

Acute cholecystitis managed in a rural surgical department: A retrospective long term outcome analysis of decision-making between early or delayed cholecystectomy and no surgical treatment

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RESEARCH

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ABSTRACT

Objectives

This study aims to define the outcome over a prolonged period of an unselected cohort of patients presenting with acute cholecystitis (AC) to a 560 bed rural hospital in Israel.

Design, setting and participants

Retrospective case series analysed from a single referral centre between 2006 and 2015. Separated into Group 1 managed by emergent cholecystectomy, Group 2 treated with antibiotics and delayed cholecystectomy, Group 3 treated with percutaneous cholecystostomy (PC) and selected delayed cholecystectomy and Group 4 managed entirely conservatively with no subsequent cholecystectomy.

Methods

Assessment of complication rates: in-hospital and delayed cause-specific morbidity and mortality along with conversion rates and the risk of intraoperative stone spillage.

Results

Of 321 patients hospitalized for AC, there were 50 in Group 1, 68 in Group 2, 59 in Group 3 and 98 in Group 4. Group 3 were older with more comorbidities and when coming to surgery had more open conversions. Intraoperative stone spillage was more common in Groups 2 and 3. The length of hospital stay was greater for Groups 1 and 3. Of the Group 4 cases, 63.2 per cent remained asymptomatic over a median follow-up of 78 months. Of those with recurrent biliary symptoms, 58.3 per cent were ASA Grade III/IV with 25/36 late deaths 80 per cent of which were from non-biliary causes.

Conclusion

In the management of AC, early cholecystectomy is favoured with non-operative approaches like PC drainage or antibiotic treatment alone being reserved for frailer comorbid cases. The absolute need for subsequent cholecystectomy is not supported by this series and requires further investigation.

Key Words

Acute cholecystitis, conservative treatment, percutaneous cholecystostomy

What this study adds:

1. What is known about this subject?

Despite an absence of categorical guidelines for optimal AC management, early laparoscopic cholecystectomy is considered to be the treatment of choice.

2. What new information is offered in this study?

This study describes the actual reality of the management of AC in a typical surgical service of a 550 bed hospital in Israel.

3. What are the implications for research, policy, or practice?

This study supports the advantages of early cholecystectomy in most patients and calls for further investigation whether surgery is mandatory in all cases.

Background

As the patient population ages, there has been a commensurate increase in the number of cases presenting to most surgical departments with acute cholecystitis (AC). About one-third of cholecystectomies are performed for AC with a principal debate concerning the timing of the surgical procedure.¹ Despite an absence of categorical guidelines for optimal AC management,² there is a general consensus that early laparoscopic cholecystectomy (LC) remains the treatment of choice for the majority during the acute phase of the illness³ and that this approach can selectively be extended with safety to the elderly.⁴ In this respect, although there is debate as to what is meant by the term early, an LC performed during the acute admission results in a shorter overall hospital stay and reduced costs without any significant negative impact on postoperative morbidity.^{5,6} Increasing laparoscopic experience has also resulted in a general reduction in the rates of conversion to an open procedure during the acute phase of the illness,^{7,8} where the performance of a delayed LC may on occasion be technically demanding with the potential risk for bile duct injury (BDI).

In some patients with significant coincident comorbidities, an alternative AC management approach with a percutaneous cholecystostomy (PC) should be considered.⁹ Despite the fact that there is no hard evidence concerning the benefit of PC in critically ill patients¹⁰ it is highly effective at AC resolution in the acute phase of inflammation.¹¹ For such cases, PC drainage may be used either as a bridge towards a delayed LC or in higher-risk patients (ASA Grades III and IV) as definitive therapy.^{12,13} The role in selected patients of an entirely conservative approach demands further prospective study. In this respect, Hatzidakis et al.¹⁴ showed no difference in outcome when comparing PC plus antibiotic therapy with conservative treatment alone with Akyurek and colleagues¹⁵ suggesting that PC followed by early LC has a generally more favourable outcome than conservative treatment and a delayed LC approach. Our study retrospectively analysed the long-term outcome of an unselected cohort of patients

treated for AC in a single referral surgical department by a range of consultant and trainee surgeons between 2006 and 2015. Outcomes were assessed in the operated groups with comparisons between those managed with early surgery (Group 1), those receiving intravenous antibiotics and then undergoing a delayed cholecystectomy, (Group 2) patients initially treated with PC drainage followed by selective surgery (Group 3) and those managed entirely conservatively without surgery (Group 4).

