fisher's exact test when appropriate, and continuous variables were compared with Student's *t* test. $P < 0.05$ was considered statistically significant.

RESULTS

Characteristics of patients

Median overall follow-up duration in young group was significantly longer than elderly group (144.1 months vs. 76.3 months, $p<0.001$, TABLE 1.). The mean age at ES was 63.7±12 in young group and 84.5±3.5 in elderly group. The number of patients who died during the course of follow-up was significantly larger in elderly group (58 patients, 75.3%) than in young group (91 patients, 36.4%, $p<0.001$). Patients in elderly group had a tendency to have lager primary CBDS than in young group (9.9±6.5mm vs.

14.8±9.4mm, $p<0.001$). The frequency of bilirubinate stone was higher in elderly group than in young group (74.2% vs. 90.2%, $p<0.001$). Patients' backgrounds including the gender, number of CBDS, presence or absence of duodenal diverticulum, choledocoduodenal fistula, the use of precut and early complications was not significantly different between two groups.

Cumulative incidence of late biliary complications

The 5-year cumulative incidence of overall biliary complications was significantly lower in cholecystectomized patients than in patient with gallbladder in situ (6.2% vs. 12.0%, $p=0.0032$, Figure 1.). Examining this result from the viewpoint of age, the 5-year cumulative incidence of overall biliary complications was significantly lower in cholecystectomized patients than in patients with gallbladder in situ in young group (6.1% vs. 15.6%, $p=0.0037$, Figure 2. A), but not different in elderly group (8.3% vs. 7.4%, $p=0.92$, Figure 2. B).

Details of late biliary complications

To investigate the difference in the incidence of overall biliary complications between young group and elderly group, we analyzed the details of late biliary complications (TABLE 2.). The frequency of acute cholecystitis in patients with gallbladder in situ was 11.7% overall, and was significantly lower in elderly group than

in young group (3.2% vs. 18.7%, $p<0.001$). Recurrence of CBDS was noticed in 19 patients (5.8%) overall. One patient in young group developed acute cholangitis. Common bile duct cancer developed in one patient in young group 166 months after ES. We did not have any patients with acute pancreatitis or liver abscess developing late after ES.

Cumulative incidence of acute cholecystitis and recurrence of CBDS

The most of the late biliary complications were acute cholecystitis and recurrence of CBDS. Therefore we analyzed the incidence of recurrence of CBDS and acute cholecystitis in two groups. The 5-year incidence of recurrent CBDS was not different between two groups (4.7% in young group vs. 4.3% in elderly group, $p=0.71$). The 5-year incidence of acute cholecystits was significantly lower in elderly group than in young group (4.1% vs. 16.0%, $p=0.011$).

Cumulative probability of death in young group and elderly group

In a recent prospective randomized study, Lau et al. [8] demonstrated that late mortality was higher in a group with gallbladder in situ than in a post cholecystectomy group. Therefore, we investigated whether cholecystectomy after ES and common bile duct clearance improves the mortality after ES in both groups. The 5-year cumulative mortality was significantly lower in cholecystectomized patients than in patients with

gallbladder in situ in young group (11.5% vs. 24.5%, p=0.0004, Figure 3. A), but not different in elderly group (36.0% vs. 50.2%, p=0.185, Figure 3. B). Most causes of death were not associated with biliary sepsis except for only one death in elderly group directly attributable to acute cholecystits.

DISCUSSION

The present study of the validity of cholecystectomy after ES for CBDS in very elderly patients demonstrated that (1) the cumulative incidence of overall biliary complications was significantly lower in cholecystectomized patients than in patients with gallbladder in situ, (2) the cumulative incidence of overall biliary complications in young group was significantly lower in cholecystectomized patients than in patient with gallbladder in situ but no difference was seen in elderly group, and (3) cumulative mortality was significantly lower in cholecystectomized patients than in patients with gallbladder in situ in young group, but not different in elderly group.

In two randomized comparative trials between ES followed by cholecystectomy and ES alone in patients with cholecystocholedocholithiasis, the incidence of late biliary complication after ES was significantly higher in patients with gallbladder in situ than in cholecystectomized patients [7, 8]. In those studies the rates of biliary complications in

patients with gallbladder in situ was 47% and 24%. Those were higher than that in our study (12.0%). This discrepancy can be explained by definition of biliary complications. We excluded biliary pain from biliary complication because it might arise from the digestive tract other than the biliary tree, cardiovascular system, urinary tract, or musculoskeletal system.

