Original Investigation

Natural Course vs Interventions to Clear Common Bile Duct Stones

Data From the Swedish Registry for Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (GallRiks)

Mats Möller, MD; Ulf Gustafsson, MD, PhD; Finn Rasmussen, MD, PhD; Gunnar Persson, MD, PhD; Anders Thorell, MD, PhD

IMPORTANCE The optimal strategy for common bile duct stones (CBDSs) encountered during cholecystectomy is yet to be determined.

OBJECTIVE To evaluate the outcomes after various interventional techniques to clear the bile ducts and the natural course of CBDSs found during intraoperative cholangiography.

DESIGN, SETTING, AND PARTICIPANTS In a large retrospective cohort analysis, we analyzed data from the Swedish Registry for Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (GallRiks). We included all patients with CBDSs found on intraoperative cholangiography during cholecystectomy from May 1, 2005, through December 31, 2009.

EXPOSURES Presence of CBDSs on intraoperative cholangiography.

MAIN OUTCOMES AND MEASURES Relation between strategies for handling CBDSs in terms of complication rates and/or incomplete clearance with need of intervention (ie, unfavorable outcomes).

RESULTS In 38 864 cholecystectomies, CBDSs were found in 3969 patients, of whom 3828 underwent analysis. Earlier or ongoing symptoms were more common with increasing stone size ($P < .001$). In total, postoperative unfavorable outcomes were found in 14.9% but less frequently for patients with smaller stones ($P < .01$). Among patients in whom no intraoperative measures were taken (representing natural course), the risk for unfavorable outcomes was 25.3%. This risk was significantly lower in patients in whom any measure was taken to clear the ducts (12.7%; odds ratio, 0.44 [95% CI, 0.35-0.55]). The same was found when small (<4 mm) and medium (4-8 mm) stones were analyzed separately (odds ratio, 0.52 [95% CI, 0.34-0.79] and 0.24 [95% CI, 0.17-0.32], respectively).

CONCLUSIONS AND RELEVANCE The high rates of unfavorable outcomes associated with taking no measures when CBDSs are found during cholecystectomy suggest that the natural course might not be as favorable as earlier suggested. This finding implies that, in general, efforts should be made to clear the bile ducts.

Invited Commentary page 1014

CME Quiz at jamanetworkcme.com and CME Questions page 1096

Author Affiliations: Department of Surgery, Ersta Hospital, Stockholm, Sweden (Möller, Gustafsson, Thorell); Department of Clinical Sciences, Karolinska Institutet, Danderyds Hospital, Stockholm, Sweden (Möller, Gustafsson, Thorell); Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden (Rasmussen); Department of Surgery, Ryhov Hospital, Jönköping, Sweden (Persson).

Corresponding Author: Mats Möller, MD, Department of Surgery, Ersta Hospital, PO Box 4622, S-11691, Stockholm, Sweden (mats.moller@erstadiakoni.se).

JAMA Surg. 2014;149(10):1008-1014. doi:10.1001/jamasurg.2014.249
Published online August 13, 2014.

Copyright 2014 American Medical Association. All rights reserved.

Cholecystectomy is one of the most common surgical interventions in the western world, and in Sweden alone, 12 000 to 13 000 patients undergo this procedure annually. In Sweden, most surgical units routinely perform intraoperative cholangiography during cholecystectomy, and in 10% to 15%, common bile duct stones (CBDSs) are encountered.[1] What measures should be taken in response to the intraoperative finding of CBDSs is controversial. Common bile duct stones might cause serious morbidity, such as pancreatitis and/or cholangitis; therefore, many surgeons traditionally advocate compulsory clearance of the bile ducts.[2] The interventional alternatives available are by themselves associated with various risks for morbidity and even mortality,[3-6] and no consensus exists as to which is superior.[7-10] The relation between risks associated with the interventions and the risk for complications due to CBDSs left without measures taken is not known. Data from several small studies suggest that spontaneous clearance rates of such CBDSs without complications might be higher than previously believed,[11-13] which raises the question whether an expectant strategy should be recommended, at least for small CBDSs.

In Sweden, the nationwide Registry for Gallstone Surgery and Endoscopic Retrograde Cholangiopancreaticography (GallRiks) was established on May 1, 2005. The aims of GallRiks were to obtain as complete a registration as possible for all procedures performed in Sweden and to provide the participating hospitals with information on results, including complications.