Patients and Methods

Ethical permission for this retrospective study was provided by the local hospital ethics committee (EMC-0010-12). The analysis was conducted on patients derived from the Department of Surgery at the Haemek Medical Center, Afula Israel, a 560-bed University affiliated referral institution. Patients examined included all those admitted with a diagnosis of AC between January 2006 and December 2015. Cases with AC were identified using the ICD disease coding (9th Revision) incorporating codes 574.0, (calculous cholecystitis variants) 574.3, (AC plus choledocholithiasis) 574.6, (calculus of the gallbladder and bile duct with AC) 575.0, (complicated AC including abscess of the gallbladder, emphysematous cholecystitis, gallbladder gangrene and empyema) 575.12 (combined acute and chronic cholecystitis) and 575.4 (perforated gallbladder).¹⁶ The diagnosis of AC was made utilizing a combination of patient history, physical examination, laboratory analyses, routine ultrasonography and selective CT scan confirmation. All patients with AC were managed with intravenous antibiotics, most commonly using a combination of Cefuroxime (Glaxo Smith Kline, Israel) and Metronidazole (Sanofi Aventis, Israel) with standard analgesics.

The study was a retrospective analysis with all practical management decisions for AC patients made at the discretion of each individual surgeon as the principal arbiter. For the purposes of analysis, the cohort was separated into groups with Group 1 undergoing cholecystectomy within 24 hours of admission, Group 2 including those patients treated with intravenous antibiotics followed by a delayed cholecystectomy and Group 3 incorporating mainly high-risk patients initially managed with PC drainage and then selectively operated. Non-operated patients were identified as Group 4. The main indication for early PC insertion was for patients deemed a poor surgical risk and/or relatively long standing symptoms (longer than five days) of AC, with later PC insertions being performed in those clinically unresponsive patients or in those cases deteriorating under conservative management. All PC placements were performed by a consultant

interventional radiologist under ultrasonographic or CT guidance. In general, a transhepatic approach to the gall bladder was preferred, however, a trans-abdominal approach was occasionally used if the gallbladder was distended and adherent to the abdominal wall or when unfavourable anatomy precluded a transhepatic approach. Placement of a PC drain was accomplished under local anaesthesia using a Seldinger guidewire technique first dilating the tract and then deploying either a 6Fr or an 8Fr pigtail catheter (Argon Medical Devices, Athens, TX USA) depending upon the viscosity of the gallbladder contents. Aspirated bile was sent for bacteriological culture.

There was some variation in the management of the PC drain, however, in general patients were discharged with the PC to open drainage. A cholangiogram was usually performed via the PC at 2–3 weeks following discharge. If the cystic duct was patent with no signs of distal obstruction and the patient was considered fit and willing to undergo an elective cholecystectomy then elective surgery was organized and performed. In this situation, the PC tube was closed but left in place until the operation. In those patients deemed to be a prohibitive surgical risk (or in those declining surgery), the PC tube was then removed. In those with initial cystic duct obstruction on cholangiography, the PC tube was left open and a repeat cholangiogram was performed in a further 2-3 weeks. If cystic duct obstruction was still evident the tube was left open and elective surgery was organized.

Demographic patient data were collected as well as relevant laboratory analyses and information concerning coincident co-morbidities. Patients were classified in accordance with their American Society of Anesthesiologists (ASA) Grade with comparison between ASA Grades I and II (combined) and ASA Grades III and IV (combined). Operative information was collated including operation type (commencement laparoscopically, commencement open or laparoscopic conversion) and the presence of intraoperative adverse events and/or stone spillage. Postoperative general and wound complications were also noted. In-hospital peri-procedural mortality was charted for those cases dying before discharge or within 30 days of discharge. Data concerning procedural complications, in-hospital morbidity, outcome and elective surgical disposition were all collated. Patients were excluded from analysis if there was a presentation of cholangitis, known choledocholithiasis, associated hepatobiliary malignancy or gallstone pancreatitis. Data for all non-operated patients was collected and assessed by their available medical records and by recent telephone interview.

Statistics

The SPSS software (Version 22.0 IBM Armonk, NY) was used for statistical analysis. Categorical data were expressed as means and standard deviations (SD) and compared using the Chi-square or Fisher's exact test where appropriate. Continuous variables were examined by the Wilcoxon rank sum test. For all analyses a two-tailed P value <0.05 was considered to be statistically significant.

