World J Surg (2018) 42:73–81
DOI 10.1007/s00268-017-4147-8

ORIGINAL SCIENTIFIC REPORT

How Safe is Performing Cholecystectomy in the Oldest Old? A 15-year Retrospective Study from a Single Institution

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Published online: 24 July 2017

Abstract

Background Globally, the number of people aged 80 years or over, the "oldest old," is the fastest growing population group. Because of the strong association between age and gallstone disease, both prevalence and incidence of this disease are increasing. The feasibility of the cholecystectomy in octogenarians has been evaluated in several studies that confirmed the safety of the operation. However, the safety of this procedure in nonagenarians is still controversial. The aim of this study was to evaluate the safety of cholecystectomies in nonagenarians and identify related predictors for postoperative hospital length of stay (LOS) and in-hospital mortality up to 30 days postoperatively.

Methods More than 500 cholecystectomies, both open and laparoscopic, were performed between January 2000 and September 2015 at our institution in patients 80 years and older. These statistics include both elective and emergent admissions. A retrospective review of charts over the last 15 years was conducted to compare mortality and length of postoperative stay among two patient groups: 319 octogenarians and 36 nonagenarians. Parameters evaluated include demographics, surgical presentation, American Society of Anesthesiologists (ASA) score, main diagnosis, comorbidities, type of surgery performed, LOS and in-hospital mortality. All data were analyzed with STATA (v.13) software, using a multivariate logistic regression after determining the statistically significant variables through a stepwise regression.

Conclusions We found out that being nonagenarian, compared to octogenarian, is not a significant risk factor in terms of LOS and in-hospital mortality within 30 days postoperatively. Despite that, the mortality rate among nonagenarians is still remarkably high as almost every patient was admitted in an emergent setting. The most remarkable predictor for mortality among the two groups was an "afternoon/night emergency" surgical presentation (OR 25.5, CI 1.53–42.35, $p = 0.02$). Thus, the surgical emergency management for gallbladder disease at our institution should be critically reevaluated. Performing the procedure in laparoscopy predicted a significant reduction (-5 days, CI -8.5 to -1.4, $p = 0.006$) of LOS, while presenting with "gallbladder and bile duct stones" (+6.3 days, CI 1.5–11.1, $p = 0.01$) or "acalculous cholecystitis" (+4.7 days, CI 0.4–9.2, $p = 0.03$) had the opposite effect. Despite the remarkable mortality rate of our series, being nonagenarian should not be considered as a reason to avoid gallbladder surgery in case of need. Our study suggests that nonagenarians are more suitable surgical candidates than may have previously expected.

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Introduction

Data from the most recent United Nations (UN) aging reports (2013 and 2015) [1, 2] clearly confirm the ongoing worrisome scenario predicted in recent years as the "Silver Tsunami" [3–6].

Globally, the "*oldest old,*" defined by the UN as "people aged 80 years or over" [1], is the fastest growing population group. In 2015, there were almost a billion of "old" people, defined as any women or men aged 60 or over, worldwide.

Aging is taking place in the world's adult population and within the older population itself. This is a result of both improved longevity and aging of large cohorts, that is, the "baby boomers" born during the post-World War II period. The share of the older population that is aged 80 years or over has already doubled from 7% in 1950 to 14% in 2015 [19]. This proportion of "oldest old" is expected to reach 20% in 2050 and 28% in 2100. If this projection is realized, there will be 830 million persons aged 80 years or over by the end of the century, seven times as many as in 2013.

The United Nations emphasize that changes are needed around the globe to continue adapting health systems to serve a growing number of older persons and to maximize health and well-being at all ages [2].

According to the NHANES III [7] (National Health and Nutrition Examination Survey), over 20 million Americans (6.3 million men and 14.2 million women aged 20–74) are estimated to have gallbladder disease (defined as the presence of gallstones on transabdominal ultrasound or a history of cholecystectomy).

Gallstone disease is one of the most common and costly of all digestive diseases. Large ultrasound-based studies from Europe have characterized both gallstone prevalence and incidence. As an example, in the Multicenter Italian Study of Cholelithiasis (MICOL) the overall rate of gallstone disease was 18.8% in women and 9.5% in men [8]. In all genders, age was found to be the key risk factor for developing gallstone disease [8–10].

