



ORIGINAL ARTICLE

Management of complicated gallstones in the elderly: comparing surgical and non-surgical treatment options

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Abstract

Objective: The aim of this study was to evaluate the differences in clinical outcomes of endoscopic retrograde cholangiopancreatography (ERCP), ERCP followed by cholecystectomy (EC) and percutaneous aspiration (PA) in the elderly population with choledocholithiasis.

Methods: We included a total of 43 338 elderly patients aged 60 years or older and 45 295 patients younger than 60 years for comparison in our study. Data were obtained from the Nationwide Inpatient Sample (Healthcare Utilization Project) for years 2001–14 by identifying patients who were admitted for gallstone complications based on the ICD 9 diagnostic code. Multiple logistic regression was used to calculate the odds of in-hospital mortality and to detect statistical differences among the treatment groups, age groups and between male and female patients. Univariate ordinary linear regression was used to compare the length of hospital stay and readmission frequency among the different age groups.

Results: The age of the patient affected mortality and the length of hospital stay after any type of procedure of gallstones removal. In a manner independent of the patient's age, PA was associated with the highest risk of death and length of stay, while the EC was characterized by lowest mortality and ERCP by the shortest length of stay. Neither age of the patient nor the type of procedure affected the likelihood of readmission. The odds of death and the probability of readmission were not affected by patient sex. However, in patients aged between 60 and 79 years, the female gender predicted a shorter duration of stay in the hospital.

Conclusions: A patient's age negatively affects the treatment outcomes of cholelithiasis with associated complications. The EC procedure appears to be the method of choice for the management of complicated gallstones in patients of all ages.

Key words: Gallstone disease; elderly; cholecystectomy; endoscopic retrograde cholangiopancreatography; percutaneous aspiration

Introduction

Cholelithiasis or gallstone disease is characterized by high prevalence ranging from 7 to 15% [1–3]. The treatment and morbidity associated with this condition constitute a significant financial burden [4, 5]. In 2012, there were almost 400 000 admissions for

cholelithiasis with cholecystitis in the USA alone, and the aggregate expenses for in-hospital treatment exceeded 4 billion dollars [4]. Almost 2000 deaths (0.5%) were reported among the patients suffering from gallstone disease [4]. Moreover, although the causal mechanism is unknown, the presence of

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cholelithiasis is associated with a 30% higher all-cause mortality, mostly due to cardiovascular events and cancer [3].

Between 5 and 30% of cholelithiasis patients have concurrent choledocholithiasis or gallstones lodged in the common bile duct (CBD) [6–8]. Endoscopic retrograde cholangiopancreatography (ERCP) is used for both diagnosis and treatment of choledocholithiasis [9–12]. It can be implemented prior to, during or after cholecystectomy and is considered to represent a low-risk intervention. Annually, 1.3 million procedures are performed and an overall complication rate is 5–10% [13, 14]. Patients undergoing either ERCP or cholecystectomy have a 70% lower risk of biliary disease recurrence within 1 year [15]. In another study, ERCP alone was shown to reduce the recurrence by 37% [16]. These data are consistent with the conclusion that ERCP only is not sufficient to reach an optimal treatment outcome and that ERCP should be combined with cholecystectomy for adequate stone clearance [17]. In comparison with ERCP alone, a smaller number of stones remain in the CBD after cholecystectomy [18]. However, cholecystectomy after ERCP appears not to be necessary for patients with acalculous cholecystitis [19].

With the increase in the age of the population [20], the number of elderly patients undergoing treatment for symptomatic gallstones is expected to increase [21]. In fact, the proportion of emergency and elective surgical cases involving older patients is on the rise [22]. Of relevance, elderly surgical patients are characterized by higher indices of comorbidities than younger subjects [23–25], posing an additional challenge in the management of gallbladder stones. Although the mortality rate after cholecystectomy remains low (0.2–0.3%) [26–28], this fraction is increased in the older population and with increasing comorbidities. In fact, elderly patients were 7–10 times more likely to die post-operatively [26, 29]. Additionally, approximately 1% of patients who undergo laparoscopic cholecystectomy suffer from a procedure-related CBD injury. This adverse event is more common in the elderly and results more often in death in this age group [30]. Patients affected by diseases of the heart, lungs and kidneys, as well as type 2 diabetes—conditions more frequent in the older population—are more likely to die following cholecystectomy [27, 29, 31].