Our results indicate that cholecystectomy after ES reduces late biliary complication and should be recommended in patients of all ages. Although there are some reports showing that the severity of gallbladder disease, rather than the chronologic age influences perioperative outcomes, and even the elderly tolerate biliary tract operations quite well [12, 13], many investigators do not recommend cholecystectomy in elderly patients due to their comorbid diseases and low performance status [8, 9]. In this study we assessed whether cholecystectomy after ES makes benefit for elderly patients in view of the prophylactic effect on late biliary complications and mortality. Surprisingly, although cholecystectomy after ES significantly prevents late biliary complications in young group, elderly patients did not receive a benefit of cholecystectomy. To disclose this difference between young and elderly groups, we analyzed the incidence of CBDS recurrence and acute cholecystitis which account for the majority of late biliary complications. In this study the incidence of CBDS recurrence in cholecystectomized

patients was not significantly different from patients with gallbladder in situ. This might be because the incidence of recurrent CBDS was relatively low and number of patients was small to investigate the impact of cholecystectomy on recurrence of CBDS. In young group the rate of cholesterol stones was higher and the size of CBDSs was smaller than in elderly group. These results indicate that the proportion of secondary CBDSs migrated from the gallbladder is estimated to be higher than that in elderly. That might be one of the reasons why cholecystectomy after ES prevents recurrence of CBDS only in young group. The rate of acute cholecystits, the other main late biliary complication, was significantly lower in elderly group in this study. Although we examined details of patients' data and previous literatures, we could not find the reason for the low incidence of acute cholecystits in this very elderly group. In very elderly patients, older than 80 years, the gallbladder contractile function might have declined and might rarely develop acute cholecystitis. Iso et al.[14] reported that the percentage of individuals favoring fatty food, known as a trigger of developing acute cholecystitis, decreased substantially with age. This may be one of possible explanations for the low frequency of acute cholecystitis in elderly group.

In a recent randomized study the cumulative mortality rate at 5 years was reported to be higher in a gallbladder in situ group than in a cholecystectomy group (21% vs. 9.2%,

log-rank, p=0.1) [8]. In the present study the cumulative mortality rate in young group was significantly higher in patients with gallbladder in situ than in cholecystectomized patients, but no significant difference was seen in elderly group. Although the poorer prognosis in patients with gallbladder in situ was expected to be caused by the high rate of late biliary complications, most causes of death were not associated with biliary sepsis. Although our study was a retrospective study and might have selection bias, this result was consistent with that of a previous randomized prospective study [8]. There may be some unknown causal relationship between cholecystectomy and prognosis, but it must await future study.

In conclusion, in very elderly patients the incidence of acute cholecystitis is low even when the gallbladder is preserved after endoscopic treatment of CBDS and preserving the gallbladder does not increase the risk of CBDS recurrence. Furthermore, cholecystectomy does not decrease biliary events and mortality in very elderly patients. Cholecystecomy after ES for CBDS should not be recommended in very elderly patients.

REFERENCES

1. Dubois F, Icard P, Berthelot G, et al. Coelioscopic cholecystectomy. Preliminary report of 36 cases. Ann Surg 1990;211:60-2.
2. Tanaka M, Ikeda S, Yoshimoto H, et al. The long-term fate of the gallbladder after endoscopic sphincterotomy. Complete follow-up study of 122 patients. Am J Surg 1987;154:505-9.
3. Kageoka M, Watanabe F, Maruyama Y, et al. Long-term prognosis of patients after endoscopic sphincterotomy for choledocholithiasis. Dig Endosc 2009;21:170-5.
4. Pereira-Lima JC, Jakobs R, Winter UH, et al. Long-term results (7 to 10 years) of endoscopic papillotomy for choledocholithiasis. Multivariate analysis of prognostic factors for the recurrence of biliary symptoms. Gastrointest Endosc 1998;48:457-64.
5. Sanjay P, Yeeting S, Whigham C, et al. Endoscopic sphincterotomy and interval cholecystectomy are reasonable alternatives to index cholecystectomy in severe acute gallstone pancreatitis (GSP). Surg Endosc 2008;22:1832-7.
6. Lee KM, Paik CN, Chung WC, et al. Risk factors for cholecystectomy in patients with gallbladder stones after endoscopic clearance of common bile duct stones. Surg Endosc 2009;23:1713-9.
7. 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;360:761-5.
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, Stuifbergen WH, et al. Endoscopic management of common bile duct stones leaving the gallbladder in situ. A cohort study with long-term follow-up. Dig Surg 2004;21:60-4; discussion 5.
10. Hammarstrom LE, Holmin T and 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.
11. Kwon SK, Lee BS, Kim NJ, et al. Is cholecystectomy necessary after ERCP for bile duct stones in patients with gallbladder in situ? Korean J Intern Med 2001;16:254-9.
12. Kim HO, Yun JW, Shin JH, et al. Outcome of laparoscopic cholecystectomy is not influenced by chronological age in the elderly. World J Gastroenterol 2009;15:722-6.
13. Pigott JP and Williams GB. Cholecystectomy in the elderly. Am J Surg 1988;155:408-10.

