Risk factors of conversion in laparoscopic cholecystectomies for lithiasic acute cholecystitis. Results of a monocentric study and review of the literature.

Facteurs de risque de conversion dans les cholécystectomies laparoscopiques pour cholécystite aiguë lithiasique. Résultats d'une étude monocentrique et revue de la littérature

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RÉSUMÉ

Introduction : De nos jours, la cholécystectomie coelioscopique est devenue la voie d'abord de choix dans la prise en charge des cholécystites aiguës lithiasiques. Cependant, le taux de conversion en laparotomie reste considérable, plus important que celui des lithiases non compliquées. Certains facteurs, en rapport avec le patient, avec la maladie ou avec le chirurgien, sont associés à un risque élevé de conversion.

Objectif : Déterminer les facteurs associés à un risque significatif de conversion dans les cholécystectomies coelioscopiques pour cholécystite aiguë lithiasique.

Méthodes : Entre Janvier 2011 et Décembre 2015, tous les patients opérés pour cholécystite aiguë au Service de Chirurgie Générale et Digestive du CHU Farhat Hached de Sousse - Tunisie ont été répartis en deux groupes : A pour la voie coelioscopique et B ayant nécessité une conversion. Nous avons procédé à la comparaison des deux groupes.

Résultats : Le taux de conversion était de 21.9% (43 patients). Au terme de ce travail, le taux de conversion était significativement augmenté en cas de sexe masculin (p=0.044), de maladie ulcéreuse (p=0.004), de tabagisme (p=0,004), de score ASA=II (p=0.005), de défense abdominale (p=0.001), de fièvre (p=0.001), d'épanchement péri-vésiculaire à l'échographie (p=0.041), de signe de Murphy échographique (p=0.023), de délai de cholécystectomie retardé (p=0.038), d'adhérences péri-vésiculaires (p<10-3) et de cholécystite gangréneuse (p=0.009).

Conclusion : La conversion est parfois mal acceptée par le chirurgien. Cependant, elle ne doit en aucun cas être considérée comme un échec, mais plutôt un changement de stratégie afin d'assurer la sécurité du patient. La conversion ne doit pas être retardée, surtout que des facteurs de risque ont été clairement identifiés.

Mots-clés

Cholécystite aiguë lithiasique ; Coelioscopie ; Conversion ; Facteurs de risque

SUMMARY

Introduction. Nowadays, laparoscopic cholecystectomy has become the gold standard in the management of lithiasic acute cholecystitis. However, the rate of conversion to laparotomy remains considerable, greater than that of uncomplicated lithiasis. Some factors, related to the patient, the disease or the surgeon, are associated with a high risk of conversion.

Aim: To identify the factors associated with a significant risk of conversion in laparoscopic cholecystectomy for acute cholecystitis.

Methods. Between January 2011 and December 2015, all patients operated on for acute cholecystitis at the Department of General and Digestive Surgery of Farhat Hached University Hospital of Sousse - Tunisia were divided into two groups: A for the laparoscopic approach and B for conversion. We compared the two groups.

Results. The conversion rate was 21.9% (43 patients). At the end of this work, we found that the conversion rate was significantly increased for males (p = 0.044), ulcerative disease (p = 0.004), smokers (p = 0.007), ASA score = II (p = 0.005), abdominal guarding (p = 0.001), fever (p = 0.001), perivesicular effusion on ultrasound (p = 0.041), ultrasound Murphy's sign (p = 0.023), delayed cholecystectomy (p = 0.038), perivascular adhesions (p <10-3) and gangrenous cholecystitis (p = 0.009).

Conclusion. The conversion is sometimes badly perceived by the surgeon. However, it should in no way be considered a failure, but rather a change of strategy to ensure patient safety. Conversion should not be delayed, especially as risk factors have been identified.

Key-words

Lithiasic acute cholecystitis; Laparoscopy; Conversion; Risk factors

INTRODUCTION

The laparoscopic approach has shown its feasibility and effectiveness in the surgical treatment of lithiasic acute cholecystitis. Nowadays, it has become the gold standard for the treatment of this relatively common pathology, which reduces postoperative morbidity and the hospital stay. However, laparoscopic cholecystectomy is sometimes not feasible for some patients because of anatomical lesions, or per-operative difficulties, obliging the surgeon to convert to laparotomy. Thus, pre-operative and intraoperative risk factors for conversion to laparotomy have been clearly identified.