In order to lessen the risk of morbidity and mortality associated with cholecystectomy, elderly patients are recommended to undergo laparoscopic instead of open cholecystectomy [32]. Elective surgeries are preferred over emergency surgery, as they have a lower perioperative risk [33]. ERCP was found to be safe and effective for the elderly [10, 12, 34, 35]. However, combining this method with laparoscopic cholecystectomy, while improving the removal of gallbladder stones, may lead to increased complications such as bile leaks or adhesions [36, 37]. Alternatively, the reason for these complications might not be the ERCP itself, but pre-existing pathologies that prompted the use of ERCP in the first place [38]. Regardless of the underlying cause-and-effect relationships, the use of ERCP positively correlates with the necessity for conversion from laparoscopic to open surgery [39–42].

To date, only one study compared the outcomes of patients who underwent ERCP with and without cholecystectomy among the elderly and concluded that cholecystectomy after the ERCP does not provide a benefit to patients older than 80 years [43]. In view of the limited information regarding the impact of various types of treatment of gallbladder disease in the oldest patients, we have designed a study aiming at the comparison of in-hospital mortality, length of hospital stay and readmission rates after ERCP alone and ERCP followed by

laparoscopic cholecystectomy in patients 60 years of age or older. Patients undergoing percutaneous aspiration (PA) were also included in the comparisons, since this protocol is considered to be a third-line option for the management of complicated gallstone disease in surgically high-risk patients [44]. Since the female gender was postulated to have a protective role against the complications of gallstone treatment [15, 16], the differences by gender were analysed as well.

Methods

Study design

This retrospective cohort study was performed using the Healthcare Cost and Utilization Project–Nationwide Inpatient Sample (HCUP-NIS) data from the years 2001–14. The HCUP-NIS is a national database of patients admitted to hospitals across the USA. The study included patients 60 years of age or older who were assigned the ICD 9 diagnostic codes of cholelithiasis with associated complications such as choledocholithiasis (574.xx). Three treatment groups were analysed: patients who underwent ERCP with cholecystectomy, patients who underwent ERCP only and patients who were treated with PA only. Subjects with incomplete data and those who had complications of gallbladder perforation were excluded from the analysis. Patients with open cholecystectomy were excluded. A total of 43 338 patients satisfied the inclusion and exclusion criteria of the study; 20 462 patients underwent ERCP with laparoscopic cholecystectomy (the EC group), 21 938 patients underwent ERCP alone (the ERCP group) and 938 patients underwent percutaneous aspiration (the PA group). For comparison with the younger population, data of 45 295 patients younger than 60 years was included (mean age: 40.49 ± 13.02 years) for comparison.

Statistical analysis

Statistical analysis was performed with the SAS statistical package, version 9.4. Multiple logistic regression was used to calculate the odds of in-hospital mortality and to detect statistical differences among the treatment groups (EC, ERCP and PA), among the age groups (less than 60 years, 60–69 years, 70–79 years and 80 years or older) and between male and female patients. Univariate ordinary linear regression was used to compare the length of hospital stay and readmission frequency among the groups. In all analyses, the results were corrected for confounding variables, such as the age at admission, gender and comorbidities; a full list of performed adjustments is included under each table. Data are presented as a mean \pm standard deviation. A *P*-value ≤ 0.05 was considered statistically significant.

Results

Patients

The average age of the elderly patients included in the study was 75.6 ± 8.7 years. Small but statistically significant differences in age were present among the treatment groups, with the EC patients being the youngest and the PA patients being the oldest. Males constituted a majority of EC and ERCP patients, while both genders were equally represented in the PA group. In each treatment group, the patients were predominantly Caucasian, and the proportion of Caucasian patients did not differ among the groups. Approximately half of the EC procedures