14. Iso H, Date C, Noda H, et al. Frequency of food intake and estimated nutrient intake among men and women: the JACC Study. J Epidemiol 2005;15 Suppl 1:S24-42.

FIGURE LEGENDS

Figure 1. Cumulative incidence of overall biliary complications

Kaplan–Meier estimates of the likelihood that overall biliary complications would occur

cholecystomized patients, solid line; patients with gallbladder-in-situ, dotted line

Figure 2. Cumulative incidence of overall biliary complications in young group and elderly group

Kaplan–Meier estimates of the likelihood that overall biliary complications would occur

A) young group, B) elderly group

cholecystomized patients, solid line; patients with gallbladder-in-situ, dotted line

Figure 3. Cumulative mortality in young group and elderly group

Kaplan–Meier estimates of the likelihood that death would occur

A) young group, B) elderly group

cholecystomized patients, solid line; patients with gallbladder-in-situ, dotted line

TABLE 1. Characteristics of patients

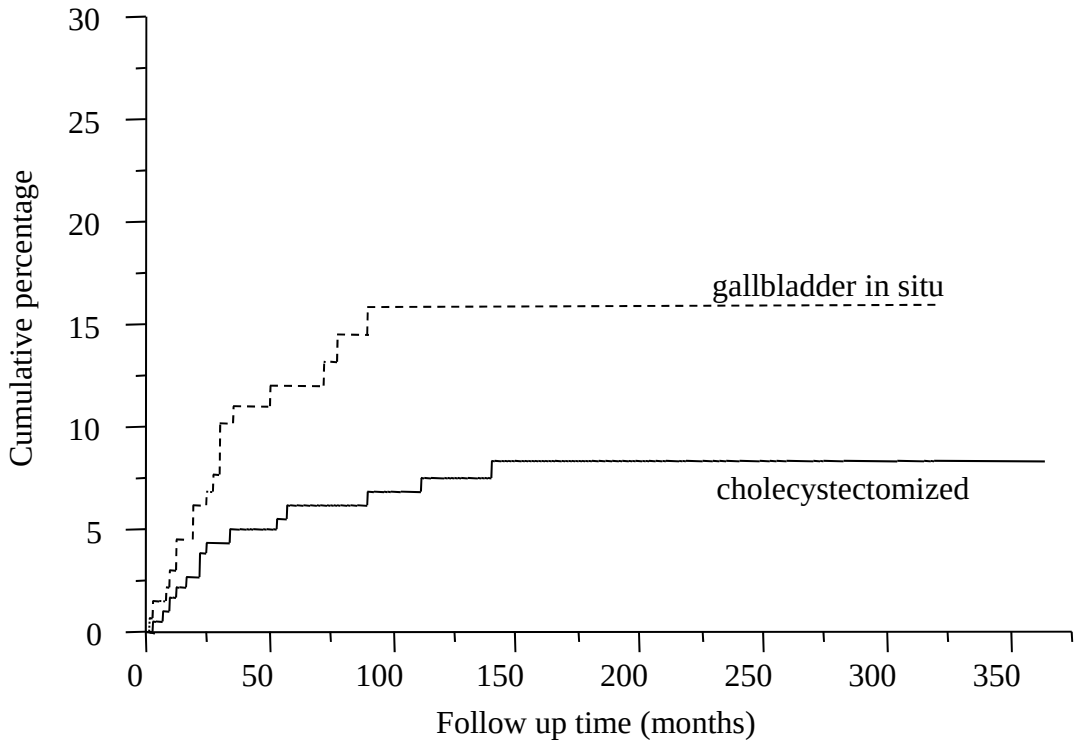
		Young group n=250	Elderly group n=77	*p* value
Age (year±SD)		63.7±12	84.5±3.5	<0.001
Sex (ratio)	Male/Female	134/116 (1.2:1)	36/41 (1:1.1)	0.29
Follow-up duration (month±SD)		144.1±74.6	76.3±55.9	<0.001
Death during follow-up (%)		91 (36.4)	58 (75.3)	<0.001
Number of CBDS (ratio)	Single/Multiple	150/100 (1.5:1)	46/31 (1.5:1)	0.97
Size of CBDS (mm)		9.9±6.5	14.8±9.4	<0.001
Type of primary CBDS (ratio)	Cholesterol/Bilirubinate	48/138 (1:2.9)	5/46 (1:9.2)	0.015
Diverticulum (%)		92/234 (39.3)	34/71 (47.9)	0.20
Choledocoduodenal fistula (%)		9/226 (4.0)	4/68 (5.9)	0.50
Diameter of CBD (mm±SD)		13.1±5.6	14.0±4.4	0.085
Precut (%)		20 (8.0)	4 (5.2)	0.41
Early complication (%)	Total	21 (8.4)	4 (3.9)	0.19
	Bleeding	5 (2.0)	2 (2.6)	0.75
	Acute pancreatitis	8 (3.2)	1 (1.3)	0.37
	Acute cholangitis	5 (2.0)	0 (0.0)	0.21