We used data from GallRiks with the following 2 aims: (1) to investigate what measures were taken when CBDSs were found intraoperatively in Sweden from May 1, 2005, through December 31, 2009; and (2) to analyze the outcomes in terms of complications and success rates of bile duct clearance in relation to various stone sizes and strategies used.

Methods

GallRiks

GallRiks is financially supported by the Swedish National Board of Health and Welfare and approved by the Swedish Surgical Society. GallRiks uses an Internet platform (http://www.ucr.uu.se/gallriks/) with online registration of the procedures and a 30-day follow-up. Data from participating centers can be uploaded at any given time for analysis and comparison with national data. A continuously increasing number of Swedish centers have joined the registry. Thus, data in GallRiks from the years 2007, 2008, and 2009 represent approximately 70%, 80%, and 90%, respectively, of all cholecystectomies performed in Sweden compared with plain registration of surgical procedures from the Swedish National Board of Health and Welfare. Representatives for GallRiks perform audits at the participating units for validation of the data on a regular basis. In 2009, 67 of the participating 72 centers had been visited by such representatives, who confirmed a complete match of registered data with medical journals in 98%.[1]

Data Collection

The study was approved by the regional ethics committee of Stockholm. We collected data on age, sex, American Society of Anesthesiologists (ASA) physical status classification, acute or elective admission to the hospital resulting in procedures, present or previous symptoms of CBDSs (ie, pancreatitis, jaundice, or confirmed CBDS), size of CBDSs found on intraoperative cholangiography, strategy chosen for handling the CBDS, postoperative complications related to the CBDS within 30 days and/or known incomplete clearance of the bile ducts at 30 days postoperatively (unfavorable outcomes [UOs]), and the indication for and findings at any endoscopic retrograde cholangiopancreatography (ERCP) performed during or at any time after the cholecystectomy. Strategies, complications, clearance of the bile duct, and UOs were assessed separately.

The following 7 possible alternatives are given in GallRiks to register the selected CBDS strategy:

1. No measures taken intraoperatively or planned postoperatively
2. Preparation for postoperative ERCP
3. Laparoscopic choledochotomy
4. Open choledochotomy
5. Laparoscopic transcystic stone extraction
6. Intraoperative ERCP
7. Flushing and/or manipulation of CBDSs into the duodenum

At the 30-day follow-up after the cholecystectomy, several different complications can be registered. Postoperative pancreatitis, cholangitis, or obstruction of bile duct/jaundice could be assumed to be related to the CBDS intervention or any remaining CBDSs and were therefore included in the analysis as present or absent. The presence of 1 or more of these categories was classified as a complication within 30 days.

Clearance of the bile ducts is normally evaluated only if remaining CBDSs are suspected postoperatively. Patients with such symptoms in whom CBDSs were confirmed were classified as having incomplete clearance at the 30-day follow up. Moreover, if an ERCP was performed at any time during the entire follow-up (0 days to 4 years) that was not a part of the primary strategy or otherwise planned, the result of that ERCP was evaluated. If a CBDS could be confirmed, the patient was also considered to have incomplete clearance. If a patient had incomplete clearance and/or complications within 30 days as defined above, this patient was considered to have a UO related to the strategy chosen for handling of the CBDSs.

Statistical Analysis

Results are presented as percentages, mean (SD), and odds ratios (95% confidence intervals) where appropriate. We used the 2-tailed *t* test for crude group comparisons of continuous variables. Crude associations between categorical variables were analyzed with χ^2 tests or the Fisher exact test as appropriate. Baseline characteristics were analyzed to determine the univariate predictors of the UO variable. We then used multiple logistic regression to assess the adjusted association between specific interventions and outcome. The adjustment variables included age, sex, and ASA. $P < 05$ was considered statistically significant. All data were analyzed using commercially available software (STATA, version 10.0; StataCorp). Missing data for stone size excluded patients from analyses involving size. We had no reason to believe that the patients with missing data for stone size were unevenly distributed in the material.

Copyright 2014 American Medical Association. All rights reserved.

Table 1. Characteristics of Study Patients Undergoing Cholecystectomy Registered in GallRiks

Characteristic	Patients With CBDSs (n = 3828)	All GallRiks Patients (n = 38 864)[a]
Sex, No. (%)		
Male	1248 (32.6)	33
Female	2580 (67.4)	67
Admission for acute illness, No. (%)	1879 (49.1)[b]	30
Age, mean (SD), y		
Male	57.8 (17.0)	55
Female	50.3 (18.1)	49
ASA, No. (%)		
1	2038 (53.2)	NA
2	1469 (38.4)	NA
3	291 (7.6)	NA

Abbreviations: ASA, American Society of Anesthesiologists; CBDSs, common bile duct stones; GallRiks, Swedish Registry for Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography; NA, not applicable.