Table 1. Patient characteristics

	EC (N = 20 462)	ERCP (N = 21 938)	PA (N = 938)
Age (years, mean \pm SD)	74.4 \pm 8.3	76.7 \pm 8.9 ^a	77.4 \pm 9.1 ^{a,b}
Gender, n (%)			
Male	8925 (44.9)	9327 (42.5) ^a	471 (50.2) ^{a,b}
Female	11 537 (55.1)	12 611 (57.5) ^a	467 (49.8) ^{a,b}
Ethnicity			
White	13 131 (75.7)	13 902 (63.3)	599 (63.9)
Black	968 (5.6)	1024 (5.6)	79 (9.5)
Hispanic	2135 (12.3)	2012 (11.0)	97 (11.7)
Asian or Pacific Islander	589 (3.4)	844 (4.6)	21 (2.5)
Native American	67 (0.4)	82 (0.5)	3 (0.4)
Other or unknown	461 (2.7)	487 (2.7)	29 (3.5)
Procedure in a major operating room			
Yes	10 613 (51.9)	640 (2.9) ^a	94 (10.0) ^{a,b}
No or unknown	9849 (48.1)	21 298 (97.1) ^a	844 (90.0) ^{a,b}
Chronic disease			
Ischemic heart disease	4982 (24.4)	6058 (27.6) ^a	387 (41.3) ^{a,b}
Heart failure	2283 (11.2)	3221 (14.7) ^a	302 (32.2) ^{a,b}
Chronic obstructive pulmonary disease	3231 (15.8)	3603 (16.4)	195 (20.8) ^{a,b}
Cancer	757 (3.7)	1582 (7.2) ^a	87 (9.3) ^{a,b}
Any of the above	8499 (41.5)	10 496 (47.8) ^a	628 (7.0) ^{a,b}

ERCP, endoscopic retrograde cholangiopancreatography; EC, ERCP followed by cholecystectomy; PA, percutaneous aspiration.

^{a,b}Indicate a statistically significant difference vs EC and ERCP groups, respectively.

were performed in a fully equipped operating room, while a significantly higher fraction, more than 90%, of ERCP and PA treatments took place outside operating rooms. Patients undergoing ERCP and PA were more likely to be affected by a chronic disease than those subjected to EC (Table 1). The incidence of ischemic heart disease, heart failure, chronic obstructive pulmonary disease and cancer was, respectively, 71, 178, 32 and 116% higher in PA than in the EC patients. All differences among the treatment groups were accounted for in subsequent analyses that were corrected for confounding variables.

In-hospital mortality

In comparison with the younger group, less than 60 years of age, the rate of death following removal of gallbladder stones was significantly increased in patients aged 60 years or older (Table 2 and Supplementary Table 1). Specifically, the unadjusted in-hospital mortality in the age group greater than 60 years of age compared to those less than 60 years old was 12.1-fold (1.21 vs 0.1%), 4.3-fold (2.09 vs 0.49%) and 1.7-fold (18.87 vs 11.14%) higher in patients undergoing EC, ERCP and PA, respectively. In all age groups, ERCP carried higher odds of death than EC and PA was associated with higher odds of death than EC and ERCP (Table 2).

Among the older cohort of patients, stratified by 10-year age intervals, the effect of age on the rate of death was dependent on the type of procedure performed. In comparison with patients 60–69 years old, the odds of in-hospital death after EC were 2.65-fold higher in the 70- to 79-year-old group and 4.82-fold higher in patients 80 years of age or older. However, in patients undergoing ERCP, the age had a much smaller impact on the rate of death; corresponding values were, respectively, 1.16-fold and 1.36-fold, and only the latter change was statistically significant. Moreover, there was no difference in the rate of death following the PA treatment among the three age groups. In comparison between the groups of 70- to 79-year-old patients and those aged 80 years or older, higher mortality was noted only in the EC group, but not in the ERCP and PA groups

(Supplementary Table 2). When comparing patients by 10-year age intervals, patients aged 60–69 years of age undergoing ERCP only had an increased in-hospital mortality rate 7.30 times higher than those undergoing EC. Patients undergoing PA in this age group had a 100.89 times higher risk of in-hospital mortality compared to those undergoing EC. In patients aged 70–79, ERCP only was associated with a 2.95-fold higher in-hospital mortality than those undergoing EC. PA in this age group was associated with a 25.74-fold higher risk of in-hospital death when compared to EC. In the 80+ age group of patients, those who underwent ERCP only had a higher mortality rate of 2.03-fold higher mortality rate than the EC group. Patients in this age group undergoing PA had a 17.24-fold higher in-hospital death rate than those undergoing EC (Table 2).

A patient's gender did not affect the rate of death after EC, ERCP or PA, regardless whether all patients 60 years or older were considered together or were stratified according to their age using the 10-year intervals. The overall pattern of the impact of the type of procedure on the risk of death, with PA being associated with the highest odds, followed by ERCP and EC, was not changed when the analysis was performed separately for male and female patients (Supplementary Table 3).