CBD; common bile duct, CBDS; CBD stone

TABLE 2. Details of late complication

	Total n=327	Young group n=250	Elderly group n=77	*p* value
Total late complications (%)	32 (9.8)	27 (10.8)	5 (6.5)	0.27
Acute cholecystitis (%)	16/137 (11.7)	14/75 (18.7)	2/62 (3.2)	<0.001
Recurrence of CBDS (%)	19 (5.8)	16 (6.4)	3 (3.9)	0.41
Cholangitis without CBDS (%)	1 (0.3)	1 (0.4)	0 (0)	0.58
Malignancy (%)	1 (0.3)	1 (0.4)	0 (0)	0.58
Acute pancreatitis (%)	0 (0)	0 (0)	0 (0)	NS
Liver abscess (%)	0 (0)	0 (0)	0 (0)	NS

CBD; common bile duct, CBDS; CBD stone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Cumulative percentage
gallbladder in situ
cholecystectomized
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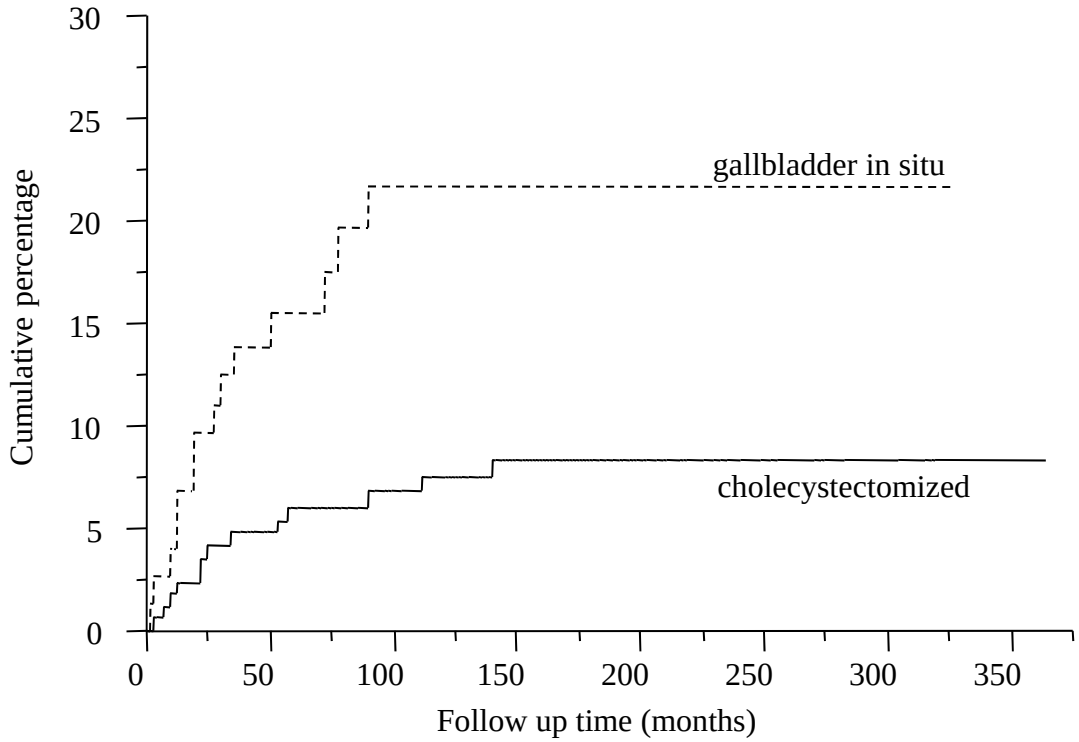
Follow up time (months)