Considering that prevalence of gallstone disease is over 80% in nonagenarians [11] and the rapid aging rate of the global population, we may assume that the overall prevalence of gallstone disease will soon increase and thus there will be a larger demand for gallbladder surgery in the near future.

The feasibility of the cholecystectomy in octogenarians was evaluated in different studies that confirmed the safety of the operation [8, 11–24]. However, we were able to find just one study among scientific literature that supported the safety of cholecystectomy [11] in a group of nonagenarians. No similar studies were completed ever since; therefore, the safety of gallbladder surgery on such a high-risk age group is still controversial.

In light of the most recent UN aging reports [1, 2] and the epidemiology of gallbladder disease, we believed that it would be both interesting and useful to examine our clinical records from the past 15 years (i.e., from 2000 to 2015) to understand what have been the outcomes of patients aged 80 years or over at our institution who underwent cholecystectomy. By critically analyzing our own data and sharing the results, we hope to provide a significant contribution to improve the surgical management of these patients and thus be more prepared for approaching "Silver Tsunami" [3–6].

Methods

More than 500 cholecystectomies were performed at the Sant'Orsola-Malpighi Hospital between January 2000 and September 2015 on patients aged 80 years or over. These were performed by different surgeons in thirteen "General Surgery" and "Surgical Emergency" units that varied throughout the 15-year time lapse. To create consistent data, those who received a secondary (i.e., "incidental") cholecystectomy (e.g., concomitant cholecystectomy to colon cancer excision) were excluded, ensuring that the primary reason for surgery was exclusively a gallbladder and/or biliary tree issue. Ultimately, 355 patients with a main diagnosis of gallbladder and/or biliary tract disease and who underwent gallbladder surgery at some time in their clinical history were included in this retrospective record review.

In our study, age group was the primary independent variable. The 355 patients were divided into two groups according to age at admission: 319 octogenarians (aged 80–89) and 36 nonagenarians (aged 90 or older).

The parameters that were recorded from the chart review were demographics, surgical presentation, ASA score, main diagnosis, comorbidities, type of cholecystectomy performed (open or laparoscopic), postoperative hospital length of stay (LOS) and in-hospital mortality within 30 days postoperatively.

Each chart also recorded the degree of urgency for cholecystectomy at presentation. Surgical presentation was stratified into three possible variables:

- *Elective* Planned surgical procedure, no urgency required for the case.
- *Urgency* Urgent treatment needed for the patient during morning shift.
- *Afternoon/night urgency* Urgent treatment needed during afternoon/night shifts.

To evaluate the impact of comorbidities on LOS and in-hospital mortality, we classified patients into one or more comorbidity "classes" as follows:

1. Cardiovascular comorbidities which included congestive heart failure, previous ischemic heart disease (chronic and acute), previous transitory ischemic attack, heart bundle branch, valvulopathy, deep vein thrombosis (and pulmonary embolism) and conditions treated with an implanted artificial cardiac pacemaker.*
2. Pulmonary comorbidities which included COPD (chronic obstructive pulmonary disease), previous lung surgery, previous and/or current lung cancer, pulmonary failure, pulmonary fibrosis, chronic bronchitis and pleural effusion.
3. Renal comorbidities which included chronic renal failure (with and without hemodialysis ongoing treatment), acute renal failure and symptomatic renal cysts.
4. Diabetic comorbidities which included diabetes mellitus type I and II.

*Paroxysmal atrial fibrillation was not included in this group as it was considered a minor and largely diffuse comorbidity that would have likely disrupted the statistical impact of the cardiovascular comorbidity class.

In our statistical analysis, we aimed to compare the data of the two groups to evaluate what were the main predictors that influenced the cholecystectomy results in terms of LOS and in-hospital mortality.

A secondary endpoint evaluated whether there had been a statistically significant improvement in the surgical management of such patients during the 15-year time frame we analyzed. This analysis compared the outcomes of the surgical procedures in terms of LOS and in-hospital mortality against the year the patient underwent the procedure.