Post-operative hospital length of stay

The length of stay in the hospital after the treatment differed between patients aged 60 years or older and the younger group (Table 3 and Supplementary Table 4). The unadjusted length of stay was 22% (7.8 vs 6.1 days) and 11% (7.2 vs 6.5 days) longer in older patients undergoing EC and ERCP, respectively. In contrast, older patients subjected to PA were characterized by 16% shorter hospital stay (15.5 vs 18.4 days) than the younger group treated by the same protocol. In patients 60 years or older, ERCP was associated with shorter length of stay than EC and PA in all age groups including 60–69, 70–79 and 80+ age groups; the latter procedure was characterized by almost two-fold longer hospital stay than EC and ERCP (Table 3).

Table 2. In-hospital mortality

Age, years	Treatment	No. of patients	Deaths, n (%)	Odds ratio (95% CI) ^a	P-value
<60	EC	27 597	27 (0.10)	Reference	–
	ERCP	17 357	85 (0.49)	6.37 (3.77, 10.76)	<0.001
	PA	341	38 (11.14)	111.25 (60.51, 204.52)	<0.001
≥60	EC	20 462	156 (1.21)	Reference	–
	ERCP	21 938	459 (2.09)	3.07 (2.46, 3.85)	<0.001
	PA	938	177 (18.87)	29.97 (22.95, 39.15)	<0.001
60–69	EC	7453	19 (0.25)	Reference	–
	ERCP	6279	100 (1.59)	7.30 (4.17, 12.77)	<0.001
	PA	244	52 (21.31)	100.89 (54.70, 186.07)	<0.001
70–79	EC	7596	58 (0.76)	Reference	–
	ERCP	7541	154 (2.04)	2.95 (2.04, 4.28)	<0.001
	PA	313	52 (16.61)	25.74 (16.22, 40.85)	<0.001
≥80	EC	5413	79 (1.46)	Reference	–
	ERCP	8118	205 (2.53)	2.03 (1.46, 2.83)	<0.001
	PA	381	73 (19.16)	17.24 (11.47, 25.90)	<0.001

ERCP, endoscopic retrograde cholangiopancreatography; EC, ERCP followed by cholecystectomy; PA, percutaneous aspiration; CI, confidence interval.

^aAdjusted for age, gender, ethnicity (white/others), major operating room procedure (yes/no), ischemic heart disease, heart failure, chronic obstructive pulmonary disease and cancer.

Table 3. Post-operative hospital length of stay (LOS)

Age, years	Treatment	No. of patients	LOS, days	Odds ratio (95% CI) ^a	P-value
<60	EC	27 597	6.1 ± 4.9	Reference	–
	ERCP	17 357	6.5 ± 8.1	6.37 (3.77, 10.76)	<0.001
	PA	341	18.4 ± 19.6	12.16 (11.45, 12.87)	<0.001
≥60	EC	20 462	7.8 ± 5.9	Reference	–
	ERCP	21 938	7.2 ± 7.5	0.13 (–0.05, 0.31)	0.16
	PA	938	15.5 ± 14.4	8.06 (7.59, 8.54)	<0.001
60–69	EC	7453	7.1 ± 5.6	Reference	–
	ERCP	6279	7.0 ± 8.4	1.06 (0.72, 1.39)	<0.001
	PA	244	17.7 ± 16.4	10.99 (10.04, 11.94)	<0.001
70–79	EC	7596	7.8 ± 6.0	Reference	–
	ERCP	7541	7.2 ± 7.2	0.22 (–0.06, 0.51)	0.13
	PA	313	16.7 ± 15.6	9.42 (8.62, 10.22)	<0.001
≥80	EC	5413	8.7 ± 6.0	Reference	–
	ERCP	8118	7.2 ± 7.3	–1.03 (–1.35, –0.71)	<0.001
	PA	381	13.4 ± 11.9	4.58 (3.84, 5.32)	<0.001

ERCP, endoscopic retrograde cholangiopancreatography; EC, ERCP followed by cholecystectomy; PA, percutaneous aspiration.

^aAdjusted for age, gender, ethnicity (white/others), major operating room procedure (yes/no), ischemic heart disease, heart failure, chronic obstructive pulmonary disease and cancer.

Among the patients undergoing the EC treatment, those aged 80 years or more had the longest duration of stay in the hospital after surgery, followed by the 70- to 79-year-old and 60- to 69-year-old patients. The differences between these three age groups were statistically significant. In contrast, the length of stay after ERCP was not dependent on age. Patients undergoing PA who were aged 80 years or older were staying in the hospital for approximately 3 days (~25%) shorter period than patients aged 60–69 and 70–79 years (Supplementary Table 5).