Figure 1.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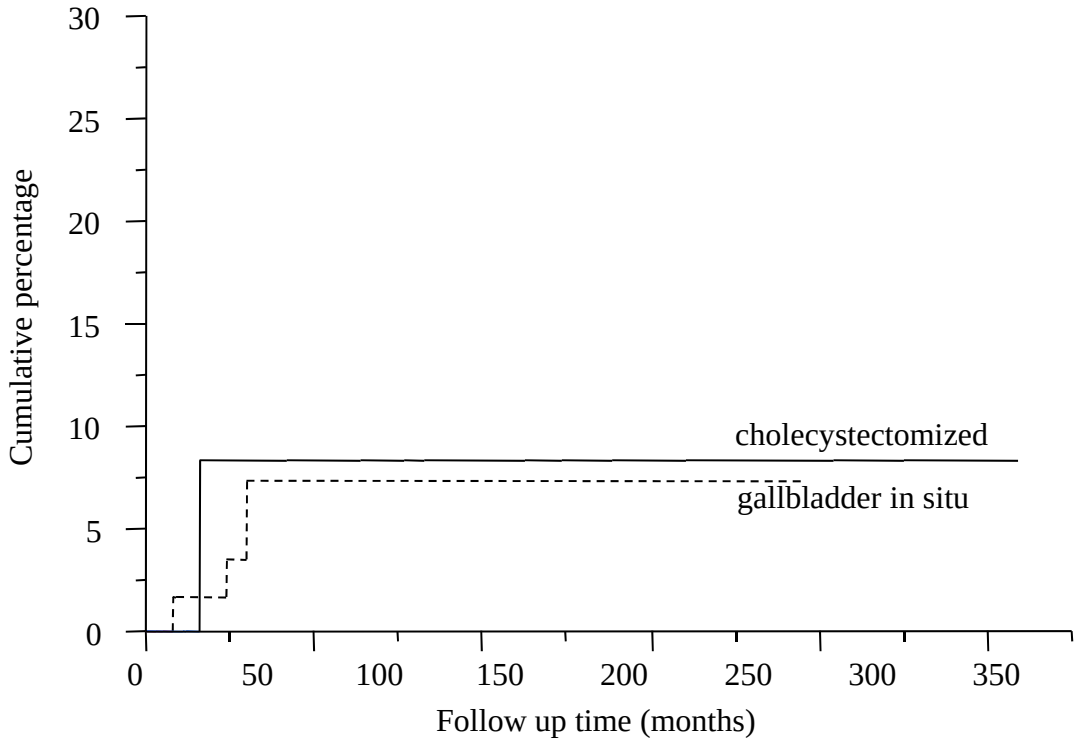
Follow up time (months)