Results

Figure 1 is a flow chart showing the basic disposition of the patient cohort. Of the total of 321 patients hospitalized for AC, 177 underwent surgery in our Department with 50 patients (15.6 per cent) undergoing urgent surgery all within 24 hours of admission (Group 1). A further 68 patients (21.2 per cent) underwent elective surgery 4–16 weeks after initially settling with antibiotic therapy (Group 2) and 59 patients (18.4 per cent) underwent elective surgery after initially being treated with antibiotic therapy and PC drainage within 48 hours of admission (Group 3). Of the remaining 144 patients, 98 (30.5 per cent) were managed conservatively (Group 4) with 33 undergoing surgery in another hospital that were not included in any of the study groups as well as other 13 cases that were lost to follow-up.

Table 1 shows associated co-morbidities for the 3 operated group dispositions. Overall, Group 3 patients are significantly older than the other two groups (60.5+14 years vs. 52+18.8 years for Group 1 and 49.6+16 years for Group 2, respectively) with significantly more co-morbidities, most notably hyperlipidaemia, diabetes and chronic obstructive pulmonary disease. Table 2 shows the type of operative approach and recorded intra-operative complications. Overall, there was a greater likelihood for cases in Group 3 to undergo an open approach with also a higher rate of open conversion for those initially operated upon laparoscopically. Part of this effect was due to the heterogeneity of the surgeon pool. During the period of time of the study, 5/7 of the Departmental consultant surgeons were replaced and with rotating residencies, overall, 17 different surgeons were involved in comprising the operator data. One of the Consultant surgeons with limited minimally invasive operative experience was the source of part of the bias performing 4/7 cases (in Group 1) and 1/6 cases (in Group 3) as open operations.

More patients in Group 3 undergoing delayed cholecystectomy, also experienced significant bile duct injuries. Stone spillage was more likely to have occurred in both groups undergoing a delayed cholecystectomy (6 per cent for Group 1 vs. 16.2 per cent for Group 2 and 13.6 per

cent for Group 3, respectively) although this did not reach statistical significance. Overall more men (24/42 cases) than women (14/42 cases) were likely to need open conversion following an initial laparoscopic approach with nine conversions in Group 1 (five males), nine in Group 2 (six males) and 20 in Group 3 (13 males). Table 3 shows the non-specific and specific postoperative complications for each group. In general there were more patients where a postoperative fever at any time was recorded with a higher risk of intra-abdominal infection in Group 3 cases and a more prolonged hospital stay in both this group and those immediately operated upon. The length of hospital stay (LOHS) was greater in both Groups 1 and 3 when compared with Group 2 patients.

Figure 2 is a flowchart showing the outcomes of the 98 non-operated cases. Thirty-six patients (36.7 per cent) suffered from recurrent biliary symptoms (mean age 67 years) including 28 cases initially managed in the first admission with PC drainage. In this recurrent group, there was a high incidence of frailty (28/36; 77.8 per cent) with 27 ASA Grade III/IV cases and 1 ASA Grade V patient. Of the biliary related deaths in this group, all were ASA Grade IV and all had declined surgery with their first recurrence occurring within 24 months of the initial AC bout. Sixty-two patients (63.2 per cent) remained asymptomatic following their initial hospital discharge (mean age 75 years) over a median follow-up of 78 months (range 10–107 months) with 36 (58 per cent) of the cases ASA Grades III/IV. Amongst this group 20 cases had been initially managed with PC drainage. Overall, 48/98 (48.9 per cent) of all Group 4 cases were initially managed with PC drainage, with 28 (58.3 per cent) cases readmitted with recurrent AC or biliary symptoms. Of the patients overall presenting with recurrent biliary symptoms there were 25 late deaths, five of which occurred in hospital from biliary-related causes. Of this small group of five patients, three had undergone prior PC drainage. Of the asymptomatic group, all 12 deaths during follow-up were from non-biliary causes.

Discussion

This retrospective assessment of an unselected group of patients presenting to a referral centre with acute cholecystitis (AC) over a prolonged time period showed advantage for patients managed with emergent cholecystectomy as the standard of care. There was less need for open conversion after an initial laparoscopic approach, with less chance of intraoperative stone spillage and less risk for bile duct injury (BDI) when compared with the two other groups undergoing a delayed cholecystectomy. There was a higher rate for open

conversion following an initially laparoscopic approach in males when compared with females. Those patients deemed particularly high-risk who underwent successful PC drainage and some of whom then underwent a delayed cholecystectomy, were significantly older with more attendant comorbidities and when subsequently operated upon, they experienced a slightly higher rate of intra-abdominal sepsis. Two-thirds of cases initially managed conservatively remained asymptomatic over the relatively long follow-up period. Nearly half of these cases were managed with PC drainage where there was a high incidence of patient frailty (ASA Grades III/IV) and where follow-up showed a high late mortality from non-biliary causes.