[a] Data were obtained directly from the annual report of all patients registered from May 1, 2005, through December 31, 2009, for whom distribution of ASA classification is not given.

[b] $P < .001$ vs all patients.

Table 2. Distribution of Size of CBDSs Encountered During Cholecystectomy in 3452 Patients[a]

CBDS Size, mm	No. (%) of Patients		
	All	Symptomatic[b]	With Unfavorable Outcome[c]
<4	904 (26.2)	362 (40.0)[d]	101 (11.2)[e]
4-8	1923 (55.7)	980 (51.0)[f]	295 (15.3)
>8	625 (18.1)	425 (68.0)	117 (18.7)
All	3452 (100.0)	1767 (51.2)	513 (14.9)

Abbreviation: CBDSs, common bile duct stones.

[a] Includes patients in whom CBDS size was registered.

[b] Includes pancreatitis, jaundice, or confirmed CBDSs.

[c] Defined as incomplete clearance and/or complications within 30 days after cholecystectomy.

[d] $P < .001$ vs 4 to 8 and greater than 8 mm.

[e] $P < .01$ vs 4 to 8 and greater than 8 mm, χ^2 test.

[f] $P < .001$ vs greater than 8 mm, χ^2 test.

Results

From the start of the registry on May 1, 2005, through December 31, 2009, 38 864 cholecystectomies were registered in GallRiks. Intraoperative cholangiography was performed in 34 200 procedures (88.0%), and, in 3969 of these (11.6%), 1 or more CBDSs were found. Two centers using GallRiks (Uppsala and Kalmar) were known to not register data on ERCP during this period, and all data (n = 141) from these units were therefore excluded from the study. Remaining data from GallRiks included 3828 patients with CBDSs for analysis.

The distributions of age and sex in the 3828 patients with CBDSs were similar compared with all patients undergoing cholecystectomy during the study period (**Table 1**). However, a larger proportion of procedures in which CBDSs were found were performed during an admission for acute illness (Table 1).

In 3452 of the 3828 procedures in which CBDSs were found (90.2%), the size of the largest stone was recorded in 1 of the following 3 categories: less than 4, 4 to 8, and greater than 8 mm (**Table 2**). More than 50% of CBDSs were classified as being 4 to 8 mm in size. With increasing stone size, we found a statistically significant increase in rates of stones reported as symptomatic.

The distribution of UOs in relation to stone size is also given in Table 2. In total, UOs were encountered in 513 of 3452 patients in whom CBDSs were found (14.9%). The rate of UOs increased with increasing stone size. However, the difference was statistically significant only between the smallest stones and the other 2 categories ($P < .01$). For each of the 3 stone size groups, we found no significant differences in rates of UOs between those patients classified as symptomatic or asymptomatic (data not shown).

Strategies Used

The distribution of different strategies used is shown in **Table 3**. For all CBDSs irrespective of size, strategy 1 was chosen in 15.5%. Intraoperative or postoperative ERCP was the most commonly used strategy, and open choledochotomy was used in 20.4% of all procedures. With increasing size of CBDSs, we found a trend toward more invasive strategies used. Almost one-third of the smallest stones were left without measures taken (strategy 1), whereas slightly less than half of patients with stones of 4 to 8 mm underwent intraoperative or postoperative ERCP, and almost half of the patients with the largest stones underwent open choledochotomy.

Unfavorable Outcomes

All CBDS Sizes

The rates of UOs, irrespective of stone sizes, are shown in **Table 4**. After the use of strategy 1, UOs were recorded in 25.3% of patients. In a multivariate analysis adjusted for age, sex, and ASA classification, the alternative of taking any measure (strategies 2-7) was associated with a risk reduction of 56% for UOs compared with strategy 1 (odds ratio, 0.44 [95% CI, 0.35-0.55]) (Table 4). Moreover, all individual strategies (2-7) were found to be associated with reduced risk for UOs compared with strategy 1 (odds ratio range, 0.18-0.66).

