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Predictive factors for the type of surgery in acute cholecystitis

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Abstract

Background: Whereas early cholecystectomy is accepted as the optimal timing for surgery, the best treatment modality for acute cholecystitis (AC) is still under debate. In this series, we aimed to assess the current treatment of AC in a single institution. In addition, preoperative criteria were defined predicting the severity of inflammation.

Methods: From January 1995 to June 1999, 236 patients undergoing cholecystectomy for AC were prospectively evaluated. Outcome measures were the treatment modality, the severity of inflammation, white blood cell (WBC) count, C-reactive protein (CRP), morbidity, and hospital stay.

Results: There were 115 laparoscopic cholecystectomies (LC), 77 primary open cholecystectomies (OC), and 44 conversions (CON) to OC. Patients with LC were significantly younger, in better condition, with a shorter duration of symptoms and lower CRP levels and WBC counts compared with OC and CON (P <0.001). Postoperative complications, reinterventions, and mean hospital stay were significantly increased after OC and CON (P <0.001). Overall mortality was 2.5%. Advanced AC was predominantly found in OC and CON (P <0.001). Patients with advanced AC were significantly older, predominantly male, and had a prolonged duration of symptoms as well as increased CRP levels and WBC counts (P <0.001). The conversion rate increased from 10% for mild AC up to 48% for necrotizing AC.

Conclusions: Based on laboratory (CRP, WBC), demographic (age, sex), and individual (American Society of Anesthesiologists classification, duration of symptoms) findings, it is possible to reliably predict the severity of inflammation. Therefore, an individualized surgical approach can be used for each patient and type of AC.

Keywords: Acute cholecystitis; Laparoscopic cholecystectomy; Open cholecystectomy; C-reactive protein

Surgical treatment of symptomatic gallstones has completely changed in the last decade since the successful advent of laparoscopic surgery [1–3]. Elective laparoscopic cholecystectomy (LC) for symptomatic gallstones has almost replaced (>90%) the conventional open procedure (OC), and various studies have confirmed its safety and efficacy [4,5]. The laparoscopic approach for acute cholecystitis (AC) was initially considered to be a relative contraindication [3,6]. Inflammatory tissue reactions make the dissection difficult, thus increasing the hazard of serious complications as well as the conversion rate [1,6–8]. Increased conversion rates may diminish the potential medical and socioeconomic advantages of the minimal invasive approach [9]. However, early conversion (CON) may prevent fatal surgical complications, and therefore protect the patient's safety [10]. In experienced hands LC has been recently shown to be a safe and effective treatment for AC in a randomized series [11]; nevertheless, OC remains a proven alternative [12].

The main purpose of this prospective study was to assess the current emergency treatment of patients with AC who were admitted to a single university teaching institution. In addition, we aimed to define preoperative criteria to predict the surgical strategy for managing AC as well as the severity of inflammation.

Patients and methods

Patients

As shown in Table 1, 236 patients with acute cholecystitis (calculous and acalculous related inflammation) were admitted to our department between January 1995 and June 1999. There were 134 male and 102 female patients (male/female ratio 1:3), with a mean age of 61.4 years (range 23

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Table 1
Characterization of patients and surgical procedures

	Number
Patients	236
Male	134
Female	102
Sex ratio (M/F)	1.3
Age (years)	
Mean	61.4
Range	23–95
ASA classification (%)	
I/II	159 (67)
III/IV	77 (33)
Surgical procedures (%)	
Laparoscopic cholecystectomy	115 (49)
Conversion (laparoscopic to open)	44 (19)
Open cholecystectomy	77 (33)

ASA = American Society of Anesthesiologists.

to 95). The clinical diagnosis was preoperatively made from the patient's history with acute onset of right upper abdominal pain and tenderness, fever, leucocytosis, increased C-reactive protein (CRP) levels, and a positive ultrasonography (thickened gallbladder wall, pericholecystic fluid collection, positive Murphy's sign). The preoperative diagnosis was confirmed by the histopathological examination of the removed specimen.

