

Original Article

Complications associated with late acute cholecystectomy

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ABSTRACT

INTRODUCTION. Gallstone-related diseases are common in Denmark, with acute cholecystitis being a painful presentation. Historically, cholecystectomy was performed within five days of symptom onset. In 2022, national guidelines abandoned this limit due to evidence suggesting similar outcomes for early and delayed surgery. This study aimed to assess the impact of an extended surgical window on the frequency of acute cholecystitis operations, complication rates and patient outcomes.

METHODS. All cholecystectomies performed between 1 June 2022 and 31 May 2023 were identified using the procedural codes KJKA20 and KJKA21. Patients with gallstone pancreatitis, biliary colic or choledocholithiasis were excluded. Medical records were reviewed, and a statistical analysis was conducted.

RESULTS. Among 180 patients identified, 128 met the inclusion criteria. Thirty-nine patients had >5 days of symptoms at the time of surgery. No significant differences were observed in operative duration, hospital stay, reoperation, conversion to open surgery or mortality. However, complications graded Clavien-Dindo > 1 were more frequent in the group with a duration of > 5 days (28.2% versus 10.1%, $p = 0.009$). Multivariate analysis showed that long symptom duration and older age were associated with an increased risk ($p < 0.05$).

CONCLUSIONS. Extended symptom duration before surgery was associated with a higher rate of post-operative complications. Larger, multicentre studies are needed to confirm these findings and guide clinical decisions.

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Approximately 20% of the Danish population has gallstones [1]. A smaller percentage, approximately 3%, will develop cholecystitis [2], a painful condition characterised by possible fever, nausea and vomiting. Cholecystitis is defined by the Tokyo Guideline as a definite diagnosis when there is a sign of local inflammation (Murphy's sign or mass/pain/tenderness in the upper right quadrant), a systemic sign of inflammation (fever, elevated CRP level or elevated white blood cell count) and an imaging finding [3]. The treatment of cholecystitis has traditionally been open or laparoscopic removal of the gallbladder [4].

Previously, the operating window was limited to approximately five days from symptom onset. This was due to increased technical difficulties and fear of an increased risk of complications from delayed emergency surgery. Patients were therefore treated non-operatively, with intravenous antibiotics and referred for delayed cholecystectomy [5].

In 2022, new Danish guidelines extended the operating window and reported no evidence of recommending an upper limit for patient-reported symptom duration before emergency surgery [6]. This is due to the risk of

readmission during the interval and the lack of a significant difference in post-operative complications between acute and planned interval operations. These recommendations are based on a meta-analysis of studies that included patients with a history of up to seven days.

This study aimed to assess the number of operations for acute cholecystitis, complication rate and grade of complications developed since the extension of the operation window was introduced by the new national guidelines.

Methods

This study was designed as a quality assurance project and approved by the Department of Surgery, Kolding Hospital, part of Lillebaelt Hospital and the Quality Department, Lillebaelt Hospital.

It investigated patients undergoing surgery due to acute cholecystitis. The primary outcome was post-operative complications. The secondary outcomes were intraoperative complications, duration of post-operative hospital stay and rate of reoperation and rehospitalisation.

Using the Danish National Health Service's Classification System (NOMESCO - SKS) [7], we identified all patients who had undergone surgery, including gallbladder removal procedure codes for open cholecystectomy (KJKA20) and laparoscopic cholecystectomy (KJKA21). The investigation period spanned 12 months, from 1 June 2022 to 31 May 2023, at the Department of Surgery, Kolding Hospital – a part of Lillebaelt Hospital, Denmark. Patients operated on for the indication of gallstone pancreatitis, gallstone colic or choledocholithiasis, and patients receiving elective surgery for chronic cholecystitis were excluded, leaving only patients undergoing cholecystectomy for acute cholecystitis.

Patient records from the electronic patient record system (EPJ SYD) were reviewed to obtain the following parameters: patient age, sex, weight, height, patient-reported duration of symptoms, date of consultation, date of surgery, surgeon charge, American Society of Anesthesiologists (ASA) score, diabetes status, intraoperative complications, duration of surgery, post-operative complications (the most extensive complication graded by the Clavien-Dindo Classification) [8, 9], reoperation rate, duration of post-operative hospital stay and rehospitalisation rate (90 days post-operatively).