CBDSs of Less Than 4 mm

Rates of UOs after each strategy for CBDSs of less than 4 mm are shown in **Table 5**. For strategy 1, the rate of UOs was 15.9%. Again, in multivariate analysis, all interventions together (strategies 2-7) were associated with lower rates of UOs. Regarding individual techniques, strategies 5, 6, and 7 by themselves were found to be associated with a reduced risk for UOs by 50% to 78% (odds ratio range, 0.22-0.50) compared with strategy 1 ($P < .001$), whereas no statistically significant difference was seen for strategies 2 to 4 (Table 5).

CBDSs of 4 to 8 mm

Rates of UOs after each strategy for CBDSs of 4 to 8 mm are shown in Table 5. For strategy 1, UOs were found at a rate of

Copyright 2014 American Medical Association. All rights reserved.

Table 3. Distribution of Treatment Strategies Chosen for CBDSs

Strategy	Patients With CBDSs, No. (%)[a]			
	All Sizes	<4 mm	4-8 mm	>8 mm
1. No intraoperative measures	594 (15.5)	289 (32.0)	222 (11.5)	34 (5.4)
2. Postoperative ERCP	572 (14.9)	76 (8.4)	341 (17.7)	101 (16.2)
3. Laparoscopic choledochotomy	141 (3.7)	12 (1.3)	56 (2.9)	14 (2.2)
4. Open choledochotomy	781 (20.4)	50 (5.5)	359 (18.7)	300 (48.0)
5. Transcystic extraction	512 (13.4)	102 (11.3)	337 (17.5)	43 (6.9)
6. Intraoperative ERCP	889 (23.2)	152 (16.8)	517 (26.9)	128 (20.5)
7. Flushing/manipulation	339 (8.9)	223 (24.7)	91 (4.7)	5 (0.8)
Total	3828 (100.0)	904 (100.0)	1923 (100.0)	625 (100.0)

Abbreviations: CBDSs, common bile duct stones; ERCP, endoscopic retrograde cholangiopancreaticography.

[a] Percentages have been rounded and may not total 100.

36.9%, which was significantly higher than those for each of the other strategies ($P < .001$). Notably, UOs were seen only in 7.1% after the use of strategy 5 (transcystic extraction).

CBDSs of Greater Than 8 mm

Rates of UOs after each strategy for CBDSs of greater than 8 mm are shown in Table 5. Strategy 1 was associated with the highest risk for UOs (26.5%). Again, the lowest rates of UOs were seen after transcystic extraction, but owing to the relatively small number of patients within each category of intervention, no multivariate analysis comparing individual strategies was performed. However, when comparing strategy 1 with all other strategies together (2-7), no significant difference in the risk for UOs could be confirmed.

Table 4. Unfavorable Outcomes for Each CBDS Strategy Chosen in 3828 Patients[a]

Strategy	Unfavorable Outcome, No./ Total No. (%) of Patients[b]	OR (95% CI)[c]
1. No intraoperative measures	150/594 (25.3)	1 [Reference]
Strategies 2-7	411/3234 (12.7)	0.44 (0.35-0.55)
2. Postoperative ERCP	103/572 (18.0)	0.66 (0.49-0.87)
3. Laparoscopic choledochotomy	8/141 (5.7)	0.18 (0.08-0.37)
4. Open choledochotomy	141/781 (18.1)	0.65 (0.49-0.85)
5. Transcystic extraction	35/512 (6.8)	0.23 (0.15-0.33)
6. Intraoperative ERCP	98/889 (11.0)	0.37 (0.28-0.49)
7. Flushing/manipulation	26/339 (7.6)	0.26 (0.17-0.41)
Total	561/3828 (14.7)	NA

Abbreviations: CBDS, common bile duct stone; ERCP, endoscopic retrograde cholangiopancreaticography; NA, not applicable; OR, odds ratio.

[a] Includes all patients with CBDSs encountered during cholecystectomy, irrespective of stone size.

[b] Defined as incomplete clearance and/or complications within 30 days after cholecystectomy.

[c] Multiple logistic regression was used to assess the adjusted association between specific interventions and outcomes. Adjusted for age, sex, and American Society of Anesthesiologists classification.

Discussion

In this study consisting of 3828 unselected patients with CBDSs encountered during cholecystectomy, the strategies chosen for handling the stones varied markedly among the different sizes of stones. For all stones, the rate of UOs, as defined above, was 14.9%. This rate was significantly lower for smaller stones but was not associated with earlier or ongoing symptoms/signs of CBDSs. The major finding was that, for small stones, the choice of taking no measures was associated with a surprisingly high risk for UOs compared with intervention to clear the bile ducts, implying that the natural course for CBDSs found during cholecystectomy is not as favorable as earlier suggested.[11-13] For larger stones, several treatment options might be similarly recommendable, whereas for small stones (<4 mm), transcystic stone extraction and flushing/manipulation of the stone into the duodenum seem to be associated with the most favorable outcome.

