Factors predisposing to conversion from laparoscopic to open cholecystectomy

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Abstract: The conversion of a laparoscopic cholecystectomy (LC) to an open procedure seems to be multifactorial, be affected by factors related to the patient, the gallbladder's pathology and the surgeon. Among the more than twenty parameters which have been studied as possible predisposing factors for conversion, current literature addresses that: a male patient, above 65 years old, with American Society of Anaesthesiology (ASA) score ≥3, suffering from acute cholecystitis, with a thickened gallbladder's wall on preoperative CT and an impacted stone in infundibulum or Mirizzi syndrome as intraoperative finding, who was operated on more than 72 hours from the onset of symptoms, by a non-laparoscopic surgeon, represents the most likely candidate for conversion from LC to open surgery. The probability increases further in the presence of malnutrition and/or cirrhosis. The proposed predictive scores for conversion have not yet found worldwide acceptance and their use is limited to theoretical or training purposes. Even patients with maximum predictive score, do not have a 100% probability for conversion. An experienced surgeon can complete a difficult LC successfully in high-risk surgical patient using the subtotal LC. The need for conversion to laparotomy should be considered as neither a failure nor a complication, but as an attempt to be avoided intra- or post-operative complications. The present review attempts to present the most recent knowledge on the field "conversion from LC to open surgery".

Keywords: Laparoscopic cholecystectomy (LC); conversion

Introduction

Laparoscopic cholecystectomy (LC) represents the "gold-standard" for the treatment of symptomatic gallstones disease, being the most common intra-abdominal operation performed in Western nations (1).

A conversion rate 5% to 10% has been reported on a nationwide basis (2). Depending on specific circumstances, a conversion can be characterized as either elective, which is defined as the surgeon's decision to resort a laparotomy (because of obscure anatomy or lack of progress of the laparoscopic procedure) before being forced to do so as a result of a major intraoperative complication or as enforced, when an intraoperative emergency such as uncontrollable bleeding or bile duct injury, occurs (3).

The most recognizable causes for conversion are: obscure biliary anatomy, presence of dense pericholecystic adhesions, intraoperative bleeding, failure of the progression and suspicion of choledocholithiasis (4,5).

Several factors such as male gender, age greater than 65 years, diabetes mellitus, obesity, acute cholecystitis, gallbladder's wall thickness, previous abdominal surgery, cirrhosis, etc. have been studied as predisposing for conversion, but contradictionary results have been published. Predictive scoring systems based on these factors (6-8), although did not gained worldwide acceptance, have been proposed as useful in selection of cases for residents training (3).

Discussion

Literature addresses that the factors predisposing to

conversion can be classified as patient related, disease related and surgeon related (3).

Patient related factors include age, gender, obesity, diabetes mellitus, previous upper abdominal surgery, presence of cirrhosis and several coexisting comorbidities.

As disease related predisposing factors have been proposed the recurrent episodes of biliary colic, the gallbladder's wall thickness, the acute cholecystitis as well as the presence of empyema or gangrenous cholecystitis, the biliary pancreatitis, the Mirizzi syndrom, the gallbladder's cancer and the presence of concomitant common bile duct (CBD) stones. Laboratory parameters such as, C reactive protein, white blood cell count, liver function tests (LFTs) and serum albumin have also been studied.

Finally, as surgeons related predisposing factors have been proposed the surgeon's experience and the development of serious intraoperative complications.

Patient related factors

Age and gender

Systematic reviews and meta-analyses (3,9-13) steadily disclosed male gender and patient's age above 65 years old as the two most recognizable predisposing factors for conversion. It has been proposed that inflammation and fibrosis were more extensive in men than in women causing difficult dissection at Calot's triangle during LC, fact predisposing to conversion (14). Particularly for elderly patients, it has been postulated that the longer the history of symptomatic gallstones disease, the more the delay in the presentation (15), thus; the more the untreated episodes of acute or even gangrenous cholecystitis, the higher the incidence of dense adhesions formation, the greater the incidence of anatomical difficulties and the higher the probability for a vulnerable dissection at Calot's triangle (16-18).