If common bile duct stones were suspected preoperatively, an endoscopic retrograde cholangiography (ERC) with papillotomy and stone removal was performed prior to surgical treatment, as laparoscopic bile duct clearance has not yet been adopted as standard technique in cases of acute inflammation.

Early cholecystectomy within 48 hours after admission was always preferred because delayed surgical management (open or laparoscopic) may be associated with an increased complication rate as well as an increased overall hospital stay and costs [13–18]. Therefore, cholecystectomy was performed as a general policy, even the patient did improve after correction of fluid or electrolyte imbalances. All operative procedures were performed under antibiotic coverage, which was prolonged for at least 24 to 48 hours postoperatively. A liquid diet was normally started within the first 2 postoperative days.

The choice of LC or OC was determined by the patient's risk or previous operations, the suspected severity of AC, and, in particular, the surgeon's experience in laparoscopic surgery. Thus, there were no strict preoperative criterias or guidelines determining the surgeon's decision. However, a laparoscopic attempt was usually made if there were no strict contraindications for a laparoscopy (cardiopulmonary restrictions, coagulation disorder). The operative procedures were performed by 14 surgeons with various degrees of surgical training, whereby all surgeons had some experience with elective LC (at least 20 cases). All operations performed by residents (25%) were supervised by a consultant surgeon.

Operative technique

LC was performed as described previously using a standard four-trocar technique [2]. In brief, the patient was placed in the French position, with the surgeon standing between the patient's legs. Decompression of the gallbladder was routinely performed. The dissection was started at Calot's triangle; and the cystic duct, the common bile duct, and the cystic artery were exposed and divided between clips. Intraoperative cholangiography was only performed selectively if either common bile duct stones were suspected or to clarify the anatomical site of the bile ducts. The gallbladder itself was carefully mobilized from the liver bed using electrocautery. An endobag was always used to remove the gallbladder, thus preventing wound contamination. A drain was inserted into the liver bed before the trocars were removed, and the fascial defects were closed.

OC was either performed through a right subcostal or a midline incision. After decompression of the gallbladder, the dissection was started to identify the cystic duct and the common bile duct. In cases of advanced local inflammatory reaction, the dissection was performed from the fundus towards Calot's triangle. Intraoperative cholangiography was only performed selectively. Finally, the gallbladder was removed from the liver bed. Before the abdominal wall was closed, the abdominal cavity was irrigated, and a drain inserted into the liver bed.

Histopathological classification of AC

All the resected specimens were sent for histopathological examination. The severity of AC was then classified as type I, II, or III according to the extent of inflammatory changes in the gallbladder wall. In type I, only the mucosa was inflamed (erosive or ulcerous inflammation), whereas in type II mucosa and submucosal parts of the gallbladder wall were involved (phlegmonous inflammation). Finally, in type III, the whole gallbladder wall was destroyed (gangrenous or necrotizing inflammation).

Data collection and statistical analysis

Data were prospectively collected (medical records, operative reports, and histopathological reports) using a previously created protocol with selected criteria from the literature and analyzed with standard software package (S-PLUS 4.5 for Windows, MathSoft Inc., and SAS Software Release 6.12, SAS Institute Inc., Cary, North Carolina). Results are expressed as mean values and ranges.

Univariate statistical methods were used for comparison of different treatment modalities (LC versus OC or CON) and severity of AC. The Kruskal-Wallis rank sum test and the F test were used for quantitative measurements, and categorical data were analyzed with Pearson's chi-square test with Yates' correction. Preoperative criteria to predict the severity of inflammation were determined with a logit