When analysis in the combined group of older patients was performed separately for men and women, the length of stay continued to be shortest after ERCP and longest after PA in both sexes. Of relevance, females 60 years or older had a shorter hospital stay following any type of treatment than men. However, when the patients were stratified according to their age using the 10-year intervals, the gender difference was present only in patients 60–69 years old, but not in patients aged 70–79 and more than 80 years (Supplementary Table 6).

Readmission related to gallbladder disease

For this analysis, data of patients admitted in 2010 and followed up until 2014 were utilized. There were no statistically significant differences in the rates of hospital readmission due to complications of gallbladder disease among those patients who underwent ERCP, those who underwent ERCP with cholecystectomy and those who were subjected to PA in any of the age groups studied (Table 4 and Supplementary Table 7). In addition, neither age nor gender had an effect on the fraction of patients that had to be readmitted (Supplementary Tables 8 and 9).

Discussion

The results of the present study indicate that the age of the patient is a significant factor determining the likelihood of death and the length of hospital stay after any type of procedure of gallstones removal. In a manner independent of the patient's age, PA is associated with the highest risk of death and length

Table 4. Hospital readmission after the treatment

Age, years	Treatment	No. of patients	No. of revisits	Revisiting patients, n (%)	Change, % (95% CI) ^a	P-value
<60	EC	4203	341	286 (6.80)	Reference	–
	ERCP	2527	173	153 (6.05)	–18.3 (–45.2, 21.8)	0.32
	PA	53	6	6 (11.32)	42.4 (–29.4, 187.6)	0.32
≥60	EC	3196	251	217 (6.79)	Reference	–
	ERCP	3364	275	232 (6.90)	19.0 (–13.9, 64.5)	0.29
	PA	153	12	10 (6.54)	15.6 (–28.1, 85.9)	0.55
60–69	EC	1189	85	74 (6.22)	Reference	–
	ERCP	1020	82	65 (6.37)	3.4 (–39.2, 75.7)	0.90
	PA	41	6	5 (12.20)	74.4 (–25.1, 306.2)	0.20
70–79	EC	1164	99	87 (7.47)	Reference	–
	ERCP	1061	87	75 (7.07)	31.6 (–24.4, 129.0)	0.33
	PA	43	1	1 (2.33)	–14.8 (–64.7, 105.6)	0.72
≥80	EC	843	67	56 (6.64)	Reference	–
	ERCP	1283	106	92 (7.17)	16.7 (–36.5, 114.4)	0.62
	PA	69	5	4 (5.80)	6.9 (–51.4, 135.3)	0.87

ERCP, endoscopic retrograde cholangiopancreatography; EC, ERCP followed by cholecystectomy; PA, percutaneous aspiration.

^aAdjusted for age, gender, ethnicity (white/others), major operating room procedure (yes/no), initial admission month (January through December), ischemic heart disease, heart failure, chronic obstructive pulmonary disease and cancer at the time of initial admission.

of stay, while the EC with the lowest mortality and ERCP with the shortest length of stay. Neither age of the patient nor the type of procedure affects the likelihood of necessity for hospital readmission for issues related to gallbladder disease. A patient's sex does not affect the odds of death after the treatment and the probability of being readmitted to the hospital. However, in patients aged between 60 and 79 years, the female gender predicts a shorter duration of stay in the hospital.

Additional relevant information was obtained when sub-analysis by age group was performed. Although mortality was found to be significantly higher in ERCP compared to EC in patients 60–79 years old, death rates were found to be comparable between these two protocols in patients more than 80 years old. Therefore, ERCP with cholecystectomy was found to be more beneficial than ERCP alone for patients of all age groups. Of note, a similar conclusion was reached in a study by Yasui *et al.* [43], who found a comparable rate of complications and recurrence of stones between patients who did and did not undergo cholecystectomy.

Several other studies provide information relevant to the interpretation of the current results. The rate of conversion to open surgery was shown to be highest in the population of octogenarians [45], which may be an additional factor contributing to higher mortality and longest in-hospital stay reported here for the oldest group of subjects. In another study, data obtained in patients aged more than 65 years indicated that the relapse of gallstone-related disease was two times more frequent in ERCP patients than in those undergoing cholecystectomy [46]. A much smaller, 16.8%, difference was seen in our analysis, and it did not reach statistical significance; the reason for this discrepancy remains to be established. In agreement with our results, a study including 152 patients did not find differences in the rate of complications following cholecystectomy between a group of older (average age 78 years) and younger (average age 68 years) patients [47]. Finally, it has been reported that age over 65 years is strongly associated with a higher probability of bile duct injury [48]; this might have been an additional factor contributing to longer in-hospital stay of older patients documented in the current study.