There have been a number of meta-analyses comparing early with delayed LC for patients presenting with AC.^{1,3,6,10,17-20} These studies are quite similar showing no real differences between the two groups in the incidence of serious complications like BDI, intra-abdominal sepsis or the risk for open conversion.

Although several studies have reported a reduced LOHS for those undergoing early LC,^{10,17,19-21} our study failed to show such a reduction advantage in those patients undergoing emergent surgery, with the shortest LOHS noted unexpectedly in those actually undergoing a delayed cholecystectomy. Differences here may partly be logistic where some have shown a lower rate of bile leakage associated with early surgery⁶ and partly cultural, where the family and social conditions of our patients in a rural hospital setting may on occasion preclude early discharge.

Following a LC, the rate of minor BDI has variably been reported at between 0.1–1.7 per cent and of major BDI at between 0.1-0.9 per cent overall.⁶ In this situation, obesity, perioperative bleeding, coincident pancreatitis and the severity of local inflammation will all increase the BDI risk.²² Recently, this issue has been retrospectively assessed by Hogan et al.²³ who showed over time with increasing laparoscopic experience that there has been a reduction in the number of BDI's following performance of an LC which are referred to a tertiary hepatobiliary unit. This has, however, been accompanied by a shift towards a greater BDI complexity as peripheral surgeons take on more difficult laparoscopic cases.

Concerning conversions of laparoscopic to open surgeries, our study showed bias where there were a range of surgeons involved in patient care, each with different operative experience and personal preferences concerning

acute biliary management. In this regard, patient outcomes reflect the nature of our surgical facility which serves a typical Israeli rural community. Here, the logistic structure of the hospital operating suite also affects outcome measures where in our institution there are six operating rooms available during the day and 1-2 available at night without a dedicated emergency operating room. The operating service functions out of hours frequently with a shortage of available anaesthetists and nursing staff so that the performance of a LC either during a night shift (or on occasion performed within 24 hours of admission), is impractical. The impact of these factors on the early performance of PC drainage may also explain our moderately high rate of use of this approach when compared with other series.^{24,25} The rate of conversion will affect operative times, postoperative morbidity and hospital costs with Tang and Cuschieri in a systematic review, showing older age, morbid obesity, cirrhosis, prior upper abdominal surgery and the need for emergent surgery to all increase the conversion risk.²⁶

Others have reported the same finding as in our study, namely that male gender was also associated with a higher conversion risk^{7,27-29} where this effect is most probably linked to a more frequent incidence of severe acute and chronic disease in men. In our series, spilled stones were more common in the delayed cholecystectomy groups (2 and 3) and were recorded less frequently in those undergoing an emergent LC. Our spillage rate is similar to that reported worldwide of around 10 per cent³⁰ although the perforation rate of the gallbladder which was not uniformly recorded in our cohort will be somewhat higher. Spillage of stones tends to occur during dissection of the gallbladder off the liver bed, upon tearing of its wall with energy dissecting instrumentation, with conventional grasping forceps and to a lesser extent during extraction of the gallbladder through one of the port sites. This latter mechanism was prevented in our series by the routine use of retrieval bags.

Successful resolution of acute inflammation with PC drainage in patients presenting with AC either in cases non-responsive to antibiotic therapy or in those deemed high-risk for surgery (ASA Grades III and IV) has been extensively reported.¹³ Our data showed that in such high-risk cases that even when a PC drain was deployed during the first admission, that the need for elective surgery can be selective³¹ and that PC drainage can act as definitive management.^{32,33} Although the treatment options are competitive, these patient groups are not, however, strictly comparable. As in our study those undergoing an interval

cholecystectomy had a lower death rate than those definitively managed with PC drainage, reflecting the inherent physiological differences between these two groups along with commoner deaths from non-biliary causes in PC-treated cases. This issue may potentially be resolved by the ongoing Dutch randomized CHOCOLATE trial comparing PC drainage with early LC in highly morbid patients.³⁴