To our knowledge, this report constitutes the largest data set to evaluate the outcome related to various treatment strategies when CBDSs are found during cholecystectomy. The rate of UOs increased with increasing size of CBDSs when strategy was not taken into account. The observation of a more frequent admission for acute illness in patients with CBDSs is a consistent finding in GallRiks.[1]

Previous or ongoing symptoms caused by CBDSs were seen in 51.2% of included patients and were reported to be more common with increasing size of CBDSs. The risk for UOs was not influenced by occurrence of symptoms. This finding might seem unexpected because the presence of symptoms might have called for preparations with proper equipment and surgical competence. We could not, however, confirm any differences in strategies chosen depending on symptoms (data not shown).

When CBDSs are encountered during cholecystectomy, a decision on how to handle this finding is necessary. To make this decision, information is needed on the relation between risks associated with various interventional strategies and those associated with leaving the stone. Such information is, however, lacking today, primarily because the natural course of CBDSs found during cholecystectomy is largely unknown. To combine the risks associated with a specific strategy, we defined the composite variable UO as described above. A possible shortcoming with this variable is that it does not distinguish between the negative outcomes associated with a complication resulting from a primary interventional strategy itself or a complication caused by any remaining CBDSs. However, any of these complications could be considered a direct consequence of the decision to choose a particular strategy for CBDSs, and therefore the variable UO gives an estimate of the total risk for negative outcomes associated with that strategy.

Copyright 2014 American Medical Association. All rights reserved.

Table 5. Unfavorable Outcomes for Each Strategy Chosen According to Size of CBDSs

Strategy	Unfavorable Outcome, No./ Total No. (%) of Patients[a]	OR (95% CI)[b]
CBDSs <4 mm (n = 904)		
1. No intraoperative measures	46/289 (15.9)	1 [Reference]
Strategies 2-7	55/615 (8.9)	0.52 (0.34-0.79)
2. Postoperative ERCP	18/76 (23.7)	1.73 (0.93-3.22)
3. Laparoscopic choledochotomy	1/12 (8.3)	0.48 (0.06-3.86)
4. Open choledochotomy	9/50 (18.0)	1.10 (0.49-2.46)
5. Transcystic extraction	5/102 (4.9)	0.29 (0.11-0.75)
6. Intraoperative ERCP	13/152 (8.6)	0.50 (0.26-0.95)
7. Flushing/manipulation	9/223 (4.0)	0.22 (0.11-0.47)
Total	101/904 (11.2)	NA
CBDSs 4-8 mm (n = 1923)		
1. No intraoperative measures	82/222 (36.9)	1 [Reference]
Strategies 2-7	213/1701 (12.5)	0.24 (0.17-0.32)
2. Postoperative ERCP	62/341 (18.2)	0.37 (0.25-0.55)
3. Laparoscopic choledochotomy	5/56 (8.9)	0.17 (0.06-0.44)
4. Open choledochotomy	58/359 (16.2)	0.30 (0.20-0.45)
5. Transcystic extraction	24/337 (7.1)	0.13 (0.08-0.22)
6. Intraoperative ERCP	52/517 (10.1)	0.19 (0.13-0.29)
7. Flushing/manipulation	12/91 (13.2)	0.28 (0.14-0.56)
Total	295/1923 (15.3)	NA
CBDSs >8 mm (n = 625)		
1. No intraoperative measures	9/34 (26.5)	1 [Reference]
Strategies 2-7[c]	108/591 (18.3)	0.68 (0.30-1.55)
2. Postoperative ERCP	19/101 (18.8)	NP
3. Laparoscopic choledochotomy	2/14 (14.3)	NP
4. Open choledochotomy	61/300 (20.3)	NP
5. Transcystic extraction	4/43 (9.3)	NP
6. Intraoperative ERCP	21/128 (16.4)	NP
7. Flushing/manipulation	1/5 (20.0)	NP
Total	117/625 (18.7)	NA

Abbreviations: CBDSs, common bile duct stones; ERCP, endoscopic retrograde cholangiopancreaticography; NA, not applicable; NP, not performed; OR, odds ratio.