Table 2
Characterization of the three patients groups and preoperative findings

	LC (n = 115)	CON (n = 44)	OC (n = 77)
Sex			
Male	53	27	54
Female	62	17	23
Sex ratio	0.9†	1.6†	2.3†
Age (years)			
Mean	55.1†	65.7†	68.5†
Range	23–89	25–93	29–95
ASA classification (%)			
I/II	99 (86)	31 (71)	29 (38)
III/IV	16 (14)	13 (29)	48 (62)
Preoperative duration of symptoms (days)			
Mean	2.2†	4.0†	3.2†
Range	1–14	1–21	1–14
Laboratory findings			
Mean WBC count in $\times 10^9$/L	11.2*	12.9*	14.5*
Range WBC count in $\times 10^9$/L	4.5–27.4	6.0–21.3	6.3–24.0
Mean CRP in mg/L	37.0†	127.1†	132.2†
Range CRP in mg/L	2–294	2–330	10–400

Statistical tests used for age, ASA, preoperative duration of symptoms and laboratory findings: Kruskal-Wallis rank sum test and F test. Statistical tests used for sex ratio: Pearson's chi-square with Yates' correction.

* $P < 0.05$ (LC versus OC and CON).

† $P < 0.001$ (LC versus OC and CON).

LC = laparoscopic cholecystectomy; OC = open cholecystectomy; CON = conversion; ASA = American Society of Anesthesiologists; WBC = white blood cells (normal range 3×10^9/L to 5×10^9/L); CRP = C-reactive protein (normal range <3 mg/L).

model for a ordinal response variable. The optimal treatment modality (LC or OC) was assessed by multivariate discriminant analysis (according to Agresti A. Categorical data analysis. Wiley, 1990; and Christensen R. Log-linear models and logistic regression. Springer, 1997).

Differences were considered statistically significant at $P < 0.05$.

Results

Patient characteristics and preoperative findings

Among the 236 patients were 159 (67%) who underwent a laparoscopic approach. In 115 of these, the gallbladder was completely removed laparoscopically, whereas in the remaining 44 cases (28%) the laparoscopic approach was converted to an open procedure (CON). Seventy-seven patients (33%) primarily underwent OC. The main reasons for OC were increased patient risk (39%), preoperatively suspected advanced local inflammation (46%), and previous upper abdominal surgery (29%). The baseline data of these three patient groups with different treatment modalities (LC, CON, and OC) are summarized in Table 2. Patients in both the OC and CON groups were >10 years older than patients in the LC group ($P < 0.001$), and they had a significantly increased individual patient risk (according to the American Society of Anesthesiologists [ASA] classification) than LC ($P < 0.001$). The sex ratio between groups also changed significantly ($P < 0.001$). In CON, and particularly in OC, there were more male than female patients (male/female ratio 1:6 and 2:3, respectively).

The preoperative laboratory findings showed significant differences for WBC count and CRP levels between the open and laparoscopically treated patients. In particular, increased CRP levels were predominantly found in OC and CON. Similarly, the preoperative duration of symptoms was prolonged in OC and CON compared with LC ($P < 0.001$). WBC counts rapidly increased with the occurrence of clinical symptoms, but there was only a slight increase with advanced inflammation such as necrosis formation and perforation. In contrast, CRP levels increased with the preoperative duration of symptoms, whereby the highest levels were found in patients with gangrenous cholecystitis.

Operative findings, morbidity, and mortality

The mean operating time was 92.1 minutes (range 25 to 240) in LC and 128.1 minutes (range 50 to 290) in OC ($P < 0.001$). CON resulted in a longer mean operating time of 135.8 minutes (range 60 to 260) compared with LC ($P < 0.001$) but not to OC. In LC, CON, and OC, there were 12 (10%), 12 (27%), and 7 (9%) intraoperative complications, respectively. The commonest by far were perforation of a friable gallbladder and some minor bleeding in the liver bed. There were no common bile duct injuries and no intraoperative deaths. Although acute inflammation of the gallbladder was found intraoperatively in all patients, histopathological examination revealed significant differences in severity between the groups ($P < 0.001$). Patients who successfully underwent LC predominantly had mild AC (type I, 68%), whereas CON and OC revealed advanced inflammatory disease (type II/III, 75% and 74%, respectively).