The purpose of this work was to determine the factors associated with a significant risk of conversion in cholecystectomy for acute gallstone cholecystitis.

METHODS

This is a retrospective descriptive doneover 5 years that included all patients with clinical, biological and radiological criteria of acute cholecystitis and operated on laparoscopically at the Department of General and Digestive Surgery of the Farhat Hached University Hospital of Sousse (Tunisia), between January 1st, 2011 and December 31st, 2015.

All patients were operated on laparoscopically following the same procedure: a supine position, legs apart, the operator positioned between the legs and the attending on the left of the patient. Four trocars were used: epigastrium and right hypochondrium (5 mm), umbilicus and left hypochondrium (10 mm). Pneumoperitoneum is maintained at 12 mmHg. In case of conversion, the approach was a right subcostal incision. The duration of the intervention was measured in minutes beginning at the moment of insufflation until the time of carbon dioxide exsufflation for laparoscopy and the moment of parietal closure when converted to laparotomy. By distinguishing two groups of patients we identified:

• Group A: Patients who were operated by laparoscopic approach (153 cases);

• Group B: Patients who required a conversion to laparotomy during the same procedure (43 cases).

We compared the two groups (A and B) in order to identify factors associated with a significant risk of conversion.

The analysis was carried out using software package Epi Info (version 8). The comparisonof quantitative and qualitative variables was performed by adopting Student's t-test and Chi-squared test (if application conditions of Chi-squared test were not satisfied, correction with Yates'

chi-squared test or F-test was conducted). Statistical significance was set at the 5%.

RESULTS

We selected 196 patients who met the criteria for inclusion and non-inclusion. Table 1 summarizes demographics, preoperative, intraoperative and postoperative data in both study groups. We were interested in clinical, biological, radiological and operative data. We also considered immediate operative follow-up.

The mean time between onset of symptoms and cholecystectomy in our study population was 117.6 hours, with extremes of 24 hours and 320 hours; for group A the average time was 113.8 hours and for group B it was 131.1 hours. We noted a statistically significant difference between the two groups with p = 0.038 (Table 1)

Comparing sex, history and lifestyle in groups A and B, we found a statistically significant difference for the male sex (30.1% Vs 46.5%, p = 0.044), the history of ulcer disease (3.9 % Vs 16.3%, p = 0.004) and smoking (11.2% Vs 31.4%, p = 0.007).

On clinical examination, abdominal guarding was found in 37.9% of patients in group A against 67.4% in group B (p = 0.001). Fever was reported in 43.1% of group A cases compared with 72.1% of group B cases (p = 0.001). For the rest of the clinical examination, we found no statistically significant difference between the 2 groups.

Biologically, no significant difference between the two groups was observed for WBC, CRP, cholestasis markers, or markers of cytolysis.

An abdominal ultrasound was performed on all patients. Perivesicular effusion was found in 11.1% of group A cases and 23.3% of group B cases (p = 0.041). The US sign of Murphy was noted in 24.2% of cases in group A Vs. 41.9% of cases in group B (p = 0.023).

In our series, conversion from laparoscopy to right subcostal laparotomy was required in 43 patients (21.9%). The reported causes of the conversion were dissection difficulties (34 cases), intraoperative bleeding (15 cases), technical problems (4 cases), anesthetic problems (1 case) and Mirizzi's syndrome (1 case). The average conversion time was 54 minutes with extremes of 20 and 180 minutes. The placement of a trans-cystic drain was performed in 10 patients (5.1%) including 4 patients in group A (2.6%) and 6 patients in group B (14%).

Table 1. Comparison of patient characteristics, clinical data, exploratory data and surgical specifics in both groups.