A shorter hospital stay was observed in patients after ERCP compared to EC. This contradicts the findings of a meta-

analysis of eight trials that showed comparable results between ERCP and EC [18]. Previous studies also reported that the number of retained stones is lower when surgical treatment is done [17, 18]. However, the present work does not support this notion, since readmission rates were found to be comparable between ERCP and EC. The readmission rate was only 7% even if the stones were removed via ERCP. It must be noted, however, that this rate is considerably lower in comparison with a study by Bergman *et al.* [15], in which a third of the patients experienced a recurrence of the disease within 2 months.

The accumulated data indicate that the management of cholelithiasis with associated complications poses a challenge in elderly patients. The clinical relevance of the finding of the current analysis is further broadened by the fact that the prevalence of gallstone disease increases with age [21, 49] and the human population is aging; the number of people aged 65 years or more is predicted to double by 2050 [20]. A combination of these two trends can be expected to result in a dramatic increase in the incidence of gallbladder disease in the near future. Therefore, the paucity of data on the clinical outcomes of different types of treatment is disconcerting. The only published study involving a large number of patients from multiple healthcare establishments provided valuable information regarding the impact of the age of patients on clinical outcomes but failed to analyse the contribution of the type of procedure employed [49]. Also, the important question of whether the patient's gender affects the outcome was not addressed.

The available data on gender differences in the outcomes of the treatment of gallbladder disease are conflicting. A study utilizing the large HCUP-NIS database documented that women admitted with cholecystitis had lower in-hospital mortality than men and shorter length of in-hospital stay [50]. However, the women included in that study were younger and had fewer comorbidities than men, and the racial composition was different in the two sex groups. These variables might have influenced the gender difference in mortality, which was not detected in our study. In agreement with the present work, the length of post-operative hospital stay was shown to be longer in men when patients undergoing laparoscopic cholecystectomy were analysed [47]. Another study, also focused on laparoscopic

cholecystectomy, failed to identify gender differences in clinical outcomes of the procedure [51]. In contrast, in a North Korean population, complications of the laparoscopic protocol, such as hydrops, empyema, pericholecystic abscess and gangrene, were more frequent in males [52]. It is unclear whether this difference is related to the ethnicity of the patients or reflects the specific types of complications that were taken into account. In this regard, male gender was shown to be associated with a higher incidence of local post-operative complications of laparoscopic cholecystectomy, but not with systemic complications [33]. It should be emphasized that the present study has the advantage of analysing the gender difference in the context of age and the type of procedure performed. Such a comprehensive approach to the question of gender differences in the outcomes of gallbladder disease treatment was never before applied.

Limitations of the current study have to be acknowledged. The specific type of complications associated with cholelithiasis was not taken into account. By design, the study did not include outpatient cholecystectomy procedures, which are likely to include less complicated cases [40]. It must also be noted that, because of the large size of the patient population, not all statistically significant findings must be inevitably clinically meaningful. Lastly, the skills of the medical personnel could affect patient outcomes. However, the large number of facilities that generated the data deposited in the HCUP-NIS database minimizes the impact of this potential variability. The nature of this database prevents yielding specific information about the procedures involved and other comorbidities that may have contributed to mortality of the patients included in the study. This creates inherent bias that is unfortunately unavoidable due to the nature of the database.

Supplementary data

Supplementary data is available at *Gastroenterology Report* online.

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Conflict of interest

None declared.