Conversion from LC to OC was necessary in 44 of the 159 patients. The decision to convert was usually taken within 15 to 30 minutes of beginning the laparoscopy in order to avoid difficult dissection with its increased bile duct injury risk. In 36 cases (82%), the anatomy of Calot's triangle was either severely distorted by the advanced inflammatory reaction or hidden by adhesions, thus making the dissection hazardous. Two patients (5%) had a perforation of the transverse colon that was caused by trocars. Both injuries were immediately recognized and successfully repaired openly. Another 2 patients had dense adhesions due to previous operations. Two further patients developed severe intraoperative hypercapnea and atrial fibrillation, and another needed a common bile duct stone removed, which was performed not laparoscopically. Finally, 1 patient had severe bleeding from the liver bed (Table 3).

LC was successful in 82%, when the operation was performed within 24 hours of the onset of clinical symptoms. After 48, 72, and 96 hours, the rate of LC decreased

Table 3
Operative findings, intraoperative complications, and conversion rate

	LC (n = 115)	CON (n = 44)	OC (n = 77)
Histopathological severity of AC (%)			
Type I	78 (68)†	11 (25)†	20 (26)†
Type II	21 (18)†	16 (36)†	26 (34)†
Type III	16 (14)†	17 (39)†	31 (40)†
Operating time (min)			
Mean	92.1†	135.8†	128.1†
Range	25–240	60–260	50–290
Intraoperative complications			
Total (%)	12 (10)	12 (27)	6 (9)
Perforation of the gallbladder	9	7	3
Bleeding	3	1	2
Perforation of the transverse colon	0	2	0
Atrial fibrillation	0	1	1
Other	0	1	0
Conversion rate (%)		44 of 159 (28)	
Reasons for conversion			
Inflammatory tissue reaction and adhesions		36	
Perforation of the transverse colon		2	
Bleeding		1	
Bile duct stone		1	
Adhesions of previous surgery	2		
Hypercapnea	1		
Atrial fibrillation	1		

Statistical tests used for operating time: Kruskal-Wallis rank sum test and F test. Statistical tests used for histopathological severity of AC: Pearson's chi-square with Yates' correction.

* $P < 0.007$ (LC versus OC and CON).

† $P < 0.001$ (LC versus OC and CON).

LC = laparoscopic cholecystectomy; OC = open cholecystectomy; CON = conversion; AC = acute cholecystitis.

Table 4
Postoperative complications, reinterventions, and hospital stay

	LC (n = 115)	CON (n = 44)	OC (n = 77)
Postoperative complications			
Total (%)	15 (13)*	7 (16)*	27 (35)*
Minor			
Wound infection	0	0	2
Local hematoma	1	1	0
Major			
Major intraabdominal bleeding	1	0	1
Cardiopulmonary dysfunction	3	4	7
Pulmonary embolism	0	0	1
Bowel obstruction	0	0	1
Intraabdominal infection (abscess)	0	0	2
MOF	0	0	5
Sepsis	0	0	3
Major bile duct injury	0	0	0
Bile leakage	1	1	2
Retained common bile duct stones	5	0	1
Intraabdominally lost drain	1	0	0
Other	3	1	2
Reinterventions (%)	10 (9)*	3 (7)*	19 (12)*
Relaparotomy	2	1	4
Relaparoscopy	1	0	0
Intervention (ERC, percutaneous drainage)	7	2	5
Mortality	0	0	6*
Hospital stay (days)			
Mean	6.3*	9.7*	14.1*
Range	3–17	4–21	4–81

Statistical test used: Kruskal-Wallis rank sum test and F test.

* $P < 0.001$ (LC versus OC and CON).

LC = laparoscopic cholecystectomy; OC = open cholecystectomy; CON = conversion; ERC = endoscopic retrograde cholangiography; ERCP = ERC and papillotomy; MOF = multiorgan failure.

to 45%, 21%, and 33%, respectively. Therefore, the conversion rate increased from 4.5% (24 hours) to 33% (48 hours), 61% (72 hours), and 45.5% (96 hours), respectively. When the patient's complaints had gone on for more than 96 hours, there were no successful LCs.