To refine our results we used a stepwise logistic regression selecting only the most relevant predictors (threshold: $p < 0.10$) to include in the statistical model. Age, type of intervention, ASA score, diagnosis and comorbidities were the most important predictors and were thus taken into account in the final multivariate model. We also considered gender, as it is one of the most important socio-demographic characteristics.

Data were then evaluated using a multivariate logistic regression for the mortality outcome and multivariate linear regression for LOS.

STATA version 13 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP) was used for statistical analysis. A $p < 0.05$ was considered as statistically significant.

Results

In Table 1, we provide a concise descriptive analysis of our sample that includes demographic data, along with key clinical and surgical information. Our population of 355 individuals included 136 males (38.3% of total) and 219 females (61.69% of total) (Table 1). Patients included in the octogenarian group (group1) were $n = 319$ (89.85% of total), while in the nonagenarian group (group2) n = 36 (10.14% of total).

The overall in-hospital mortality rate was 4.78% ($n = 17$). Of these, 10 were among the octogenarian group (3.13% of group 1) and seven were in the nonagenarian group (19.44% of group 2) (Table 1). Of the 17 deaths, 15

Table 1 Descriptive analysis of the selected population

Variable name	Patients aged 80–89 years ($N = 319$)	Patients aged 90 years or more ($N = 36$)	p value
Sex (F/M)	61%	69%	$p = 0.09$
Surgical presentation (%)			
Afternoon/evening emergency	55 (17%)	18 (50%)	$p < 0.0001$
Urgency	175 (54%)	16 (44%)	
Election	89 (27%)	2 (5%)	
Mean LOS (*d*)	11 ± 14.1	22 ± 16.4	$p < 0.0001$
Main diagnosis			
Gallstones with cholecystitis	157 (49%)	14 (38%)	$p = 0.07$
Gallbladder and bile duct stones	35 (10%)	4 (11%)	$p = 0.003$
Gallstones without cholecystitis	62 (19%)	5 (13%)	$p = 0.001$
Acalculous cholecystitis	48 (15%)	7 (19%)	$p = 0.06$
Gallbladder perforation	13 (4%)	4 (11%)	$p = 0.51$
Other	4 (1%)	2 (5%)	$p = 0.49$
Type of procedure (*N*)			
Open cholecystectomy	212 (66%)	34 (94%)	$p = 0.0006$
Laparoscopic cholecystectomy	107 (33%)	2 (5%)	
In-hospital mortality (*N*)	10/319 (3.13%)	7/36 (19.4%)	$p < 0.0001$

were cardiovascular arrests, one was sudden death, and one was due to sepsis.

Mean LOS for the entire population was 12 days postoperatively, with a mode of 2 days. The mean LOS for octogenarians was 11 ± 14.1 days and 20 ± 16.4 days for nonagenarians (Table 1).

Six main diagnoses indicating gallbladder disease were considered (Table 1): "acalculous cholecystitis" ($n = 55$, 15.5% of total), "gallstones with cholecystitis" ($n = 171$, 48.2% of total), "gallbladder and bile duct stones" ($n = 36$, 10.1% of total), "gallstones without cholecystitis" ($n = 67$, 18.9% of total), "gallbladder perforation" ($n = 17$, 4.8% of total) and "other" ($n = 8$, 2.2% of total, almost all identified with a main diagnosis of gallbladder hydrops).

Only three patients among all the case examined were diagnosed with cholangitis during their hospital stay. Considering the extremely small dimensions of such sample compared to the 355 total patients, we believed that from a statistical point of view it would not have been useful focusing on patients presenting with cholangitis.

The procedures were either open ($n = 246$, 69.3% of total) or laparoscopic ($n = 109$, 30.7% of total) (Table 1).

However, the vast majority of the 36 patients diagnosed with "gallbladder and bile duct stones" were further managed with postoperative ERCP.

The surgical presentation at the time of the procedure was classified as elective ($n = 188$, 52.9% of total), afternoon/night urgency ($n = 73$, 20.6% of total) or urgency ($n = 94$, 26.5%) (Table 1).

The most common patient comorbidity was cardiovascular comorbidities ($n = 167$, 47% of the total), followed by pulmonary comorbidities ($n = 144$, 40.6% of the total), diabetic comorbidities ($n = 55$, 15.5% of the total) and renal comorbidities ($n = 50$, 14.1% of the total). The mean number of comorbidity classes assigned to the octogenarian group was 1.2 ± 0.94, while in the nonagenarian group it was 1.3 ± 0.91.