Obesity

Patients with an increased body weight have been reported to be especially prone to more severe inflammation or fibrosis of the gallbladder, making the dissection more difficult (19), while technical difficulties related to the trocars placement, the obscure anatomy because of the excessive intraperitoneal fat presence and the inability to retract the liver sufficiently, make obese patients prone to conversion. However, the role of obesity as a predisposing factor for conversion remains unclear. Other studies (20-22) disclosed body mass index (BMI) >30 as a predisposing factor for conversion, while others (23,24) state that as the surgeon's experience increases and the laparoscopic instruments improve, obesity gradually becomes even less important and should not be considered as a predisposing factor for conversion any more.

Diabetes mellitus

In theory, poorly controlled diabetes causes autonomic and peripheral neuropathy; thus diabetic patients may not develop symptoms of gallstones until later in the course of the disease, fact which may lead to a delayed diagnosis and more severe inflammation, increasing the risk for conversion during the laparoscopic procedure (8). Whether diabetes represents a predisposing factor for conversion remains controversial, since other studies (10,25) favor its predisposing role, while others (11,26) are against it. Glycosylated hemoglobin (Hba1c) plasma level >6 mg/dL has been proposed as a more predictive risk factor for conversion (27).

Previous upper abdominal surgery

Previous abdominal operations, particularly in the upper abdomen, are associated with an increased need for adhesiolysis, a prolong operating time and a higher conversion rate (3,10,28-31). However, previous upper abdominal surgery should not preclude LC as the first therapeutic option in symptomatic gallstones patients.

Cirrhosis

Cholelithiasis occurs twice as often in cirrhotic patients as in the general population. Since cirrhosis and compromised multiple organ function usually co-exist, while the hardness of the fibrotic liver and its increased vasculature secondary to portal hypertension with a high risk for bleeding, constitute major intraoperative difficulties, LC was considered as a contraindication in cirrhotic patients (32).

In 2003, Puggioni and Wong (33) enrolled 400 cirrhotic patients in a meta-analysis of the articles been published between 1993 and 2001. Among them, only 6 had been classified as Child-Pugh class C. The analysis found that compared to open cholecystectomy, LC in cirrhotic patients was associated with less intraoperative blood loss, decreased operative time and shorter postoperative hospital stay. The overall conversion rate was 7%. The authors concluded that although cirrhotic patients undergo cholecystectomy for more emergent reasons, LC can be safely and effectively applied, having advantages over open cholecystectomy and carrying an acceptable conversion rate.

In 2012, Machado (34) enrolled 1,310 cirrhotic patients

in a review of the articles been published between 1994 and 2011. Among them, 17 had been classified as Child-Pugh class C. The overall conversion rate was 4.5%, be increased up to 35% in Child-Pugh class C patients.

Currently, LC is not contraindicated in cirrhotic patients Child-Pugh class A and B, although a higher conversion rate should be expected. For cirrhotic patients Child-Pugh class C, the existing evidence is not enough for definite conclusions. However, for this particular subgroup of patients, open cholecystectomy still has an important role. Intensive preoperative optimization of the cirrhotic patient is mandatory prior to any laparoscopic or open approach.

Comorbid cardiopulmonary disease

It is well established that patients with American Society of Anaesthesiology (ASA) score 3,4 and 5, compared to them with ASA score 1 and 2 (35,36) as well as patients with comorbidities compared to low anesthetic risk ones (9,29), are at an increased—nearly double (35)—risk for conversion. Moreover, the positive pressure of pneumoperitoneum has adverse effect on the stroke volume and the cardiac index in patients with significant ischemic heart disease (37). The abdominal wall lift and the low pressure pneumoperitoneum techniques have been used to overpass the problem. Systematic reviews concluded that abdominal wall lift was not found to offer any advantage over pneumoperitoneum in low anesthetic risk patients (38), while the LC can be completed successfully using low pressure pneumoperitoneum in 90% of the patients, offering nothing to low anesthetic risk patients (39). Since the previously mentioned modifications of the laparoscopic technique have minimal effect on the conversion rate, all efforts should be focused in the preoperative optimization of the patient.