Postoperative morbidity, mortality, and overall hospital stay are shown in Table 4. There were 15 (13%), 7 (16%), and 27 (35%) postoperative complications after LC, CON, and OC, respectively. Minor complications were similar in each group (1% to 3%). There were 2 wound infections after OC and 2 local hematomas after LC and CON. Major complications occurred significantly more frequently after OC than after LC and CON. In particular, cardiopulmonary and septic complications, as well as multiorgan failure, developed more frequently in patients after OC. Major surgical complications (eg, major intraabdominal bleeding, intraabdominal abscess formation, bile leakage, and retained bile duct stones) generally needed reintervention or at least a prolonged intensive care unit stay. In LC, 2 reoperations were needed owing to major bleeding of the cystic artery and a bile leak of an aberrant bile duct; and one drain, which was poorly attached to the abdominal wall, had to be removed laparoscopically. Seven postoperative ERCs were performed; in 5 cases, stone removal was achieved. In CON, 1 patient underwent a planned second-look laparotomy to secure hemostasis. Another patient needed ERC with temporary stenting owing to cystic stump leakage. Postoperatively, a pseudo-obstruction of the colon developed in 1 patient and required an endoscopic tube insertion. In the OC group, 4 patients were reoperated on (2 for major bleeding, 1 small bowel obstruction, 1 duodenal perforation). Three patients needed postoperative ERC with stone removal, and in 1 case a plastic stent was inserted covering a bile leakage after removal of the T-tube drainage. Another patient had radiologically guided drainage of an intraabdominal abscess. After OC, 8 patients developed sepsis, which was prolonged with multiorgan failure (MOF) in 5 patients. Of these, 3 died within 2 weeks from septic complications, and 2 survived with a prolonged intensive care unit stay. There were 3 additional deaths after OC (1 pulmonary embolism, 1 respiratory insufficiency, 1 myocardial infarction). The increased mortality rate of 8% in the OC group reflected the severity of concomitant disease, whereas the overall mor-

Table 5
Comparison of different inflammatory stages of AC

	AC type I (n = 109)	AC type II (n = 63)	AC type III (n = 64)
Sex			
Male	52	36	47
Female	57	27	17
Sex ratio (M/F)	0.9†	1.3†	2.8†
Age (years)			
Mean	54.7†	63.3†	66.8†
Range	24–89	25–93	23–95
Preoperative duration of symptoms (days)			
Mean	2.2†	3.2*	3.6†
Range	1–14	1–21	1–21
Laboratory findings			
Mean WBC count in $\times 10^9$/L	11.5*	12.9*	14.1*
Range WBC count in $\times 10^9$/L	4.8–17.6	4.7–19.5	8.1–29.9
Mean CRP in mg/L	42.1†	91.0†	146.4†
Range CRP in mg/L	2–227	2–319	2–410
Operating time (min)			
Mean	99†	131†	155†
Range	30–260	30–285	25–290
Conversion rate (%)	10†	43†	49†
Complication rate (%)			
Intraoperative complications	10*	21†	17†
Postoperative complications	14†	24†	40†
Mean hospital stay (days)	7.3†	10.8†	10.5†

Statistical tests used for age, preoperative duration of symptoms, laboratory findings, complications and hospital stay: Kruskal-Wallis rank sum test and F test. Statistical test used for sex ratio: Pearson's chi-square with Yates' correction.

* $P < 0.05$ (LC versus OC and CON).

† $P < 0.001$ (LC versus OC and CON).

AC = acute cholecystitis; WBC = white blood cells (normal range 3×10^9/L to 5×10^9/L); CRP = C-reactive protein (normal range <3 mg/L); Type I = mild AC; Type II = moderate AC; Type III = advanced AC.

tality for the whole patient group was 3%, with no deaths in the LC and CON groups.

The average length of postoperative hospital stay was 6.3 days (range 3 to 17) in LC, 9.7 days (range 4 to 21) in CON, and 14.1 days (range 4 to 81) in OC ($P < 0.05$, CON and OC versus LC).