An increased in-hospital mortality using a univariate test was associated with age group, type of surgery, ASA score, main diagnosis and number of comorbidity classes (Table 2). In the final statistical model, however, in-hospital mortality was not significantly higher in the nonagenarians group compared to the octogenarians group ($p = 0.830$) (Table 3).

The most important and significant predictor of in-hospital death identified with our multivariate model was "afternoon/night emergency surgery," with a highly significant result (OR 25 CI 95% 2.13–42.34, $p = 0.02$) (Table 3).

ASA score was a predictor in the crude analysis (Table 2) but was not a predictor in the final adjusted multivariate model (Table 3). Gallbladder perforation appeared to be weakly and not significantly associated with a higher mortality rate, even in the adjusted multivariate analysis (OR 6.58 CI 95% 0.57–75.3, $p = 0.08$) (Table 3). The number of comorbidity classes identified in patients tripled their mortality risk in the crude analysis (Table 2), but statistical significance was not achieved in the multivariate analysis (Table 3).

Table 2 Outcomes for in-hospital mortality predictors—univariate crude results

Variable name	OR for mortality	CI 95%	p value
Age >90 years	8.3	2.9–24	$p < 0.001$
Surgical presentation	4.2	2.1–8.8	$p < 0.001$
ASA score	5.5	2.7–11.4	$p < 0.001$
Main diagnosis	2.3	1.5–3.5	$p = 0.03$
Comorbidities	3	1.7–5.3	$p = 0.02$
Laparoscopic procedure	0.89	0.56–2.43	$p =$ n.s.

Of note, we observed a progressive increase in the in-hospital mortality OR (0.6, 15, 25, 69, respectively, in patients with 1, 2, 3 or 4 concomitant comorbidity classes—Table 3), as the number of comorbidity classes increased. These results were nonsignificant, but may still represent a remarkable clinical parameter when patients are evaluated to be surgical candidates.

Laparoscopic procedure was not a predictor of in-hospital mortality, neither in the crude (Table 2) nor in adjusted analysis (Table 3).

Figure 1 presents the relationship between type of surgical presentation and in-hospital mortality risk, (*) with those presenting as "*elective*" representing a baseline ($y = 0$).

In the univariate regression test, an increased LOS was associated with age group, type of surgery, ASA score and main diagnosis (Table 4).

LOS was significantly higher by 10.7 days (CI 95%: 2.9–24) in the nonagenarians group, compared to the octogenarians group. However, the significance was not confirmed in the adjusted analysis (Table 4).

Although "surgical presentation" was identified as a predictor for increased LOS in the univariate model, this was not confirmed in the final adjusted model (Table 4).

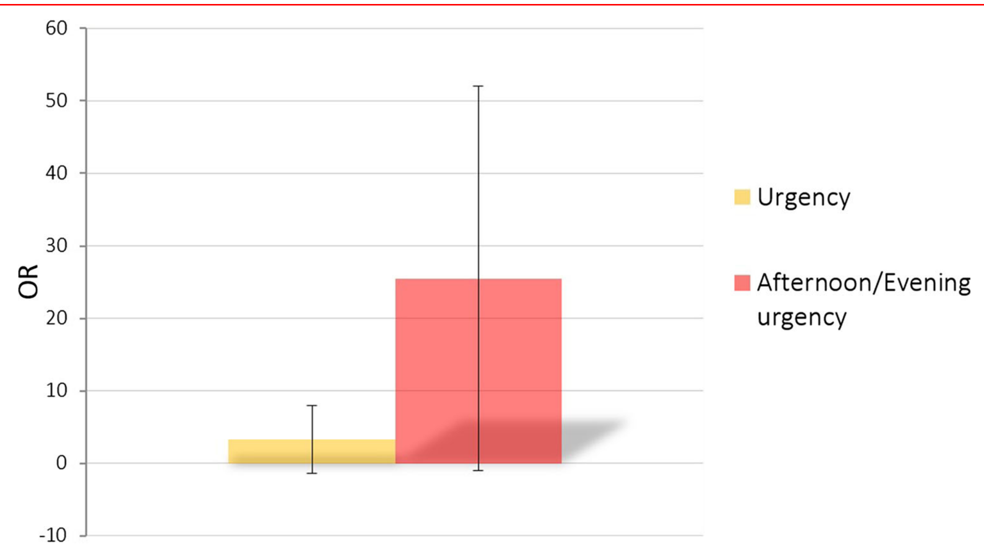
We may state the same for ASA score: The mean difference was remarkable (increase of 5.7 days per ASA score upgrade) and significant in the crude model; however, it was not confirmed in the final multivariate model (Table 4).