Included patients were divided into two cohorts based on patient-reported symptom duration at surgery (≤ 5 versus > 5 days). For patients not operated on the day of admission, the pre-surgery length of stay was added to the patient-reported symptoms to determine the total duration of symptoms. Patients without patient-reported symptom duration in the electronic chart were excluded.

Each variable obtained was compared between the two cohorts using Student's t-test for continuous variables and the χ^2 -test for categorical variables. A logistic regression analysis was performed with any complication as outcome; cohort (≤ 5 versus > 5 days of symptom duration) as the dependent variable; and age, sex, ASA score, BMI and presence of diabetes as covariates. A separate analysis was performed for each covariate, and significant variables were included in the adjusted logistic regression. $p < 0.05$ was considered significant.

All data were stored on a secure regional server, and data management and analysis were performed using STATA18 (College Station, Texas, USA).

Trial registration: not relevant.

Results

In this study, we found 180 patients who had undergone acute cholecystectomy. Fifty patients underwent surgery for reasons other than acute cholecystitis and were excluded. Among the remaining 130 patients, patient-reported symptom duration was not recorded for two patients, who were therefore excluded from the analysis.

There was no statistical difference between the two groups for age, sex, BMI, ASA score or the presence of diabetes (see Table 1).

TABLE 1 Patient characteristics.

	Symptom duration		p value
	≤ 5 days (N _{≤5} = 89)	> 5 days (N _{>5} = 39)	
Age, median (25th-75th percentile), yrs	60.0 (26.0)	55.0 (20.0)	0.269
Sex, n (%)			0.670
Female	47 (52.8)	19 (48.7)	
Male	42 (47.2)	20 (51.3)	
BMI, n (%)			0.775
BMI < 18.5 kg/m ²	2 (2.2)	0	
BMI 18.5-25 kg/m ²	15 (16.9)	6 (15.4)	
BMI 25-30 kg/m ²	30 (33.7)	12 (30.8)	
MI 30-35 kg/m ²	24 (27.0)	14 (35.9)	
BMI > 35 kg/m ²	18 (20.2)	7 (17.9)	
ASA score, n (%)			0.927
1	20 (22.5)	10 (25.6)	
2	50 (56.2)	21 (53.8)	
3	19 (21.3)	8 (20.5)	
Diabetes, n (%)	13 (14.6)	2 (5.1)	0.125

ASA = American Society of Anesthesiologists - physical status classification system.

There were no deaths within the study group within 30 days of surgery. Surgery duration, length of post-operative stay, distribution of complications by Clavien-Dindo, conversion to open surgery, reoperation and

readmission did not differ between the groups. However, the rate of post-operative complications, i.e., Clavien-Dindo ≥ 1 , was higher in the group of patients with > 5 days of symptom duration (28.2% versus 10.1%, $p = 0.009$). Readmission rates were rather high in both groups (10.1% and 20.5%, $p > 0.05$). However, these rates include every physical contact to the surgical and acute department, be it constipation, surgical site infection, acute onset of diverticulitis or post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis, etc. Most cases were managed and discharged on the same day (see Table 2).

TABLE 2 Surgical and post-operative characteristics.

	Symptom duration		p value
	≤ 5 days ($N_{\leq 5} = 89$)	> 5 days ($N_{> 5} = 39$)	
Duration of surgery, median (25th-75th percentile), min.	126.0 (48.5)	135.0 (50.0)	0.431
Post-operative length of stay, median (25th-75th percentile), days	1.0 (1.0)	1.0 (1.0)	0.063
Clavien Dindo grade, n (%)			0.079
0	80 (89.9)	28 (71.8)	
1	4 (4.5)	5 (12.8)	
2	3 (3.4)	4 (10.3)	
3b	2 (2.2)	2 (5.1)	
Conversion to open surgery, n (%)	2 (2.2)	3 (7.7)	0.143
Any complication, n (%)	9 (10.1)	11 (28.2)	0.009
Reoperation, n (%)	3 (3.4)	3 (7.7)	0.287
Readmission, n (%)	9 (10.1)	8 (20.5)	0.111

Regarding conversion to open surgery and the Clavien-Dindo score

Five patients were converted to open surgery; two due to intraoperative bleeding and two due to uncertain anatomy and poor overview. The last conversion was due to an enlarged gallbladder stretching to the pelvis.