Data	Group A (N=153)	Group B (N=43)	p
Mean age	52.3	57.5	0.066
Sex			
Male	46 (30.1%)	20 (46.5%)	**0.044**
Obesity	12 (63.2%)	4 (21.1%)	0.764
Medical history:			
Diabetes	26 (17%)	8 (18.6%)	0.805
Hypertension	47 (30.7%)	18 (41.9%)	0.170
Coronary artery disease	16 (10.5%)	3 (7%)	0.496
Respiratory failure	11 (7.2%)	1 (2.3%)	--
Renal failure	1 (0.7%)	0	--
Dyslipidemia	10 (6.5%)	5 (11.6%)	0.267
Acute pancreatitis	2 (1.3%)	1 (2.3%)	--
Hepatitis	2 (1.3%)	0	--
Stroke	7 (4.6%)	1 (2.3%)	--
Hypothyroidism	8 (5.2%)	0	--
Alcohol	2 (1.8%)	1 (40%)	--
Peptic ulcer disease	6 (3.9%)	7 (16.3%)	**0.004**
Smoking	13 (11.2%)	11 (31.4%)	**0.007**
Surgical history	26 (17%)	6 (14%)	0.634
ASA			
I	79 (52.3%)	13 (30.2%)	0.010
II	55 (36.4%)	26 (60.5%)	**0.005**
III or IV	17 (11.3%)	4 (9.4%)	0.952
Clinical examination:			
RUQ tenderness /guarding	58 (37.9%)	29 (67.4%)	**0.001**
Fever	66 (43.1%)	31 (72.1%)	**0.001**
Murphy's sign	12 (7.8%)	5 (11.6%)	0.436
Jaundice	1 (0.7%)	2 (4.7%)	--
Laboratory findings			
High WBC count (mean)	12 233.1	14 186	0.124
High CRP	47 (64.4%)	25 (83.3%)	0.057
Cytolysis	42 (32.3%)	12 (30.8%)	0.856
Cholestasis	47 (39.8%)	19 (50%)	0.270
High pancreatic enzyme	8 (8.2%)	3 (10%)	0.888
US signs			
Perivesicular effusion	17 (11.1 %)	10 (23.3%)	**0.041**
Sonographic Murphy's sign	37 (24.2%)	18 (41.9%)	**0.023**
Gallstones	151 (98.7%)	41 (95.3%)	0.171
GB Distension	143 (93.5%)	41 (95.3%)	0.649
GB wall thickening	136 (88.9%)	40 (93%)	0.429
Double layered GB wall	42 (27.5%)	10 (23.3%)	0.582
CBD stones	7 (4.6%)	3 (7%)	--
Intrahepatic bile duct dilatation	6 (3.9%)	1 (2.3%)	--
Timing of cholecystectomy (hours)	113.8 hours	131.1 hours	**0.038**
5 days delay	111 vs 42	23 vs 20	**0.04**
Surgical finding			
Gangrenous GB	34 (22.2%)	18 (41.9%)	**0.009**
GB distension	150 (98.7%)	42 (97.7%)	0.637
Pediculitis	54 (35.3%)	20 (46.5%)	0.180
CBD dilatation	7 (4.6%)	1 (2.3%)	0.513
Pancreatitis	0	1 (2.3%)	--
Peritonitis	8 (5.2%)	6 (14%)	0.128
Adhesions	59 (38.6%)	35 (81.4%)	**<10^{-3}**

ASA : American Society of anesthesiology; RUQ: Right upper quadrant; WBC: White blood cells; CRP: C-reactive protein; US: Ultrasonographic; GB: gallbladder; CBD : Common bile duct

The difference was statistically significant (p = 0.045). In our study, the mean operative duration was 102 minutes, with 92.4 minutes for group A vs. 136.6 minutes for group B. The difference between the 2 groups was statistically significant with p <10^{-3}. We also compared the two groups A and B regarding the intraoperative findings. The difference was statistically significant between the two groups for the gangrenous aspect (22.2% vs 41.6%, p = 0.009) and in case of peri-vesicular adhesions (38.6% vs 81.4%, p <10^{-3}).

The average length of stay in our population was 5.44 days with extremes of 2 and 29 days with 4.73 days for group A vs. 7.97 days for group B. The difference was statistically significant with p <10^{-3}. The mortality in our series was nil while the postoperative morbidity was 7.4% with a statistically significant difference between the 2 study groups (p = 0.01). Indeed, we counted 14 cases of postoperative complications;6 cases in group A (4.1%) and 8 cases in group B (19%). No surgical, endoscopic or radiological re-intervention was recorded.