Other comorbidities

A nationwide study (2) disclosed a higher incidence of conversion rate among patients with malignancy as well as among psychiatric ones. Immunosuppression caused by the tumor itself or its therapy and conceal of the symptoms caused by the mental disorders themselves or the drugs used to treat them, delay the diagnosis, leading to more advanced stage of the disease at the time of diagnosis, causing more intraoperative technical difficulties, finally increasing the probability for conversion.

Disease related factors

Biliary colic

It was proposed that the breakpoint of more than 10 biliary colic attacks was a highly significant predictor for conversion (40). Based on only one high-bias risk trial, a systematic review (41) concluded that an early (within 24 from the diagnosis of the biliary colic) LC carries statistically significant lower conversion rate compared to the delayed one, (0% *vs.* 20% respectively, P=0.017) when multiple recurrences of the symptoms may have been occurred. Although the statistical significance was lost in the sequel systematic review (42), it also concluded that an early LC carries lower conversion rate compared to the delayed one (0% versus 17%, P=0.07) in cases of biliary colic.

Gallbladder's wall abnormalities

The terms "thickened gallbladder's wall" and "pericholecystic fluid" are the imaging findings unspecifically used in the literature to describe preoperatively terms such as acute cholecystitis, "complicated" cholecystitis and "difficult" gallbladder.

Since the proposed sonographic signs (e.g., wall thickness, wall striations, pericholecystic free fluid, local inflammatory fat changes) are neither sensitive nor specific enough to definitively diagnose acute cholecystitis (43), the accurate diagnosis of a thickened gallbladder's wall should be based on the CT findings. A thickened wall is defined as a smooth weakly enhancing thin inner layer consistent with inflamed or sloughed mucosa and a non-enhancing thick outer layer compatible with an oedematous loose connective tissue layer (44). Based on the preoperative CT findings, Fuks *et al.* (45) clearly stated that pericholecystic fluid was not significantly associated with conversion, the absence of gallbladder's wall enhancement was associated with gangrenous cholecystitis and only the presence of a gallstone in the infundibulum was associated with conversion. Maehira *et al.*, (46) determined the CT attenuation ratio of arterial phase (ARAP) to represent the degree of transient focal enhancement of the liver adjacent to the gallbladder. They found that an increased ARAP≥1.5 is a predictive factor for difficult LC and conversion.

The "difficult" gallbladder

The term "difficult" gallbladder is mainly based on intraoperative findings and is strongly depended on surgeons' skills to handle with a thickened gallbladder's wall (difficulties to grasp and retract the gallbladder, limitations in anatomic definitions, failures in dissection) (47), adhesions, concomitant choledocholithiasis or Mirizzi's syndrome (48). Thus, meta-analyses (10-12) and clinical studies (6,49-52) encountering the objective intraoperative

findings of a "difficult gallbladder" or a "thickened gallbladder's wall" as possible parameters affecting conversion, logically concluded that a gallbladder's wall of more than 5 (11,49), 6 (50) or 7 mm (51) predicts difficulty with anatomic exposure, predisposing to conversion. Bat (48) addressed severe adhesions at Calot's triangle as the most serious problem among all difficult LC cases and their presence was directly related to the overall operative time, the conversion rate and the wound infection rate. Not surprisingly, difficult LC, particularly in the elderly, carries a 22% conversion rate, compared to only 2.5% in cases of chronic cholecystitis (53).