Two of the converted patients presented with six days of symptom duration and were operated nine and seven days after onset, respectively. Among the patients converted due to uncertain anatomy and poor overview, one patient taking anticoagulants (non-vitamin K oral anticoagulant) was postponed for two days to decrease the risk of bleeding and was ultimately operated eight days after onset. In the group of patients converted to open

surgery, only this patient needed post-operative surgery, which was performed due to gall leakage. This patient underwent ERCP and was classified as Clavien-Dindo 3b. One of the patients converted due to bleeding was observed in the intensive care unit (ICU) and given blood transfusions, resulting in a category two on the Clavien-Dindo Classification.

Regarding Clavien-Dindo 2

Two patients needed blood transfusions, and another two were infected at the surgical site and were treated with antibiotics. One developed post-operative kidney failure and infection, leading to atrial fibrillation. Another patient contracted pneumonia, and the last patient developed atrial fibrillation and was treated with digoxin.

Regarding reoperations, i.e. Clavien-Dindo 3b

Three patients were reoperated with ERCP; one patient, as mentioned above, in the group of patients converted to open surgery, and another patient, who developed gall leakage (cholascos). The two patients who developed post-operative cholascos were both in the group of patients with > 5 days of symptom duration. The third and final patient, a patient with ≤ 5 days of symptom duration, developed hyperbilirubinaemia on the fifth post-operative day and had stones in the common bile duct.

A single patient had a bowel perforation during placement of the laparoscopic trocars; a mini-laparotomy was performed, the bowel sutured, the abdomen closed and the cholecystectomy was performed laparoscopically. However, the patient was believed to have a rupture of the abdominal fascia and was taken to the operating room, where this condition was ultimately disproven.

Regarding intraoperative complications

The main issue was bleeding, which occurred 22 times and was treated with various applications, ranging from laparoscopic ligation clips to local coagulation applications, including Fibrillar, Surgicel and Veriset. However, as mentioned above, only two laparoscopic procedures were converted to open surgery due to bleeding, one in each group. Gall leakage from the liver occurred twice, once in each group, and no statistical significance was therefore observed.

In the logistic regression analysis, only age and BMI were significant covariates in the independent analysis. Therefore, the adjusted logistic regression with any complication, i.e., Clavien-Dindo ≥ 1 as outcome, included the group based on patient-reported symptom duration as the dependent variable, and BMI and age as covariates (see Table 3).

TABLE 3 Logistic regression analysis.

	Unadjusted analysis		Adjusted analysis	
	OR (95% CI)	p value	OR (95% CI)	p value
<i>Duration of symptoms</i>				
≤ 5 days	1.00 (ref.)	-	1.00 (ref.)	-
> 5 days	3.49 (1.31-9.31)	0.012*	5.56 (1.74-17.79)	0.004*
<i>Sex</i>				
Female	1.00 (ref.)	-	-	-
Male	1.37 (0.52-3.56)	0.524	-	-
Age	1.04 (1.00-1.07)	0.036*	1.05 (1.01-1.09)	0.024*
<i>ASA score</i>				
1	1.00 (ref.)	-	-	-
2	1.48 (0.38-5.79)	0.577	-	-
3	3.15 (0.72-13.72)	0.126	-	-
<i>BMI</i>				
BMI 18.5-25 kg/m ²	1.00 (ref.)	-	1.00 (ref.)	-
BMI 25-30 kg/m ²	0.27 (0.07-0.99)	0.049*	0.23 (0.07-0.96)	0.043*
BMI 30-35 kg/m ²	0.38 (0.10-1.32)	0.127	0.34 (0.09-1.32)	0.120
BMI > 35 kg/m ²	0.17 (0.03-0.96)	0.044	0.23 (0.04-1.40)	0.111
<i>Presence of diabetes?</i>				
No	1.00 (ref.)	-	-	-
Yes	0.35 (0.04-2.85)	0.329	-	-

ASA = American Society of Anesthesiologists - physical status classification system; ref. = reference.