The histopathological examination performed on all the removed biliary vesicles showed no statistically significant difference between the two groups.

After multivariate analysis, we found that the preoperative factors that significantly increase conversion's rate are fever (p = 0.012), abdominal guarding (p = 0.013), delayed cholecystectomy (p = 0.02) and ulcerative disease (p = 0.017). Intraoperatively, they were perivesicular adhesions (p <10^{-3}) and gangrene of the vesicular wall (p = 0.032). Table 2 summarizes these predictive factors of conversion.

Table 2. Predictive factors of conversion in laparoscopic cholecystectomy for lithiasic acute cholecystitis.

Factors	OR	CI$_{95\%}$	p
Pre-operative factors			
Fever	2.778	[1.25-6.15]	0.012
RUQ tenderness / guarding	2.632	[1.22-5.67]	0.013
Delay of the cholecystectomy	1.01	[1.001-1.016]	0.02
Peptic ulcer disease	4.40	[1.31-14.81]	0.017
Intra-operative factors			
Gangrenous GB	2.46	[1.082-5.582]	0.032
Adhesions	6.29	[2.701-14.632]	<10^{-3}

OR: Odds ratio; CI: Confidence interval; RUQ: Right upper quadrant; GB: gallbladder

DISCUSSION

This retrospective work finds its originality in the relatively large size of the sample (196 patients) which gives the required validity to our results and findings, with the possibility of generalizing the results. In addition, the retrospective and exhaustive character of the series made it possible to avoid a selection bias of the patients.

Our study has proven the feasibility of laparoscopic cholecystectomy for the treatment of lithiasic acute cholecystitis (78.9%). Laparoscopic management is therefore feasible and safe as a treatment for this common pathology. It has therefore become the gold standard for the management of acute cholecystitis [1]. At the end of this study, we found that the conversion rate was significantly increased for males, ulcerative disease, smokers, ASA score = II, abdominal guarding, fever, perivesicular effusion on ultrasound, ultrasound Murphy's sign, delayed cholecystectomy, perivascular adhesions and gangrenous cholecystitis.

The rate of conversion to laparotomy during laparoscopic cholecystectomy for acute cholecystitis in lithiasis varies between 2 and 25% in the literature [2-7]. In our series, it was 21.9%, which is consistent with the literature data. Conversion to laparotomy results in longer operating time, longer hospital stay and increased postoperative morbidity [6,8-12]

Currently, most surgeons recognize that the degree of inflammation of the gallbladder is the most important determinant of conversion [13]. Knowing the different risk factors for conversion can be very useful for assigning potentially more difficult cases to more experienced surgeons [14]. Especially since some authors [12, 15] have clearly identified the level of experience of the operator as being one of the primary factors in the conduct of laparoscopic cholecystectomy until the end, complication-free. Of course, other preoperative and perioperative risk factors for conversion to laparotomy have been clearly identified [16-18].

Teckchandani study [13] demonstrated that the conversion rate during cholecystectomy in male patients is significantly higher. Eldar [19] and Schäfer [8] also found that the male sex was a significant predictor of the severity of inflammation and the risk of conversion into acute cholecystitis. This is consistent with the results of our study in which there were 46 men in group A (sex ratio of 0.43) and 20 men in group B (sex ratio of 0.87) with p = 0.004. The reason why the conversion rate is higher in men remains poorly explained, but the male sex is classified as a significant risk factor in several other series [17, 20]. According to Kama [4], male patients had more intense inflammation or fibrosis, which resulted in a more difficult dissection of both the Calot's triangle and the layer separating the gallbladder from the liver. According to Sippey, this could be explained by the more delayed consultation period for men compared to women. Men would tolerate more pain and seek medical carelater, leading to a more difficult operating field and greater likelihood of conversion [6].