With the multivariate model (Table 4), a main diagnosis of "gallbladder and bile duct stones" and "acalculous cholecystitis" was associated with a significantly higher LOS by 6.3 days (CI 95%: 1.5–11.1, $p = 0.01$) and 4.7 days (CI 95%: 0.4–9.2, $p = 0.03$), respectively.

Table 3 Outcomes for in-hospital mortality predictors—multivariate adjusted results

Variable name	OR for mortality	CI 95%	*p* value
Age >90 years	1.03	0.76–1.04	$p =$ n.s.
Surgical presentation			
Emergency	3.29	0.2–55.05	$p =$ n.s.
Afternoon/night emergency	25.5	1.53–42.35	$p = 0.02$
ASA score	1.5	0.43–5.15	$p =$ n.s.
Main diagnosis			
Gallstones without cholecystitis	1.16	0.03–39.13	$p =$ n.s.
Acalculous cholecystitis	5.43	0.66–44.5	$p =$ n.s.
Gallbladder perforation	6.58	0.57–75.3	$p =$ n.s.
Number of comorbidity classes			
1	0.66	0.2–22.7	$p =$ n.s.
2	15.8	0.73–33.9	$p =$ n.s.
3	25.52	0.71–91.9	$p =$ n.s.
4	69.23	0.48-99.35	$p =$ n.s.
Laparoscopic procedure	0.22	0.02–6.28	$p =$ n.s.

Fig. 1 Mortality risk by surgical presentation (*) compared to the baseline ($y = 0$), represented by the "*elective*" surgical presentation



The laparoscopic procedure compared to the open one was found to decrease LOS by 8.9 days in the crude analysis. This outcome was adjusted to 5 days by the multivariate analysis while maintaining a high statistical significance (CI 95%: −8.5 to −4.3, $p = 0.006$) (Table 4).

In Fig. 2, we compared the mean difference (days) in LOS among predictors obtained from the multivariate regression analysis. For the "main diagnosis" variable, "gallstone with cholecystitis" was taken as baseline ($y = 0$), while the type of surgery variable used "open procedure" as the baseline for comparison against "laparoscopic procedure."

As for our secondary endpoint, we did not find any significant difference between the surgical outcomes in terms of both in-hospital mortality and LOS when categorizing patients by year of surgical procedure.

Discussion

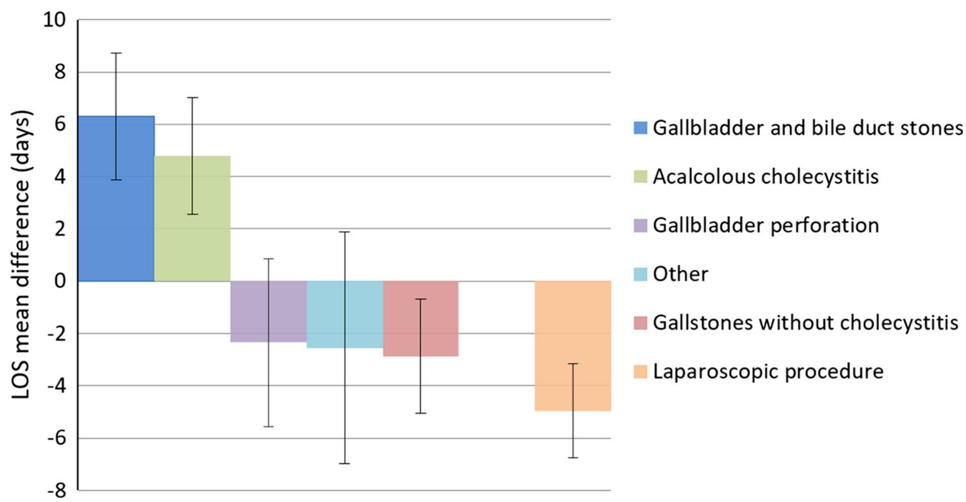
The present investigation evaluated the safety of gallbladder surgery among nonagenarians.