Our data clearly shows that entirely conservative therapy for AC is acceptable. There are two good quality randomized controlled trials addressing this matter, both from the same institution.^{35,36} This group reported that about half the patients randomized to observation only eventually underwent cholecystectomy with most of the surgery performed for pain within the first five years after the initial hospitalization. The biliary-related mortality associated with conservative treatment is very low and is consistent with other reports^{37,38} although this will depend upon the number of high-risk cases included in the conservative cohort.¹⁴ Even when the majority of conservatively-treated patients do not experience gallstone-related complications, those in the observation group will generally have more events related to gallstone disease (AC, CBD stones and acute pancreatitis) and these are more likely to occur in those where AC was their first presentation.^{35,36,39}

There are several limitations of our study. Firstly, its retrospective nature will provide important biases in the accumulation and reporting of data where there may be insufficient information concerning some of the reasons for conversion or for stone spillage. Decision-making concerning an operative or non-operative approach was personalized where in our environment there was a somewhat broad use of PC drainage as an initial treatment method. Here, the lower rate of conversion in our emergent cases (which did not quite reach statistical significance) may potentially be used as a proxy for the safety of the early LC approach. The maturation of an early LC as the preferred AC management option for most patients will reflect the Unit proficiency with laparoscopic surgery over time and will change the nature of the learning curve for more complicated cases. With this change there will be an expected reduction in BDI for more acutely performed cases although the BDI pattern itself might eventually alter. Adaptation of a surgical Unit towards a more evidence-based guideline of AC management is a slow and non-uniform process and will as in our case, reflect the local logistics of a surgical department and the available institutional resources for the performance of acute surgery. There has been in this study of an active decision-

making towards selected higher-risk and elderly cases away from the tradition of surgery where further prospective, randomized data will be required to determine the safety and economic implications of this approach and to better define those patients at a low risk for acute biliary complications. The issue of cost is important, where the decision for cholecystectomy is more expensive because of the use of resources around surgery and because of the impact of post-surgical complications. The cost benefit of either observational or conservative treatment options is diminished if these groups experience a high complication rate requiring emergency surgery, where a policy of ultimate surgery for everyone or conservative management followed by selective surgery for symptomatic patients only, will be more effective but where it will also be more costly.⁴⁰

Conclusion

In summary, our retrospective survey suggests that an early LC in AC patients is the treatment of choice, however, further work is needed to determine if this shift in management away from initial antibiotic therapy followed by a delayed LC is cost-effective along with elucidation of the reasons why emergent surgery in our Unit has not so far resulted in an expected reduction in LOHS. Additional study will also characterize the subgroup of high-risk cases where initial PC drainage can act as definitive therapy and better define those patients where no surgical intervention at all can be safely and cost-effectively employed. Within our rural environment, changes in the logistics surrounding emergency surgery and in laparoscopic proficiency will affect primary outcome measures following a presentation with AC.

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PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

ETHICS COMMITTEE APPROVAL

Ethical permission for this retrospective study was provided by the HaEmek medical center ethics committee (EMC-0010-12)

Figure 1: Flow chart of patient disposition. Group 1 cases were operated upon during the acute admission. Group 2 cases initially settled after intravenous antibiotic therapy and were then operated upon electively. Group 3 cases were initially managed by percutaneous cholecystostomy (PC) with some undergoing elective surgery and some treated by PC definitively