References

- Shabanzadeh DM, Sørensen LT, Jørgensen T. Gallstone disease and mortality: a cohort study. *Int J Public Health* 2017;**62**: 353–60.
- Stinton LM, Shaffer EA. Epidemiology of gallbladder disease: cholelithiasis and cancer. *Gut Liver* 2012;**6**:172–87.
- Ruhl CE, Everhart JE. Gallstone disease is associated with increased mortality in the United States. *Gastroenterology* 2011;**140**:508–16.
- Peery AF, Crockett SD, Barritt AS et al. Burden of gastrointestinal, liver, and pancreatic diseases in the United States. *Gastroenterology* 2015;**149**:1731–41.
- Shabanzadeh DM. Incidence of gallstone disease and complications. *Curr Opin Gastroenterol* 2018;**34**:81–9.
- Mishra T, Lakshmi KK, Peddi KK. Prevalence of cholelithiasis and choledocholithiasis in morbidly obese South Indian patients and the further development of biliary calculus disease after sleeve gastrectomy, gastric bypass and mini gastric bypass. *Obes Surg* 2016;**26**:2411–7.
- Rahal MA, Rammal MO, Karaoui W et al. Predictors of bile tree pathology in patients presenting with gallbladder disease. *Eur J Gastroenterol Hepatol* 2017;**29**:1017–21.
- Paci P, Mayo NE, Kaneva PA et al. Determinants of variability in management of acute calculous cholecystitis. *Surg Endosc* 2018;**32**:1858–66.
- Hu KC, Chu CH, Wang HY et al. How does aging affect presentation and management of biliary stones? *J Am Geriatr Soc* 2016;**64**:2330–5.
- Ukkonen M, Siiki A, Antila A et al. Safety and efficacy of acute endoscopic retrograde cholangiopancreatography in the elderly. *Dig Dis Sci* 2016;**61**:3302–8.
- Molvar C, Glaenger B. Choledocholithiasis: evaluation, treatment, and outcomes. *Semin Intervent Radiol* 2016;**33**:268–76.
- Zippi M, De Felici I, Pica R et al. Comparison of endoscopic retrograde cholangiopancreatography between elderly and younger patients for common bile duct stones. *Clin Ter* 2013;**164**:e353–8.
- Rustagi T, Jamidar PA. Endoscopic retrograde cholangiopancreatography (ERCP)-related adverse events. *Gastrointest Endosc Clin N Am* 2015;**25**:107–21.
- Loor MM, Morancy JD, Glover JK et al. Single-setting endoscopic retrograde cholangiopancreatography (ERCP) and cholecystectomy improve the rate of surgical site infection. *Surg Endosc* 2017;**31**:5135–42.
- Bergman S, Al-Bader M, Sourial N et al. Recurrence of biliary disease following non-operative management in elderly patients. *Surg Endosc* 2015;**29**:3485–90.
- Trust MD, Sheffield KM, Boyd CA et al. Gallstone pancreatitis in older patients: are we operating enough? *Surgery* 2011;**150**: 515–25.
- Huang RJ, Barakat MT, Girotra M et al. Practice patterns for cholecystectomy after endoscopic retrograde cholangiopancreatography for patients with choledocholithiasis. *Gastroenterology* 2017;**153**:762–71.
- Dasari BV, Tan CJ, Gurusamy KS et al. Surgical versus endoscopic treatment of bile duct stones. *Cochrane Database Syst Rev* 2013;CD003327.
- Kageoka M, Watanabe F, Maruyama Y et al. Long-term prognosis of patients after endoscopic sphincterotomy for choledocholithiasis. *Dig Endosc* 2009;**21**:170–5.
- He W, Goodkind D, Kowal P, U.S. Census Bureau. *An Aging World: 2015. International Population Reports*, P95/16–1, U.S. Washington, DC: Government Publishing Office, 2016.
- Agrusa A, Romano G, Frazzetta G et al. Role and outcomes of laparoscopic cholecystectomy in the elderly. *Int J Surg* 2014;**12**(Suppl 2): S37–9.
- Etzioni DA, Liu JH, O'Connell JB et al. Elderly patients in surgical workloads: a population-based analysis. *Am Surg* 2003;**69**: 961–5.
- Laor A, Tal S, Guller V et al. The Charlson Comorbidity Index (CCI) as a mortality predictor after surgery in elderly patients. *Am Surg* 2016;**82**:22–7.
- Piccirillo JF, Vlahiotis A, Barrett LB et al. The changing prevalence of comorbidity across the age spectrum. *Crit Rev Oncol Hematol* 2008;**67**:124–32.
- Turrentine FE, Wang H, Simpson VB et al. Surgical risk factors, morbidity, and mortality in elderly patients. *J Am Coll Surg* 2006;**203**:865–77.
- Sandblom G, Videhult P, Crona Guterstam Y et al. Mortality after a cholecystectomy: a population-based study. *HPB (Oxford)* 2015;**17**:239–43.