Our outcomes in terms of LOS are considerably longer compared to a study that involved almost four million Americans aged 80 or over who underwent emergency care related to general surgery issues, where the mean LOS was 4.50 days [25]. In a similar study that included subjects >65 year old, LOS was found to be 3 days on average

Table 4 Outcomes for LOS predictors—crude and adjusted analysis outcomes comparison

Variable	Mean difference (days)—crude analysis	CI 95%	p value	Mean difference (days)—adjusted analysis	CI 95%	p value
Age >90 years	10.7	2.9–24	$p < 0.0001$	1.84	−5.43–9.12	$p =$ n.s.
Surgical presentation	2.9	2.1–8.8	$p < 0.0001$	0.87	−2.5–5.7	$p =$ n.s.
ASA score	5.7	2.7–11.4	$p < 0.0001$	1.73	−0.98–4.45	$p =$ n.s.
Main diagnosis	1.7	1.5–3.5	$p < 0.0001$	4.43	1.2–10.4	$p = 0.03$
Gallbladder and bile duct stones	/	/	/	6.3	1.5–11.1	$p = 0.01$
Acalculous cholecystitis	/	/	/	4.7	0.4–9.2	$p = 0.03$
Laparoscopic procedure	−8.9	−12.1 to −5.7	$p < 0.0001$	-5	−8.5 to −1.4	$p = 0.006$

Fig. 2 LOS predictors



[26]. These differences with our data may be easily explained by the substantial portion of patients in the cited studies that did not actually receive a surgical procedure despite their acute conditions, thereby significantly diminishing their mean LOS.

Indeed, if we compare studies which analyze a smaller sample of patients more similar to ours, the mean LOS rises to 11 days [27, 28] and 12 days [29] postoperatively. These values are comparable to the mean LOS for our octogenarian group but are still considerably shorter than our nonagenarian group. Perhaps this reflects the complex management of these cases, compounded by the higher number of comorbidities.

Furthermore, our patients treated laparoscopically had a shorter LOS by 5 days compared to those who underwent open procedures. This is consistent with laparoscopic cholecystectomy being considered the "gold standard" for the surgical treatment of gallstone disease. Compared with open cholecystectomy, laparoscopic cholecystectomy reduces postoperative pain and significantly shortens hospital LOS and time away from work [16, 30–39].

Our data confirmed that laparoscopic procedure significantly shortened LOS; however, this may be related to patient selection as patients with worse disease presentation were more likely to undergo an open procedure. Indeed, in the nonagenarian group, almost all the procedures were open ($n = 34$, 94%). Many factors may explain why laparoscopy was not used in preference to open surgery. First of all in the early decade of the study, laparoscopy was not yet diffused or used at our institution, especially in an emergent setting and for elderly patients. Even in the latest years, often experienced laparoscopic attending surgeons were hardly available during afternoon/night shifts and the operations were performed by emergency surgeons or HBP surgeons with expertise in open surgery and low/moderate experience in laparoscopic surgery or laparoscopy for acute cholecystitis. Therefore, in such situations of high-risk acute cholecystitis with challenging technical issues and in elderly patients often with comorbidities, a routine open surgical approach was deemed to be safer, carrying lower risk of iatrogenic complications. On the contrary, laparoscopic surgery was the most performed ($n = 212$, 66%) in the octogenarian group. Indeed, this group was treated in election in 27% ($n = 89$) of cases compared to only 5% ($n = 2$) of the nonagenarian group.

Our statistical analysis showed that performing laparoscopy in the octogenarian group contributed to a shorter LOS compared to the nonagenarian group.

The total in-hospital mortality rate in our series was 5.1% (18 patients out of total). We should remember that this number includes patients aged 80 years and over who mostly underwent gallbladder surgery in an emergency setting.