Although the current literature is divided as to whether BMI is predictive of conversion [21-27], the possible explanations for this finding include greater difficulty with liver retraction, pneumoperitoneum, and laparoscopic instrument manipulation, given the increased thickness of the abdominal wall. According to Sippey [6] and Livingston [23], obesity (BMI> 30 kg/m^2) was a predictor of conversion. In our series, the same as in Kama series, obesity was not a risk factor for conversion (p = 0.077)

Regarding age, Eldar [19] and Schäfer [8] found that an age> 65 years was a significant independent factor associated with conversion. In another study, Low [24] also identified higher age as a predictor of a higher failure rate of laparoscopic cholecystectomy, which could be explained by the complications related to defects. But in our study, the same as in Teckchandani study [13], age was not judged as a predictor of conversion in acute cholecystitis (p = 0.07).

Although no studies in the literature have investigated peptic ulcer disease as a predictor of conversion, in our series, we have elucidated this disease in a uni-multivariate study as a factor correlated with high conversion (with p = 0.004). This could be explained by the importance of adhesions and inflammatory changes in the duodenum caused by ulcerative disease which could make the dissection of the cystic pedicle more difficult.

In the literature, having had abdominal surgery is consideredas a predictor of conversion [25]. However, whether the nature of the procedure influences the rate of conversion has not yet been determined. Fraser [26] found that scars and hernias of the abdominal wall were significantly associated with perioperative difficulty during laparoscopy, requiring conversion. Akyurek [27] found an association between perioperative bleeding and the concept of previous surgery. In our series, we counted

16.3% of patients that had a surgical history of abdominal or pelvic surgery, but we did not find a significant association with the conversion rate.

Some studies have consideredfever as a conversion factor for acute cholecystitis, and concluded that fever >= 38°C correlates with a high conversion rate [16, 28, 29]. This seems logical because the existence of fever in case of acute cholecystitis is an indirect sign of its severity. Fever is usually associated with the clinical picture of acute cholecystitis.However the correlation between the degree of fever and the severity of the disease is uncertain. Kama [4] described abdominal guarding as a severity factor in acute cholecystitis at higher risk of conversion. Indeed, this sign accompanies the occurrence of a serious complication which is biliary peritonitis.Leukocytosis is one of the biological criteria for diagnosing acute cholecystitis as recommended by Tokyo [25]. Kanaan [10] has shown that high WBC level is useful for identifying patients at risk of conversion. He has found that the conversion rate in patients with acute cholecystitis with a WBC greater than 16000 was 28% compared with only 7.5% in patients with a WBC less than 16000. Other authors indicated that other figures of WBC as predictive factor of conversion, for example Dominguez [9] and Stanisic [30] who fixed the value of 12000 elements / ml, and on the other hand Kaafarani [31] and Sippey [6] who have set the value of 11000 elements / ml. In our study, we found that the conversion rate was significantly increased with the presence of abdominal guarding (p = 0.001) and fever (p = 0.001). But we found no significant difference between the 2 groups by comparing average WBC counts.

Several studies indicate that some signs in the initial abdominal ultrasound can predict the risk of conversion to open surgery, such as the presence of cholelithiasis in the gallbladder neck, a very thickened wall, perivesicular effusion, sclero-atrophy of the gallbladder and dilation of the bile ducts [22, 25, 32]. In the Atmaram [3], Srikanth [29], Thompson [33] and Dominguez [9] studies, wall thickening (> 4 mm) was the main predictor of conversion. In our series, we also found that perivesicular effusion and the sonographic Murphy sign are correlated with a high conversion rate.

Studies by Brugere [34], Thompson [35], Lo [36] and Jarrar [37] converge on the fact that early surgery (<5 days) has fewer technical difficulties, lower morbidity a shorter hospital stay and a lower laparotomy conversion rate (10-31% vs 18-74%). Similarly, the delay in our series influenced the conversion rate, since the average time was 114 hours in group A versus 131 hours in group B, with p = 0.038. In addition, when operated on after more than 5 days, the risk of conversion seemed to increase (p = 0.04). It therefore appears with a good level of evidence that the intervention should be performed without delay, if possible within 5-6 days of onset, at the acute stage of inflammation [9].