[a] Defined as incomplete clearance and/or complications within 30 days after cholecystectomy.

[b] Multiple logistic regression was used to assess the adjusted association between specific interventions and outcome. Adjusted for age, sex, and American Society of Anesthesiologists classification.

[c] Owing to the relatively low number of patients within each category of intervention, no multivariate analysis comparing individual strategies was performed.

Choice of strategy is likely to depend on various factors such as technical equipment available, number of stones found, personal skills, and local traditions. Because the size of CBDSs is likely to influence the choice of strategy, we analyzed each of the 3 size categories separately. For small stones (<4 mm), the alternatives of no measures or flushing/manipulation were chosen in more than 50%. Somewhat surprising, the alternative to leave the stone was associated with UOs in 15.9%, which was found to be significantly higher compared with the combined alternatives (strategies 2-7) representing any intervention. This finding suggests that the natural course, also for small CBDSs found during cholecystectomy, might not be as uneventful as earlier suggested.[11-13] One possible explanation for these discrepancies might be our longer follow-up time compared with previous reports, ranging from 30 days to 4 years.

Within specific stone size categories, the choice of technique depends on variables such as available competence, equipment, time of the day, etc. Such variables are difficult to control for in a register study; therefore, comparisons on outcome between individual interventional techniques must be considered more uncertain than comparisons between any intervention (strategies 2-7) and no intervention (strategy 1). Nevertheless, for stones of less than 4 mm, postoperative ERCP was associated with a high rate of UOs (23.7%), which is comparable to those reported earlier.[14,15]

Strategies 5, 6, and 7 were the alternatives associated with the lowest risk for UOs with small CBDSs. One might speculate that manipulation of the CBDS into the duodenum was more likely be chosen for the smallest stones within the category (<4 mm), which in turn might have contributed to the benign outcome. Also, because only 1 strategy can be registered in GallRiks, any unsuccessful attempt to clear the bile ducts with the use of this or any other strategy was never recorded. Thus, if a change of strategy occurred during the surgical procedure, the replacement strategy is reported and the failure of the abandoned strategy is never documented. Laparoscopic transcystic exploration was also associated with a particularly low risk for UOs (4.9%). This finding confirms suggestions of earlier reports that this approach is a safe and effective alternative.[14]

For stones of 4 to 8 mm, more invasive measures were taken. The risk for UOs for strategy 1 was significantly higher compared with all other strategies ($P < .001$). For specific techniques, the difference in favor of intraoperative compared with

Copyright 2014 American Medical Association. All rights reserved.

postoperative ERCP remained, and transcystic extraction was associated with a particularly low risk for UOs with stones of 4 to 8 mm. In addition, laparoscopic choledochotomy resulted in low rates of UOs for small and medium CBDSs (8.3% and 8.9%, respectively).

Only 625 patients had CBDSs greater than 8 mm in our material, making comparisons between different strategies more uncertain. Invasive measures were taken even more frequently, and open choledochotomy was chosen in almost half of all procedures. The rate of UOs for these procedures was 20.3%, which is similar to the rate of UOs after the same procedure in small and medium CBDSs (18.0% and 16.2%, respectively), suggesting that this risk is associated with the procedure itself rather than the size of the stones. Although chosen in a relatively small number of procedures, transcystic extraction of CBDSs was again associated with a low risk for UO. Strategy 1 had a 26.5% risk for UOs, but in multivariate analysis we were not able to confirm any significant difference compared with strategies 2 to 7, most likely owing to the small number of patients who followed strategy 1.

Our study has a number of limitations, including lack of information regarding the severity of complications that makes the group of patients with OUs heterogeneous. The number of CBDSs found on intraoperative cholangiography, which might influence strategy chosen and outcome, was not recorded. The inability to register more than 1 technique for clearance of bile ducts might also make direct comparisons between various strategies more uncertain. Any treatment for CBDSs before cholecystectomy or any data about patients with missed stones were not included in the analysis; therefore, the results and conclusions are limited to situations in which CBDSs are found during cholecystectomy. The major strengths of the study include the large population-based material and the high rate of inclusion of patients undergoing cholecystectomy in Sweden during the study period.