In the literature, studies that evaluate mortality rates after emergency laparotomy procedures on patients aged 80 years and over report a mortality rates ranging between 20 and 24% [18, 27, 28, 40]. Such a large difference with our findings may be explained by considering that some of these studies included cases which present considerably higher mortality than primary gallbladder disease (e.g., surgery for ruptured abdominal aortic aneurysms).

Our mortality rate for the octogenarian group may be considered relatively low ($n = 11$, 3.4%) when compared to the most recent meta-analysis regarding gallbladder surgery in the elderly [14].

Unfortunately, the mortality rate among the nonagenarian group may appear to be elevated. Nevertheless, a study in the literature reported a mortality rate of 20.8% among 145 nonagenarians in the setting of emergency laparotomy procedures [29]. Our data should be interpreted in context of the relatively small sample of high-risk and multiple comorbidities emergency cases. From this point of view, it is difficult to make a scientific judgment if our mortality outcome falls within a reasonable interval. What we may state with certainty is that the large majority of our nonagenarian patients presented to the emergency department in an intolerable amount of pain, often after failure of antibiotics and/or pain medication therapy.

Planning to avoid or delay gallbladder surgery may sound as a reasonable plan in a very elderly population, but it was recently proved by Dr. Riall et al. that it produces more harm than benefit. In fact, their review of the US Medicare database of 29,818 elderly subjects with acute cholecystitis found a higher risk of mortality over the following two years in patients who were discharged without surgery compared to those who underwent cholecystectomy in the initial hospitalization (hazard ratio 1.56, 95% CI 1.47–1.65) [41].

Several studies in the literature support the fact that acute cholecystitis is an underestimated condition in the elderly and that too often the surgeon is not even consulted when the patient first presents in the emergency department [15]. Avoiding surgical treatment may lead to inappropriate discharges which promote multiple emergency readmissions, increased percentage of open procedures and also an additional payment of $7000, compared to early surgical management [41]. Moreover, evidence from large database reviews and randomized trials shows that cholecystectomy performed early during the initial hospitalization may be associated with reduced perioperative morbidity and mortality in some patients and reduced LOS and cost [16, 30–39].

Our mortality outcomes in the nonagenarians should make us reflect on what we may change today to improve our healthcare tomorrow. Considering the most recent UN aging reports and the epidemiology of gallbladder disease, we must expect increasing numbers of similar patients. Are we truly prepared to face such change from a surgical standpoint of view? In the approaching healthcare system, operating on subjects aged 90 years or over for a gallbladder disease will not be the exception, but the rule.

Our identification of comorbidities as predictors of LOS and in-hospital mortality is very similar to those founded by Rao et al. [42]. This group conducted a retrospective review on the American College of Surgeon's NSQIP (National Surgical Quality Improvement Program) database that included 15,248 patients older than 65 years of age who underwent elective laparoscopic cholecystectomy. Significant independent predictors of inpatient stay and mortality were identified: congestive heart failure, ASA class 4, bleeding disorder, COPD and renal failure requiring dialysis. A further study conducted on the NSQIP database evaluated outcomes following surgical treatment of acute cholecystitis in 5460 patients with and without diabetes [43]. Mortality among subjects with diabetes was significantly higher than in those without diabetes (4.4 vs. 1.4%). In our investigation, even though many of the in-hospital deaths were complicated by diabetes, we were not able to obtain significant data for this comorbidity class.

As in the aforementioned study [42], we were able to achieve statistical significance for predictors in relation to both LOS and in-hospital mortality thanks to the univariate regression analysis. However, when all the variables recorded are inserted in a multivariate model obtained from a stepwise analysis, the p values lose the power calculated with the previously cited test and become statistically nonsignificant ($p > 0.05$). This applied to most of our parameters interpreted as predictors of LOS and/or of in-hospital mortality, such as age group, ASA score, type of surgery, main diagnosis. These considerations underline that our model is mathematically and statistically more robust, providing much more reliable results as compared to the univariate regression alone.

By analyzing every recorded variable at the same time, we may conclude that having gallbladder surgery as an "afternoon/night emergency" played the most important role by far among the predictors in terms of short-term in-hospital mortality.