27. Scollay JM, Mullen R, McPhillips G et al. Mortality associated with the treatment of gallstone disease: a 10-year contemporary national experience. *World J Surg* 2011;**35**:643–7.
28. Pålsson S, Saliba G, Sandblom G. Outcome after cholecystectomy in the elderly: a population-based register study. *Scand J Gastroenterol* 2016;**51**:974–8.
29. Nimptsch U, Mansky T. Deaths following cholecystectomy and hemiotomy. *Dtsch Arztebl Int* 2015;**112**:535–43.
30. Halbert C, Altieri MS, Yang J et al. Long-term outcomes of patients with common bile duct injury following laparoscopic cholecystectomy. *Surg Endosc* 2016;**30**:4294–9.
31. Kiu KT, Chen HL, Huang MT et al. Outcome analysis of patients with gallstone disease receiving cholecystectomy: a population-based cohort study. *Digestion* 2017;**95**:132–9.
32. Caglia P, Costa S, Tracia A et al. Can laparoscopic cholecystectomy be safely performed in the elderly? *Ann Ital Chir* 2012;**83**: 21–4.
33. Giger UF, Michel JM, Opitz I et al. Risk factors for perioperative complications in patients undergoing laparoscopic cholecystectomy: analysis of 22, 953 consecutive cases from the Swiss Association of Laparoscopic and Thoracoscopic Surgery database. *J Am Coll Surg* 2006;**203**:723–8.
34. Kakucs T, Harsányi L, Kupcsulik P et al. The role of laparoscopy in cholecystectomy in patients 80 years old and older [in Hungarian]. *Orv Hetil* 2016;**157**:185–90.
35. Lu Y, Chen L, Jin Z et al. Is ERCP both effective and safe for common bile duct stones removal in octogenarians? A comparative study. *Aging Clin Exp Res* 2016;**28**:647–52.
36. Allen NL, Leeth RR, Finan KR et al. Outcomes of cholecystectomy after endoscopic sphincterotomy for choledocholithiasis. *J Gastrointest Surg* 2006;**10**:292–6.
37. Santaş Ü, Üstündağ Y, Baron TH. Prevention of post-ERCP pancreatitis. *Turk J Gastroenterol* 2011;**22**:449–63.
38. Çakır M, Küçükkartallar T, Tekin A et al. Does endoscopic retrograde cholangiopancreatography have a negative effect on laparoscopic cholecystectomy? *Ulus Cerrahi Derg* 2015;**31**:128–31.
39. Cinar H, Ozbalci GS, Tarim IA et al. Factors affecting the conversion to open surgery during laparoscopic cholecystectomy in patients with cholelithiasis undergoing ERCP due to choledocholithiasis. *Ann Ital Chir* 2017;**88**:229–36.
40. Nielsen LB, Harboe KM, Bardram L. Cholecystectomy for the elderly: no hesitation for otherwise healthy patients. *Surg Endosc* 2014;**28**:171–7.
41. Qasaimeh GR, Banihani MN. Laparoscopic cholecystectomy in the elderly and young: a comparative study. *Hepatogastroenterology* 2012;**59**:22–5.
42. Ahn KS, Kim YH, Kang KJ et al. Impact of preoperative ERCP on laparoscopic cholecystectomy: a case-controlled study with propensity score matching. *World J Surg* 2015;**39**: 2235–42.
43. 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.
44. Katabathina VS, Zafar AM, Suri R. Clinical presentation, imaging, and management of acute cholecystitis. *Tech Vasc Interv Radiol* 2015;**18**:256–65.
45. Lee W. Cholecystectomy in octogenarians: recent 5 years' experience. *Korean J Hepatobiliary Pancreat Surg* 2013;**17**:162–5.
46. García-Alonso FJ, de Lucas Gallego M, Bonillo Cambrodón D et al. Gallstone-related disease in the elderly: is there room for improvement? *Dig Dis Sci* 2015;**60**:1770–7.
47. Ambe PC, Weber SA, Christ H et al. Primary cholecystectomy is feasible in elderly patients with acute cholecystitis. *Aging Clin Exp Res* 2015;**27**:921–6.
48. Aziz H, Pandit V, Joseph B et al. Age and obesity are independent predictors of bile duct injuries in patients undergoing laparoscopic cholecystectomy. *World J Surg* 2015;**39**:1804–8.
49. Kuy S, Sosa JA, Roman SA et al. Age matters: a study of clinical and economic outcomes following cholecystectomy in elderly Americans. *Am J Surg* 2011;**201**:789–96.
50. Dua A, Dua A, Desai SS et al. Gender based differences in management and outcomes of cholecystitis. *Am J Surg* 2013;**206**: 641–6.
51. Bazoua G, Tilston MP. Male gender impact on the outcome of laparoscopic cholecystectomy. *JLS* 2014;**18**:50–4.
52. Lee HK, Han HS, Min SK et al. Sex-based analysis of the outcome of laparoscopic cholecystectomy for acute cholecystitis. *Br J Surg* 2005;**92**:463–6.