The role of prophylactic cholecystectomy versus deferral in the care of patients after endoscopic sphincterotomy

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Introduction: Prophylactic cholecystectomy (PC) is advised after ES and clearance of ductal calculi on the basis of a randomized controlled trial that showed a requirement for cholecystectomy in 36% of patients who defer surgery. Other studies suggest the cholecystectomy rate to be as low as 8%. **Method:** To determine the proportion of patients who deferred cholecystectomy and the outcome, we reviewed 870 consecutive patients who underwent endoscopic retrograde cholangiography and sphincterotomy; the gallbladder of 420 of these remained in situ. Patients were assigned to PC or deferred cholecystectomy (DC) groups. **Results:** Cholecystectomy was deferred in 180 of 310 eligible patients. DC patients were significantly older (66.4 v. 49.8 yr) and sicker (according to the American Society of Anesthesiology [ASA] physiological status score) and had a significantly higher mortality rate than did PC patients. Deaths were principally cardiovascular and not biliary related. After a follow-up of 24.2 (< 1–82.3) months, eventual cholecystectomy was required in 46 (24.7%) DC patients at a mean of 6 months after ES. The subgroup undergoing eventual cholecystectomy was younger (57.6 v. 69.4 yr; $p < 0.001$) fitter (ASA score of 1.98 v. 2.26; $p = 0.015$) and more likely to have residual cholecystolithiasis than were those who continued deferral. Recurrent pancreatitis was more common in DC (30%) than in PC (4.8%) patients if pancreatitis was the indication for sphincterotomy. **Discussion:** PC is advised for patients with residual cholecystolithiasis after ES. In patients with relative contraindications, the choice is balanced in favour of cholecystectomy if there is a history of pancreatitis and in favour of deferral if more than 6 months have elapsed since ES.

Introduction : À la suite d'un essai contrôlé randomisé qui a montré que la cholécystectomie s'imposait chez 36 % des patients qui reportent l'intervention chirurgicale, on conseille une cholécystectomie prophylactique après une sphinctérotomie par endoscopie (SE) et l'enlèvement des calculs canalaires. D'autres études indiquent que le taux de cholécystectomies atteint à peine 8 %. **Méthode :** Pour déterminer le pourcentage des patients qui ont reporté une cholécystectomie et les résultat du report, nous avons étudié le dossier de 870 patients consécutifs qui ont subi une cholangiographie rétrograde et une sphinctérotomie par endoscopie. La vésicule biliaire est demeurée en place chez 420 de ces patients. On a réparti les patients en deux groupes : patients ayant subi une cholécystectomie prophylactique (CP) et patients dont la cholécystectomie avait été reportée (CR). **Résultats :** La cholécystectomie avait été reportée chez 180 patients admissibles sur 310. Les patients du groupe CR étaient beaucoup plus âgés (66,4 c. 49,8 ans) et plus malades (selon le score de l'état physiologique de l'American Society of Anesthesiology [ASA]) et ont présenté un taux de mortalité significativement plus élevé que les patients du groupe CP. Les décès ont été attribuables principalement à des troubles cardiovasculaires et non biliaires. Après un suivi de 24,2 (< 1–82,3) mois, la cholécystectomie s'est imposée éventuellement chez 46 (24,7 %) des patients du groupe CR, en moyenne de six mois après la SE. Les sujets qui ont fini par subir une cholécystectomie étaient plus jeunes (57,6 c. 69,4 ans; $p <$ 0,001), en meilleur état de santé (score ASA de 1,98 par rapport à 2,26; $p = 0,015$) et plus susceptibles d'avoir une cholécystolithiase résiduelle que les sujets qui ont continué de reporter l'intervention. La pancréatite répétitive a été plus fréquente chez les patients du groupe CR (30 %) que chez ceux du

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groupe CP (4,8 %) si la pancréatite constituait l'indication de la sphinctérotomie. **Discussion :** On recommande la cholécystectomie prophylactique chez les patients qui ont une cholécystolithiase résiduelle après une SE. Chez les patients qui présentent des contre-indications relatives, le choix a penché en faveur de la cholécystectomie s'ils avaient des antécédents de pancréatite et en faveur du report s'il s'était écoulé plus de six mois depuis la SE.

Endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy are advised for the treatment of choledocholithiasis before laparoscopic cholecystectomy is considered.[1] The role of ductal pressure in biliary symptoms suggests that some patients may be managed by sphincterotomy alone because it reduces pressure in the biliary tree. In contrast, cholecystectomy without sphincterotomy elevates biliary pressure.[2] Deferral of cholecystectomy after endoscopic sphincterotomy for choledocholithiasis was first reported 20 years ago for high-risk patients.[3] Only 13% of 224 patients observed for 3 years required cholecystectomy. A more recent series observed a cohort of 447 patients for 6 years.[4] Of 164 patients whose gallbladders were left in situ, 13 (7.9%) required cholecystectomy and 11 (6.7%) had repeat endoscopic management.