*) p < 0.05 was considered significant.

Discussion

Only the parameter of any complication, i.e., Clavien-Dindo ≥ 1 , was statistically significantly different between the two groups. However, the distribution of the severity of complications did not differ, nor did conversion to open surgery, reoperation or the readmission rate. Multivariate analysis revealed that long symptom duration and age were associated with a higher rate of complications, while a BMI between 25 and 30 was associated with a lower rate of complications (p < 0.05). A study from Finland and one from Australia showed that although obesity may increase technical difficulty, the procedure was not associated with an elevated risk of post-operative complications [10, 11]. A recent large study including more than two million Americans undergoing non-elective laparoscopic cholecystectomy for acute cholecystitis also found that higher age was linked to an increased risk of complications [12]. The present study is small in comparison but seems to support the findings of the larger studies mentioned above. Whether these findings can be attributed to pre-existing comorbidities in an ageing population is unclear. We found no association with diabetes, and the two groups did not differ in this perspective either.

We found a higher rate of complications in cholecystectomy for patients with symptoms for more than five days, but the reason for this finding remains unclear. It is also unknown whether these patients would be at a higher

risk of complications if cholecystectomy were deferred to a later point in time. This deferral also increases the risk of recurrent cholecystitis during the cool-down period [6].

A large Danish single-centre retrospective study, which included 34 patients with > 5 days of symptom duration at the time of surgery, found no increase in post-operative complications [13]. However, in Japan, a single-centre prospective study with 41 patients with 4-7 days of symptom duration found increased post-operative complications [14]. Again, these numbers are relatively small and would benefit from systematic recording in a prospective national database.

The strength of this study is that it includes all consecutive patients undergoing acute cholecystectomy for acute cholecystitis at a high-volume acute surgical department for a full year. Electronic patient records were thoroughly examined, and relevant risk factors were included, including patient-reported symptom duration, which is often lacking in similar studies.

The retrospective nature of this study entails a risk of bias. Patients who underwent cholecystectomy with more than five days of symptom duration may represent a subpopulation of patients who receive antibiotic treatment, initially due to comorbidity, but where clinical deterioration resulted in a need for acute cholecystectomy. There was, however, no difference in registered comorbidities between patients with long and short symptom duration. At admission, 92.2% of patients reported a maximum symptom duration of five days. However, at the time of surgery, only 69.5% had symptoms for five days or less. This implies a delay from the beginning of admission to surgery, but the clinical consequences of this remain unknown. In addition, this study excludes patients who did not undergo surgery. However, a very small group of patients, i.e. those treated with percutaneous drainage and intravenous antibiotics alone, may represent a group with considerable complications, which could potentially question the internal validity of this study.

Furthermore, this study is relatively small. Even in acute cases, cholecystectomy has a relatively low complication rate; therefore, this study may not have enough power to detect differences in rare complications. It can also be discussed whether hyperbilirubinaemia caused by stones in the common bile duct, post-operatively requiring ERCP, constitutes a complication.

Conclusions

This study showed an increased complication rate in patients undergoing laparoscopic cholecystectomy for acute cholecystitis with a long symptom duration. Future studies on the Danish population regarding this topic should be prospective, include all cases of acute cholecystitis (regardless of treatment modality), record the reason for delays in cholecystectomy, register all medical and surgical complications and include more centres to increase the study size. This would increase the power, validity and potential clinical application of the study. To support current clinical practice, more data is necessary. Previously, all cholecystectomies in Denmark were registered in a national database. However, this practice was terminated, as the rate of bile duct injuries dropped to acceptable levels. A collective database providing clinicians with a platform to report, like in neighbouring Sweden (GallRiks), would help underpin data collection [15].

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