Comparison of different inflammatory degrees of AC

The demographic data of the three patient groups with different severity of AC are summarized in Table 5. Advanced inflammation of the gallbladder (AC type II and III) was more frequently found in elderly and male patients ($P < 0.001$). In addition, they had a significantly prolonged duration of preoperative symptoms. Advanced inflammatory stages of the gallbladder were associated with significantly increased CRP values and WBC. The overall complication and conversion rates as well as postoperative hospital stay were also significantly increased with advanced inflammation.

Table 6
Preoperative parameters predicting severity of inflammation

Variable	Odds ratio	Confidence interval
C-reactive protein	0.979	0.969–0.989
Duration of symptoms	0.861	0.759–0.977
Male gender	0.413	0.217–0.788
White blood cell count	0.993	0.987–1.000

Preoperative factors predicting severity of inflammation and determining treatment modality

Different preoperative parameters were identified using a logit model for multinomial response variables which were significantly related to the severity of inflammation and the treatment modality (Table 6). Male gender, prolonged duration of symptoms, increased WBC counts, and in particular increased CRP levels were associated with advanced inflammatory changes of the gallbladder and correlated with the severity of inflammation. The stepwise logistic regression analysis identified the following independent parameters that determine the treatment modality (laparoscopic versus open approach) for AC: CRP levels on admission, ASA classification, duration of symptoms, age, and WBC counts on admission.

According to the predictive preoperative factors that have been found in our series, there were several patients who underwent the "wrong" treatment modality. In fact, surgeons with limited laparoscopic experience revealed a tendency to overestimate the severity of inflammation and the impact of preexisting adhesions on the operative course of LC.

Comments

The purpose of our current study was to assess the treatment of patients with AC. In addition, the intention was to find preoperative parameters that predict the severity of AC. The data from this series demonstrate that different surgical modalities (LC and OC) are needed for the treatment of AC. Furthermore, we found several preoperative factors, in particular the CRP level, that help predict the severity of inflammation.

Since the late 1970s and 1980s, there has been a clear shift toward early surgical treatment of AC. Delayed cholecystectomy was found to be associated with increased morbidity and mortality rates, particularly in patients more than 65 years of age [13,14,16]. Increasing experience with laparoscopic surgery and improved technical equipment has led to a reintroduction of the "golden 72 hours" of early cholecystectomy, and several nonrandomized series have shown the safety and efficacy of LC for uncomplicated AC, although the reported conversion rate ranged up to 22% [19–21]. In addition, two recently published randomized trials have shown an even lower morbidity rate for LC compared with OC for treating gangrenous cholecystitis [11,17]. Although most of the available studies are at least partially biased by the varying skills of the laparoscopic surgeons involved, the selected patient groups, and the lack of a precise definition of AC, early LC currently represents an accepted treatment modality for AC.

Previous studies have shown that the complication rate of AC in open and laparoscopic surgery increases with age (>65 years), with a high operative risk (ASA >3), and present bile duct stones, as well as in patients with gangrenous inflammation [22–26]. The main reasons for conversion to OC were advanced age (>65 years), male sex, obesity, preoperative duration of symptoms, histologically proven degree of inflammation, and the surgeon's experience in laparoscopic surgery [7,12,27–29]. In our series, patients with OC and CON revealed similar characteristics compared with the literature. Advanced age, preoperative duration of symptoms, male sex, and the presence of concomitant disease (ASA 3 and 4) were significant risk factors predisposing for OC and CON compared with patients with successful LC who were younger and generally presented in a healthy condition. Furthermore, increased inflammatory changes of laboratory findings (WBC and CRP) were significant predictors for OC and CON.