Figure 2. A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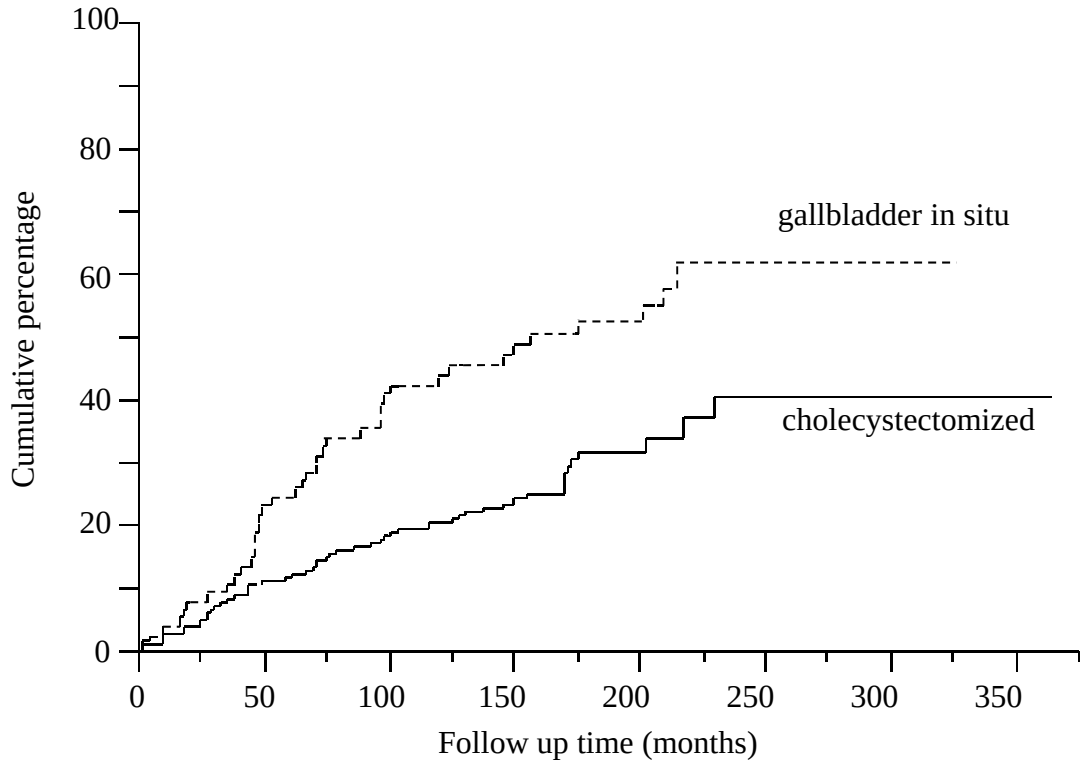
Follow up time (months)

Figure 2. B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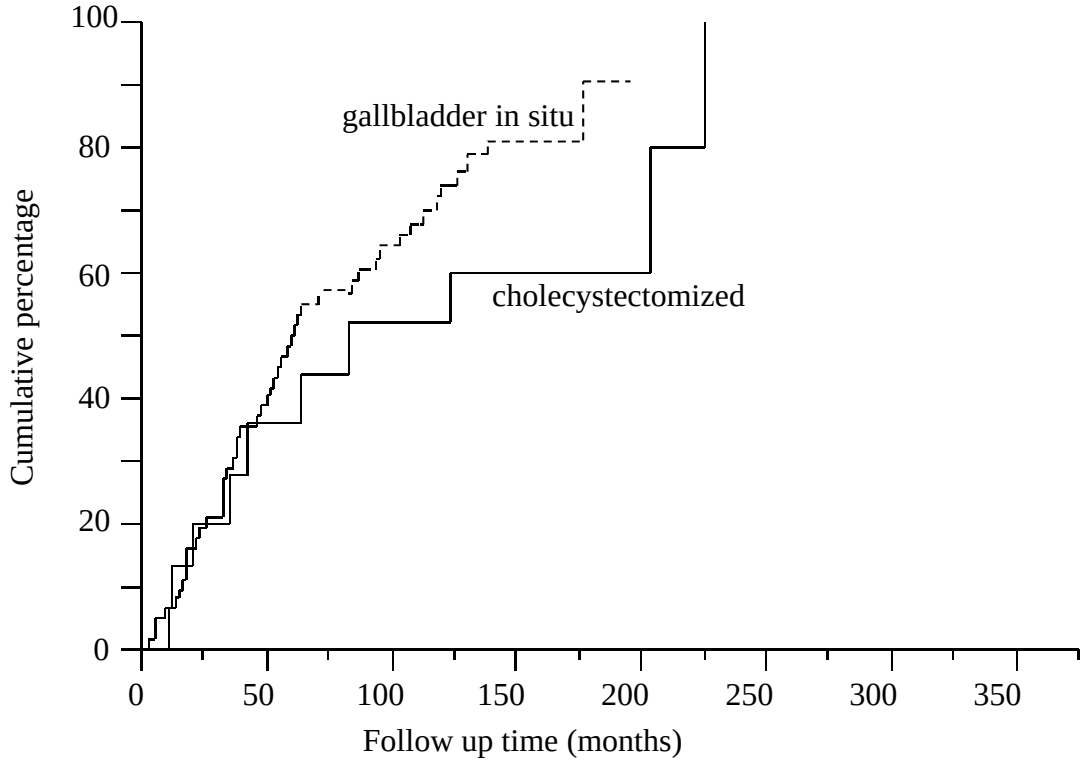
Follow up time (months)

Figure 3. A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Follow up time (months)

Figure 3. B