In patients considered to be fit for surgery, early or prophylactic cholecystectomy (PC) is advised after the clearance of ductal calculi on the basis of a recent randomized controlled trial (RCT).[5] There was some crossover in the trial between the PC and the wait-and-see group. Ten percent of the patients were lost to follow-up, but of 61 (50%) were managed by wait-and-see, 27 (44%) had at least 1 biliary symptom and 22 (36%) had cholecystectomy up to 20 months after sphincterotomy.[6] No survival or quality-of-life advantage was seen with PC.

Even though the information regarding cholecystectomy deferral was developed in the high-risk group, we felt that an increasing number of fit patients were choosing wait-and-see care over cholecystectomy. To determine whether this was so and to examine the impact, we retrospectively studied the role of cholecystectomy in the management of patients whose gallbladders were in situ at the time of ERCP.

Methods

We examined the records of all patients undergoing ERCP and sphincterotomy between January 1993 and January 2000. We excluded patients who had a prior cholecystectomy, malignancy or acute cholecystitis at the time of ERCP. An incomplete sphincterotomy, inadequate clearance of the common bile duct or the placement of an endobiliary stent were also factors for exclusion. For analysis, we chose the last ERCP in patients who had multiple procedures. Follow-up was completed by hospital chart review by mail and telephone contact with the referring and family physicians and by telephone call to the patients or their families.

Data collected included demographic details, American Society of Anesthesiology physiological status (ASA) score, indication for and findings at ERCP, time and cause of death (if applicable), time and indication for cholecystectomy (if applicable) and development of biliary symptoms or pancreatitis. We determined late post-ERCP pancreatitis to be a diagnosis of pancreatitis starting more than 1 week after ERCP to distinguish it from ERCP-related pancreatitis.

Patients were assigned to the PC or the deferred cholecystectomy (DC) group if their records showed an intention to proceed with or to postpone cholecystectomy, respectively. Where this could not be determined, patients who had a cholecystectomy within the first month of sphincterotomy without the occurrence of biliary symptoms were assigned to the PC group. Discrete data were compared with chi-square analysis and continuous data, using Student's t test with a statistical significance set at $p < 0.05$.

Results

Over the 7-year period, 870 patients underwent ERCP and sphincterotomy 422 (48.5%) of whom still had a gallbladder at the time of the procedure. Sixty-two patients were excluded for the following reasons: malignancy (40 patients), insufficient sphincterotomy (13 patients), inadequate duct clearance (7 patients) or concurrent acute cholecystitis (2 patients). Of the 340 eligible patients, adequate follow-up information was available for 310 (91.2%). Cholecystectomy was deferred in 186 (60%) of the eligible patients. The intention of the responsible physician and the patient with respect to PC or deferral was determined in 259 (83.5%) patients. Twenty-one patients were assigned to the PC group because the interval between ES and cholecystectomy was less than 1 month without symptoms; the remaining 30 patients were included with the patients who deferred cholecystectomy.

Patients who deferred cholecystectomy were significantly older (66.4; versus 49.8 yr; $p < 0.01$) and had a higher ASA score (2.19 versus 1.53; $p < 0.001$) than did patients who underwent an early cholecystectomy (Table 1). Overall mortality was 18%, occurring a mean of 16 (< 1–53.6) months after ERCP. Most deaths occurred in the group aged over 65 years, predominantly from cardiovascular and nonbiliary causes. Mortality was substantially higher in the patients who deferred cholecystectomy (26.3%), compared with

the PC group (5.3%), but this was not temporally related to ERCP or eventual cholecystectomy. Excess mortality in the DC group occurred in the lower ASA score (1–2) categories and not in patients with ASA scores of 3–5, who experienced a high mortality rate regardless of the treatment choice (Table 2).

Cholecystectomy was performed in the PC group up to 4.4 (mean 0.65) months after sphincterotomy. Biliary-type pain was more common in the DC group. Cholecystectomy was eventually required in 46 (24.7%) patients in the DC group between 0.13 and 36.4 (mean 6.4) months after sphincterotomy (Table 3, Fig. 1). These patients were significantly younger (57.6 versus 69.4 yr) and fitter (ASA 1.98 versus 2.26) than patients who did not undergo cholecystectomy (Table 4). The latter group had a substantially higher death rate. The requirement for multiple ERCP to clear the bile duct of stones was associated with eventual cholecystectomy.