Studies by Shamieh [38] and Teckchandani [13] have suggested that intra-abdominal adhesions and the modified anatomy of the Calot's triangle also play a significant role in conversion. The inability to recognize anatomy, as a result of adhesions and inflammation, unexpected operative results and iatrogenic trauma are the most incriminated criteria in the decision to convert to an open path [10]. Peters [39] found that difficult dissection, usually secondary to adhesions, severe inflammation or obscure anatomy, is the most common reason for conversion (14%). This is consistent with our study's results. In fact, we found that 35 patients (81.4%) of the converted group had adhesions with $p < 10^{-3}$.

The degree of macroscopic severity observed intraoperatively of acute cholecystitis is largely associated with the rate of conversion of cholecystectomy. This has been reported by Eldar [40], Schäfer [8] and Rattner [41]. Teckchandani [13] also showed that the intraoperative severity of acute cholecystitis was significantly lower in patients with early laparoscopic cholecystectomy than in those who underwent conversion (p=0.032). In addition, the rate of conversion is significantly increased in case of vesicular plastron or gangrenous cholecystitis, as demonstrated by Singer [42]. In our study, the gangrenous appearance of the gallbladder was also significantly found more in group B (41.9% versus 22.2% in group A, p = 0.009). This rate is related to the difficulty of exposure and vesicular gripping because the wall is friable especially during the dissection of the Calot's triangle [32].

The factors correlated with a significant risk of conversion from the literature and in our series are summarized in Table 3.

CONCLUSION

Our study has highlighted the importance of taking into account, during acute cholecystitis surgery, the possibility of conversion, which must be done before the occurrence of any complication. The conversion proved to be dependent on certain factors. It is sometimes misunderstood by

Table 3. Synthesis of the predictive factors of conversion according to the studies.

Series	N	Conversion (%)	Predictive factors
Hollyman (2016) [7]	8820	3.4	Elderly, Male, ASA, US GB wall thickening.
Sippey (2015) [6]	7242	6	Elderly, Male, Obesity, ASA III or IV, Smoking, Cholestasis.
Vivek (2014) [22]	323	7.5	Elderly, Male, Obesity, History of abdominal surgery, ERCP, Adhesion, Cytolysisor cholestasis.
Dominguez (2011) [9]	703	13.8	Male, Age >70 years, WBC> 12000, ERCP, US GB wall thickening, Delayed cholecystectomy.
Atmaram (2011) [3]	1347	5.3	Elderly, Male, Obesity, ASA III, Fever, High WBC, US GB wall thickening or perivesicular effusion.
Teckchandeni (2010) [13]	50	20	Male, High CRP, Cholestasis.
Kaafarani (2010) [31]	11669	9	Elderly, Male, ASA>= III, Smoking, History of abdominal surgery, Hypertension, Diabetes, Obesity, Renal failure, Cytolysis or cholestasis, WBC> 11000.
Kanaan (2002) [10]	161	10	Elderly, Male, History of cardiovascular diseases, Gangrenous GB, Delayed cholecystectomy, High WBC, US GB wall thickening or perivesicular effusion.
Schäfer (2001) [8]	236	18.6	Elderly, Male, ASA >=III, High CRP, High WBC, US GB wall thickening or perivesicular effusion.
Kama (2001)[4]	1000	4.8	Male, History of abdominal surgery, US GB wall thickening
Peters (1994) [39]	746	14	Age > 60 years, Male, Delayed cholecystectomy>4days
Our series	196	21.9	Male, Peptic ulcerdisease, Smoking, ASA=II, Abdominal guarding, Fever, US perivesicular effusion, US Murphy's sign, Delayed cholecystectomy, Adhesions, Gangrenous GB.

ASA : American Society of anesthesiology; US: Ultrasonographic; GB: gallbladder; ERCP: Endoscopic retrograde cholangiopancreatography; WBC: White blood cells; CRP: C-reactive protein

surgeons who consider it a strategic failure. However, it should in no way be considered as a failure of the surgeon but rather a change of strategy, which should not be delayed, in order to avoid any risk to the patient, especially that pre-operative and intra-operative risk factors for conversion to laparotomy have been clearly identified. In all cases, the patient should be warned of the risk of this conversion before undergoing surgery.

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