In our study, the "afternoon/night emergency" variable proved to be a stronger predictor than ASA score, comorbidity number and even age group, our first independent variable. This trend is confirmed in the literature by an investigation that evaluated mortality outcomes after emergency laparotomy surgery concluding "the mortality rate increased during night emergency admission compared to daytime admission" [27]. All these facts suggest that being octogenarian or nonagenarian does not imply a significant difference in terms of LOS and in-hospital mortality after gallbladder surgery.

As for our secondary endpoints, several factors and biases may have played a role in obtaining nonsignificant outcomes. Probably, the most important issue is that we may have had too small a sample size that lead to a low number of patients per year category, thereby not allowing us to reach significant results. As for biases, evaluating improvements in the surgical management of elderly people may be considered for certain aspects a paradox, as innovative surgical approaches are usually first clinically tested on noncomorbid patients, not nonagenarians.

From a statistical standpoint, the data come from our local administrative database and whenever there was a doubt in the quality of such data, it was corrected with a review of the specific charts and records of the patient involved. This may improve the overall quality of the data recorded but at the same time opens a window for human error. We were not able to achieve statistical significance in our statistical model for many parameters, despite obtaining it with the univariate regression: This is largely related to the low size of our nonagenarian sample. However, our statistical model was proven reliable as it mathematically explained most of the parameters' variance.

From a clinical view, a limitation of the study is that we are categorizing patients into six main diagnoses. Despite an accurate selection of such subjects that implied excluding 29.7% of available cases (150 out of 505), we must underline that some cases presented with symptoms that fit both categories and classifying them under only one of them may present a possible limitation to the study. Nevertheless, this classification did not affect our primary goal, the crude calculation of mortality and LOS, but only the reliability of the "main diagnosis" as a predictor of mortality and LOS.

In relation to the obtained results, we may add that we did not report if the patients had previous less invasive procedures such as ERCP interventions, percutaneous ultrasound-guided drainage, laparoscopic aspiration or cholecystostomy. Interventional Radiology service was established in our institution in the late 2000s and was only available during weekdays for a few years. Only since the end of 2012, a full service of Interventional Radiology available 24/7 was established. Moreover, we did not insert in our multivariate model the experience of the surgeon involved in the case.

It is challenging to make a scientific judgment and establish whether our in-hospital mortality and LOS outcomes fall within a reasonable interval considering the type of patient and surgery we are dealing with. We may conclude that our results for octogenarians do fall in such intervals, but we have almost no data for comparison for the nonagenarian group.

Although gallbladder surgery in the nonagenarian group appears as a risky intervention, when considering the severity of the vast majority of the cases, it was a necessary and effective intervention in resolving the excruciating conditions of these patients and restoring their previous quality of life.

Further encouraging, mortality outcomes and LOS in the octogenarian group were even more positive compared to the literature, once more confirming the safety of laparoscopic cholecystectomy in this delicate, aging population.

As for our secondary endpoint, we may conclude that an improvement in surgical management from 2000 to 2015 of the "oldest old" as far as gallbladder surgery at our institution was not detected and the reasons may lie in the limitations and biases of our study.

Finally, we may identify a few crucial take home messages. At our institution, the surgical "afternoon/night emergency" intervention should be critically reevaluated to ensure the best possible treatment for the oldest old, even in the emergency setting.

On the other hand, we must highlight that being nonagenarian compared to octogenarian is not a significant risk factor in terms of in-hospital mortality and LOS. This fact may be interpreted as positive news for the healthcare future as it means that nonagenarians are more suitable surgical candidates than may have previously expected. While the postoperative in-hospital mortality was considerably higher among the nonagenarians, it should be noted that these patients underwent the procedures always in an emergency setting. In fact, while we can draw conclusions for emergency cholecystectomies, we do not have adequate data to support the recommendation of performing elective cholecystectomies on nonagenarians.

Prospective studies should be planned to examine a larger sample of nonagenarians and elucidate what represents a reasonable in-hospital mortality and LOS in an emergency context, and thereby direct future surgical guidelines for the population of the "Silver Tsunami."

Acknowledgements We would like to thank Dr. Fabrizio Michelassi, Dr. Luca Stocchi and Sherman Kwan for their significant contribution in drafting this manuscript.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

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