Although the intraoperative complication rates for LC and OC were similar, the postoperative complication rate was higher after OC. This finding is comparable with previous studies, which also revealed a higher rate of postoperative complications for OC [21,25]. However, conversion was not associated with a higher postoperative morbidity compared with LC. The increased morbidity after OC is predominantly caused by the high incidence of major nonsurgical complications (eg, cardiopulmonary and septic complications, multiorgan failure). It can be assumed that patients selected for primary OC had an increased operative risk compared with those patients undergoing laparoscopy. The main reasons for intraoperative complications and conversion were related to inflammatory changes of the gallbladder and the adjacent structures, whereas impairment of the cardiopulmonary system was of no importance. However, conversion led to a prolonged hospital stay; thus, one main advantage of minimal access was lost. The length of the operating time for CON was strongly influenced by the surgeon's attempt to achieve LC. If there is no progress in the surgical dissection, the operation should be converted to an open approach. Otherwise, the danger of complications only increases, and unnecessary time will be lost.

Percutaneous cholecystostomy has been proposed by different authors as safe and effective alternative treatment to cholecystectomy in high-risk patients with severe concomitant comorbidity (eg, ASA 4) [30–32]. Although rapid relief of symptoms and improvement of laboratory findings might be achieved in 83% to 95%, later cholecystectomy was needed in almost 50% of patients with calculous AC, and the overall mortality rates ranged between 5.5% and 36% [31–33]. Therefore, percutaneous cholecystostomy should probably be restricted to patients unfit for surgical cholecystectomy, as surgical resection of the gallbladder can finally not be avoided in nearly half of the patients.

A broad variety of different inflammatory degrees of the gallbladder are culminated as AC, but obviously, mild inflammation at early stages of AC does not impair LC, whereas advanced necrotizing tissue reactions severely hamper safe identification and dissection of the anatomical structures. Therefore, the safety and efficacy of LC should be investigated for varying degrees of AC. In our study, we categorized the severity of inflammation into three different types according to the histological extent of gallbladder wall destruction. The three patient groups showed clear differences according to the severity of inflammation. Advanced age, male sex, prolonged duration of symptoms, and increased WBC counts and CRP levels were significant preoperative risk factors for advanced inflammation (AC type II and III). The complication rate, particularly postoperative complications, increased with the severity of the inflammation.

Using a multivariate analysis, there were several risk factors that predicted the severity of inflammation. CRP levels were the most powerful predictors, followed by the preoperative duration of symptoms, male gender, and WBC. To our knowledge, the predictive value of CRP for discriminating the degree of AC has not yet been described. However, for other intraabdominal inflammatory disease, such as acute pancreatitis and acute appendicitis, CRP levels are commonly used to predict the severity of inflammation, particularly necrosis formation, and bacterial infection [34–38]. WBCs increase within a very few hours, thus indicating the start of a gallbladder inflammation. Although there was a statistically significant difference between uncomplicated (type I) and complicated (type II and III) inflammatory disease, the diagnostic value of the WBC count was clinically limited. In contrast, protracted AC causing tissue necrosis led to different CRP levels, which were highly discriminatory for the inflammatory stage of AC. In general, CRP levels <10 mg/L are clinically unimportant for the diagnosis of AC and other acute inflammatory reactions [39]. On the other hand, CRP levels >100 mg/L are strongly related to local tissue necrosis. In our series, we did not routinely perform bacterial tests of the gallbladder wall; thus, we were not able to correlate the CRP level with the bacterial infection rate. Previous studies reported bacterial infection rates of 80% to 85% in cases of CRP levels >100 mg/L [40]. Although CRP levels and preoperative duration of symptoms correlated both in most cases with the severity of AC, the increase of CRP may not be strictly related to the duration of symptoms. Additional bacterial infection is presumably another important factor which has major influence on the development of CRP levels. Complicated AC (type II and III) was associated with both increased CRP levels and WBC. There were no patients in these two patient groups with a normal laboratory finding, whereas in type I AC about 25% of these patients showed any abnormality in the preoperative laboratory results. This is in comparison with Grönroos et al

[35] who found identical patterns of laboratory findings for uncomplicated and complicated acute appendicitis.

Based on the laboratory (CRP, WBC), demographic (age, sex), and individual (ASA classification, duration of symptoms) variables for determining the severity of inflammation, it seems possible to set preoperative conditions for laparoscopic and open cholecystectomy for AC. The validation of these predicting factors will be confirmed in a prospective trial.

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