In the present study, we focused particularly on interventional strategy 1 (no measures) because this represents the natural course of CBDSs found during cholecystectomy. When the size of the CBDS was not considered, this strategy was associated with UOs in 25.3% of patients, which was a significantly higher risk compared with the alternative of clearing the bile ducts, irrespective of the technique used. The opinion seems to be relatively widespread that, for small CBDSs, the risk associated with taking no measures is low.[11-13] This view might also be supported by the fact that the alternative to leaving the stones was chosen in almost one-third of patients with CBDSs smaller than 4 mm. The major finding of this study is that, for small stones (<4 mm), the risk for a negative outcome is 15.9%, which in turn is statistically significantly higher compared with the risk after use of an intervention aimed to clear the bile ducts ($P < .001$). This risk did not seem to be related to the occurrence of previous or ongoing symptoms.

Conclusions

High rates of unfavorable outcomes are associated with taking no measures when CBDSs are found during cholecystectomy. The natural course of CBDSs might not be as favorable as earlier implied. Together our observations suggest that, irrespective of symptoms, efforts to clear the bile ducts should be made when small CBDSs are found during cholecystectomy.

ARTICLE INFORMATION

Accepted for Publication: December 17, 2013.

Published Online: August 13, 2014. doi:10.1001/jamasurg.2014.249.

Author Contributions: Drs Möller and Thorell had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Möller, Persson, Thorell.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Möller, Gustafsson, Persson, Thorell.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Möller, Gustafsson, Rasmussen.
Obtained funding: Möller, Thorell.
Administrative, technical, or material support: Möller, Rasmussen, Thorell.
Study supervision: Möller, Persson, Thorell.

Conflict of Interest Disclosures: None reported.

Funding/Support: This study was supported by the Erling-Persson Family Foundation and the Regional Agreement on Medical Training and Clinical Research (ALF) between Stockholm County Council and the Karolinska Institutet.

Role of the Sponsor: The funding organizations had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Information: This study is registered at clinicaltrials.gov (identifier: NCT01734720).

REFERENCES

1. Persson G, Enochsson L, Sandblom G. Årsrapport 2009: Årsrapport för Svenskt kvalitetsregister för gallstenskirurgi. GallRiks website. http://www.ucr.uu.se/gallriks/. Published August 16, 2010. Accessed August 20, 2010.

2. Consensus Development Panel. NIH consensus conference: gallstones and laparoscopic cholecystectomy. *JAMA*. 1993;269(8):1018-1024.

3. Martin DJ, Vernon DR, Toouli J. Surgical versus endoscopic treatment of bile duct stones. *Cochrane Database Syst Rev*. 2006;(2):CD003327.

4. Lal D, Lane M, Wong P. Complications of endoscopic retrograde cholangiopancreatography. *N Z Med J*. 2003;116(1177):U496.

5. Costamagna G, Tringali A, Shah SK, Mutignani M, Zuccalà G, Perri V. Long-term follow-up of patients after endoscopic sphincterotomy for choledocholithiasis, and risk factors for recurrence. *Endoscopy*. 2002;34(4):273-279.

6. Andriulli A, Loperfido S, Napolitano G, et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. *Am J Gastroenterol*. 2007;102(8):1781-1788.

7. Williams EJ, Green J, Beckingham I, Parks R, Martin D, Lombard M; British Society of Gastroenterology. Guidelines on the management of common bile duct stones (CBDS). *Gut*. 2008;57(7):1004-1021.

8. Paganini AM, Feliciotti F, Guerrieri M, et al. Laparoscopic common bile duct exploration. *J Laparoendosc Adv Surg Tech A*. 2001;11(6):391-400.

9. Millat B, Fingerhut A, Deleuze A, et al. Prospective evaluation in 121 consecutive unselected patients undergoing laparoscopic treatment of choledocholithiasis. *Br J Surg*. 1995;82(9):1266-1269.

10. Clayton ESJ, Connor S, Alexakis N, Leandros E. Meta-analysis of endoscopy and surgery versus surgery alone for common bile duct stones with the gallbladder in situ. *Br J Surg*. 2006;93(10):1185-1191.

11. Collins C, Maguire D, Ireland A, Fitzgerald E, O'Sullivan GC. A prospective study of common bile duct calculi in patients undergoing laparoscopic cholecystectomy: natural history of choledocholithiasis revisited. *Ann Surg*. 2004;239(1):28-33.

12. Frossard JL, Hadengue A, Amouyal G, et al. Choledocholithiasis: a prospective study of spontaneous common bile duct stone migration. *Gastrointest Endosc*. 2000;51(2):175-179.