Late pancreatitis was more common if cholecystectomy was deferred (Table 3). Recurrent pancreatitis was more common in patients who deferred cholecystectomy in whom the indication for ERCP was pancreatitis (Table 5). Eventual cholecystectomy was required in 9 of 30 patients who had pancreatitis before ERCP, but this was not significantly different from those who did not have pancreatitis (37/156).

Discussion

Mortality in the cohort of patients studied here is substantially higher than in the RCTs.[6–8] A larger than expected proportion of patients chose to defer cholecystectomy, and they had a substantially higher mortality rate than those who underwent cholecystectomy. Cardiovascular deaths in the group aged over 65 years accounted for this difference. Patients who deferred cholecystectomy were of older age and less fit than those who proceeded to PC. Similarly, patients who deferred cholecystectomy but eventually underwent the procedure had a better survival rate, but they were also of younger age and more fit than those who continued to defer

Table 1

Patients with gallbladder in situ at the time of endoscopic retrograde cholangio-pancreatography and ampullary sphincterotomy

Characteristics	Procedure; no. (and %)* Prophylactic cholecystectomy	Deferred cholecystectomy	*p*
No. patients	124 (40)	186 (60)	
Months follow-up, mean (range)	28.5 (1.8–82.0)	24.2 (<1–82.3)	0.048
Women:men	83:41	106:80	0.08
Mean age (range) yr	49.8 (15–87)	66.4 (8–96)	< 0.001
< 50 yr	63 (50.8)	44 (23.7)	< 0.001
50–65 yr	27 (21.8)	26 (14.0)	< 0.07
> 65 yr	34 (27.4)	116 (62.4)	< 0.001
Mean ASA score	1.53	2.19	< 0.001
ASA 1–2	121 (97.6)	133 (71.5)	0.07
ASA 3–5	3 (2.4)	53 (28.5)	

*Unless otherwise indicated. ASA: American Society of Anesthesiology physiological status.

Table 2

Mortality after endoscopic sphincterotomy (ES) with gallbladder in situ

Characteristics	Procedure; no. (and %)* Prophylactic cholecystectomy	Deferred cholecystectomy	*p*
No. patients	124	186	
Mortality rate	7 (5.6)	49 (26.3)	< 0.001
Mean months after ES (range)	6.3 (1.8–12.5)	17.4 (< 1–53.6)	< 0.001
Cause of death			
Cardiovascular	0	23 (46.9)	0.03
Cancer	4 (56.1)	13 (26.5)	
Pneumonia	2 (28.6)	6 (12.2)	
Other	1 (14.3)	7 (14.3)	
Age group			
< 50 yr	0	2 (4.5)	
50–65 yr	0	4 (15.4)	
> 65 yr	7 (20)	43 (37.15)	0.07
ASA score			
ASA 1–2	6 (5.0)	26 (19.5)	< 0.001
ASA 3–5	1 (33.3)	23 (43.4)	1.00

*Unless otherwise indicated. ASA: American Society of Anesthesiology physiological status.

Table 3

Course after endoscopic sphincterotomy with gallbladder in situ

Course	Procedure; no. (%) Prophylactic cholecystectomy	Deferred cholecystectomy	*p*
No. patients	124	186	
Late pancreatitis	2 (1.6)	12 (6.5)	< 0.001
Biliary pain	17 (13.7)	72 (38.7)	< 0.001
Gallbladder cancer	2	0	

cholecystectomy. Although the difference in mortality largely reflects the high-risk population for whom the nonoperative route was chosen, the impact of PC on survival is unknown. We did not observe a biliary link to the excess mortality, but it cannot be excluded on the basis of retrospectively collected data. Because cholecystectomy was not randomly assigned, we cannot know from this review whether PC would have improved the outcome for high-risk patients.

RCTs are preferable to retrospective reviews, with respect to data collection and the elimination of bias. Their principal weakness lies in the selection of subjects. We reviewed the outcome for all patients over the study period and excluded high-risk patients from the RCTs. We found an overall mortality of 18%, compared with 0% in the trials. Therefore, if the impact of PC on survival is to be properly tested, the high-risk patient group has to be studied. Although such a trial would be difficult to complete, the advent of laparoscopy might allow such a consideration, because it has resulted in increased use of cholecystectomy in elderly, high-risk populations, with a superior outcome compared to open cholecystectomy.[9,10]

Conversely, if deferral of cholecystectomy does not impact survival or quality of life in the fit population, the information required by patient s in making the choice regarding surgery is the incidence of subsequent symptoms requiring cholecystectomy. In the RCT[please provide a reference], the requirement for cholecystectomy was higher than expected, at 37%,[6] whereas it was only 7.9% in a recent series.[4] Our finding of a 25% eventual cholecystectomy rate is similar to an earlier retrospective study by Keulemans and colleagues,[11] where they found the cholecystectomy rate to be 23%. On the basis of current information, it is reasonable to tell patients that cholecystectomy after sphincterotomy can be avoided in 70% of cases. Although this would please public tax payers, from the patients' perspective, the threshold event rate where PC should be advised is not known. Context is provided by asymptomatic cholecystolithiasis where the current consensus is to defer cholecystectomy. A recent study of patients with asymptomatic cholecystolithiasis found that 12% required cholecystectomy over a 7-year period of observation.[12] This annual rate of nearly 2% persists indefinitely without the plateau in the incidence of cholecystectomy that was seen at 6 months postsphincterotomy in our study.