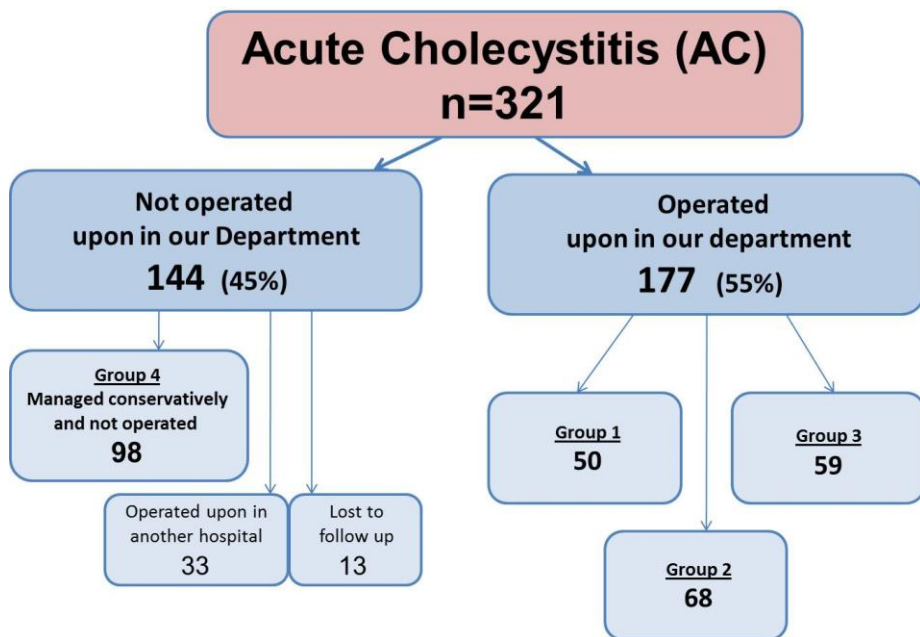
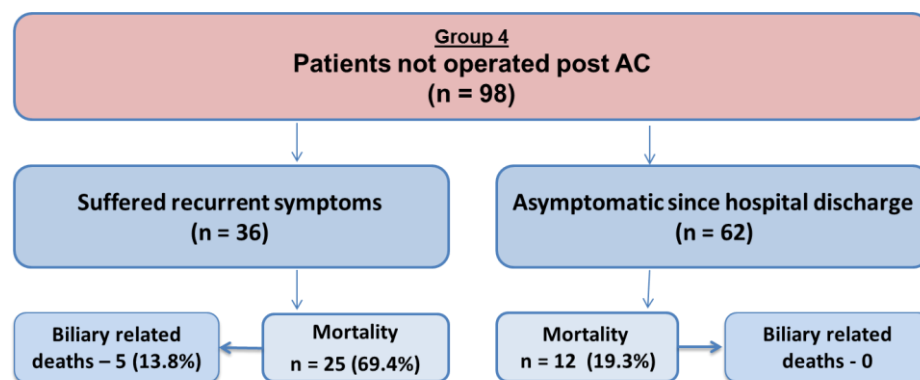


Figure 2: Group 4: Flow chart showing the outcome during follow-up of a group of 98 non-operated patients presenting with AC



Total	Age	Male Gender	ASA ≥3	ASA < 3	Mortality	Biliary related death	Group 4
98	72 (23-101)	52 (53.1%)	64(65.3%)	34	37(37.8%)	5(5.1%)	not operated post AC
62 (63%)	75 (26-101)	34 (54.8%)	36(58%)	26	12(19.3%)	0	Asymptomatic
36 (37%)	67 (23-98)	18 (50%)	28(77.8%)	8	25(69.4%)	5(13.8%)	Symptomatic

Table 1: Co-morbidities according to basic group type*

	1 (n=50)	2 (n=68)	3 (m=59)	P
Age (Years+SD)	52+18.8	49.6+16	60.5+14	0.0004
Gender (Male)	22	33	30	
Hyperlipidaemia	13	21	30	0.014
Hypertension	17	25	32	
Ischemic Heart Disease	6	7	13	
Diabetes	11	7	21	0.0028
Renal Failure	1	1	5	
Smoker	4	10	11	
Congestive Heart Failure	4	3	8	
COPD	4	2	9	0.045
Cancer	1	1	5	
Dementia	2	-	1	

Group 1 Emergent surgery group

Group 2 Elective surgery group

Group 3 PC-treated patients

*Data for group 4 is presented in Figure 2

Table 2: Operative type and intra-operative complications according to group

	Group 1	Group 2	Group 3	P
Intraoperative Events:				
Open	7(14)	33	6 (10.2)	0.002
Converted	9 (18)	13 (19.1)	20 (33.9)	0.08
Iatrogenic bile duct Injury (BDI)	1 (2)	5 (7.4)	9 (15.3)	0.042
Stone spillage	3 (6)	11 (16.2)	8 (13.6)	0.24
Postoperative Events:				
Bile Leakage	4 (8)	6 (8.8)	7 (11.9)	0.76
ERCP	2 (4)	6 (8.8)	6 (10.2)	0.53
Deaths*	1 (2)	1 (1.5)	1 (1.7)	

*All deaths occurred in ASA Grade IV cases.

() Brackets are percentages

Open Surgery commenced open

Converted Surgery commenced laparoscopically and converted to open

Table 3: Postoperative complication list (Groups 1-III)

	I	II	III	P
Fever > 380C	9 (18)	4 (5.9)	15 (25.4)	0.01
Wound infection	5 (10)	2 (2.9)	7 (11.9)	0.11
Intra-abdominal Abscess	-	2 (2.9)	7 (11.8)	0.01
Pneumonia	3 (6)	1 (1.4)	3 (5.1)	
ICU	2 (4)	-	3 (5.1)	
LOHS > 72 hours	22 (44)	11 (16.2)	22 (37)	0.003

ICU Need for intensive care unit treatment

LOHS Length of hospital stay

() Brackets are percentages for each group