13. Caddy GR, Kirby J, Kirk SJ, Allen MJ, Moorehead RJ, Tham TC. Natural history of asymptomatic bile

Copyright 2014 American Medical Association. All rights reserved.

duct stones at time of cholecystectomy. *Ulster Med J*. 2005;74(2):108-112.

14. Rhodes M, Sussman L, Cohen L, Lewis MP. Randomised trial of laparoscopic exploration of common bile duct versus postoperative endoscopic retrograde cholangiography for common bile duct stones. *Lancet*. 1998;351(9097):159-161.

15. Nathanson LK, O'Rourke NA, Martin IJ, et al. Postoperative ERCP versus laparoscopic choledochotomy for clearance of selected bile duct calculi: a randomized trial. *Ann Surg*. 2005;242(2):188-192.

Invited Commentary

Clearing Common Bile Duct Stones
One Size Does Not Fit All

Paul Montero, MD; Richard D. Schulick, MD, MBA

Möller et al[1] report on common bile duct stone (CBDS) incidence, management, and outcomes in a large retrospective cohort analysis. They find a higher rate of unfavorable outcomes when stones are encountered and no measures are taken to address them. Limitations, including the heterogenous metric of *unfavorable outcome* and the inability to compare or register more than 1 intervention technique, are acknowledged. Ultimately, their findings have very limited effect on the debatable topic of CBDS management. Variables persist in this patient population, including patient selection and preoperative suspicion; routine vs selective cholangiography; preoperative, intraoperative, and postoperative endoscopic retrograde cholangiopancreatography (ERCP); and intraoperative open and laparoscopic management. New diagnostic measures, including magnetic resonance cholangiopancreatography and endoscopic ultrasonography, are more frequently used[2] but add cost and extra procedures to the overall management. Routine intraoperative cholangiography is championed by many[3] but may result in nontherapeutic interventions in as many as one-third of cases.[4] In a compelling study by Collins et al,[4] an intraoperative cholangiographic catheter was left in place when stones were found, and repeated cholangiograms at 48 hours and 6 weeks demonstrated normal findings in more than half of the patients, suggesting false-positive intraoperative cholangiographic findings or natural passage of the stones. Iatrogenic complications, availability, and experience related to laparoscopic bile duct exploration and ERCP remain areas of concern in this management schema. Given these variables, most surgeons in our academic practice perform selective cholangiography when evidence suggestive of CBDS is low, attempt CBDS flushing and/or manipulation, and obtain postoperative ERCP when clinically significant stones persist. Anecdotally, these procedures have resulted in a low rate of complications, avoided the technical and logistic demands of laparoscopic bile duct exploration, and minimized the incidence of open incisions. The availability of pertinent equipment, specialists, and technical ability varies among institutions, and therefore management algorithms must be individualized until these variables are more uniform among all surgeons' practices.

Related article page 1008

ARTICLE INFORMATION

Author Affiliations: Department of Surgery, University of Colorado School of Medicine, Aurora.

Corresponding Author: Paul Montero, MD, Department of Surgery, University of Colorado School of Medicine, 12631 E 17th Ave, Mail Stop C313, Room 6001, Aurora, CO 80045.

Published Online: August 13, 2014. doi:10.1001/jamasurg.2014.195.

Conflict of Interest Disclosures: None reported.

REFERENCES

1. Möller M, Gustafsson U, Rasmussen F, Persson G, Thorell A. Natural course vs interventions to clear common bile duct stones: data from the Swedish Registry for Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (GallRiks) [published online August 13, 2014]. *JAMA Surg*. doi:10.1001/jamasurg.2014.249.

2. Bansal VK, Misra MC, Rajan K, et al. Single-stage laparoscopic common bile duct exploration and cholecystectomy versus two-stage endoscopic stone extraction followed by laparoscopic cholecystectomy for patients with concomitant gallbladder stones and common bile duct stones: a randomized controlled trial. *Surg Endosc*. 2014;28(3):875-885.

3. Massarweh NN, Devlin A, Elrod JA, Symons RG, Flum DR. Surgeon knowledge, behavior, and opinions regarding intraoperative cholangiography. *J Am Coll Surg*. 2008;207(6):821-830.

4. Collins C, Maguire D, Ireland A, Fitzgerald E, O'Sullivan GC. A prospective study of common bile duct calculi in patients undergoing laparoscopic cholecystectomy: natural history of choledocholithiasis revisited. *Ann Surg*. 2004;239(1):28-33.

Copyright 2014 American Medical Association. All rights reserved.