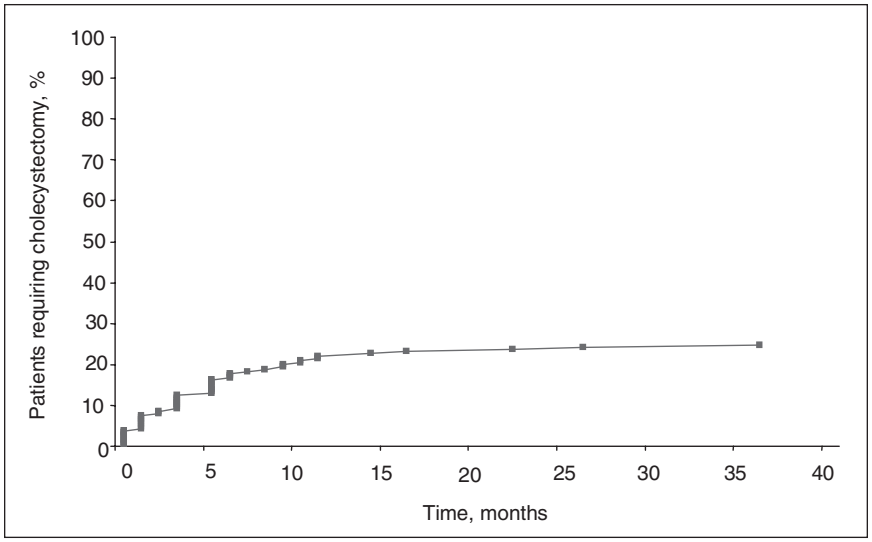

FIG. 1. Eventual cholecystectomy rate in patients who initially deferred cholecystectomy after endoscopic sphincterotomy.

Table 4

Eventual cholecystectomy in patients who defer cholecystectomy

Characteristics	Course; no. (%)*		*p*
	Eventual cholecystectomy	Continued cholecystectomy deferral	
No. patients	46 (24.7)	140 (75.3)	
Mean age (range) yr	57.6 (17–85)	69.4 (8–96)	< 0.001
Mean ASA score	1.98	2.26	0.015
Death	5 (10.9)	44 (31.4)	0.006
Cholecystolithiasis	29 (63.0)	69 (49.3)	0.12
Multiple ERCP to clear duct	19 (41.3)	19 (13.6)	< 0.001
Stones retrieved at ERCP	17 (37)	61 (43.6)	0.43

ASA: American Society of Anesthesiology physiological status, ERCP = endoscopic retrograde cholangiopancreatography.
*Unless otherwise indicated.

Table 5

Patients with pancreatitis as an indication for endoscopic sphincterotomy who defer cholecystectomy

Characteristics	Procedure; no. (%)		*p*
	Prophylactic cholecystectomy	Deferred cholecystectomy	
No. patients	21	30	0.85
Mortality	2 (9.5)	5 (16.7)	0.69
Recurrent pancreatitis	1 (4.8)	9 (30)	0.034
Cholecystectomy	21 (100)	10 (33.3)	< 0.001

Research might also focus on factors that predict recurrent biliary symptoms. Boerma and others[6] felt that the high cholecystectomy rate was due to the requirement for sonographic confirmation of residual cholecystolithiasis for study inclusion. We saw a statistically insignificant increase in cholecystolithiasis among patients who required cholecystectomy. Patients whose indication for ERC was pancreatitis had a higher incidence of recurrent pancreatitis if cholecystectomy was deferred.

Our review does not undermine the published opinion in favour of safe PC.[5] After endoscopic cholecystectomy, our current policy is to recommend cholecystectomy to patients with residual cholecystolithiasis if they do not have a contraindication to cholecystectomy. In patients with relative contraindications to surgery, the choice is balanced in favour of cholecystectomy if there is a history of pancreatitis and in favour of deferral if more than 6 months have lapsed since endoscopic sphincterotomy. We believe an RCT of PC after endoscopic sphincterotomy in patients with relative contraindications to surgery is warranted to determine its impact on the high mortality in this group when cholecystectomy is deferred.

Competing interests: None declared.

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