For this particular subgroup of patients, a modification of the LC, the subtotal laparoscopic cholecystectomy (SLC), was advocated as a safe and feasible alternative prior to conversion. By resecting either both the posterior and anterior walls of the gallbladder, usually starting from fundus in a retrograde manner, closing or not the remnant at the level of the gallbladder's neck or Hartmann's pouch and leaving the pouch behind or by excising most of the gallbladder's anterior wall, leaving part of the posterior wall attached to the liver and closing or not the remained gallbladder's stump, the conversion rates were significantly decreased (54,55). Systematic review (56) suggested that closure of the cystic duct, gallbladder remnant or both should be preferable since fewer bile leaks, less need for ERCP and less recurrent gallstones symptoms seemed to occur.

The recently published (57) 25-point definitions of a "difficult" gallbladder, potentially can become the foundation of a novel and universally accepted grading system of surgical difficulty during LC. It can possibly lead to the initiation of a multicenter clinical trial in the future that was lacking in the past owing to the absence of a gold standard frame of reference. Such a study will have far-reaching impacts in solving important clinical questions.

Acute cholecystitis

Acute cholecystitis is a severe inflammation accompanied by increased vascularity and dense adhesions that interfere with good visualization, whereas the thick-walled gallbladder is often shrunken and contracted. Therefore, the cystic duct becomes shortened and the gallbladder adherents to the CBD, making its grasp for retraction difficult and its dissection from the CBD unsafe (58). Because of the technical difficulties confronted during LC, acute cholecystitis represents a steadily predisposing factor for conversion in the majority of the studies (3,9,10,11,21,25,27,30,58). An untreated acute cholecystitis may progress to emphysematous, gangrenous, emphysematous and perforated cholecystitis. Reports from national registries (59,60) disclosed that whenever any of the above happened, the conversion rate was increased by 3-fold, compared to the simple acute cholecystitis cases.

One of the factors found to affect the conversion rate, was the timing for cholecystectomy in acute cholecystitis cases. A Cochrane review (61), outlined the benefits of LC within 7 days from the onset of symptoms, others (13) addressed that the conversion rate was significantly lower in patients who underwent LC within 96 hours from the onset of symptoms, while others (62,63), advocated LC within the "golden 72 hours" of symptoms duration. Despite the obvious benefits, the feasibility of performing LC within 72 hours is often questioned due to a multitude of factors such as the possible attempts by patients to self-medicate with which may result in the late recognition of the condition, and that in a substantial group of patients with significant co-morbidities is required time for adequate pre-operative assessment and optimization (64), Current evidence support that is beneficial for the patients an early, within 72 hours from the onset of symptoms, rather than an interval LC and it should be offered as a therapeutic option in all non-high surgical risk acute cholecystitis patients.

Mirizzi syndrome

Mirizzi syndrome is encountered in 0.3–3% of all LC (65), For accurate diagnosis of the disease a high index of suspicion is required, and it should be suspected in any case of empyema, mucocele or stone impaction in the infundibulum (66), Mirizzi syndrome was considered as a contraindication for laparoscopic approach (65), since it was carrying a conversion rate of up to 74% for Type I and up to 100% for Type II (67). Since the introduction of the SLC technique, the conversion rates decreased to 16% for Type I and to 28% for Type II (68), indicating that a successful laparoscopic management by using the SLC technique, avoiding the conversion, can be achieved in selected cases (66,68,69)

Gallbladder cancer

Gallbladder cancer is mainly an incidental diagnosis. In the vast majority of the patients is diagnosed postoperative on the histological examination and exceptionally rare constitutes an intraoperative finding during LC. The incidence of the disease has been reported as low as 0.05% in simple LC, increasing to 0.60% in converted LC (70) The 5% conversion

rate for cholecystectomies performed for benign diseases, increases to 58% in cases of malignancy (71). Study from USA (70) addressed that incidental gallbladder cancer should be suspected in female patients, older than 65 years old, with elevated alkaline phosphatase level. Study from Europe (72) stated that the disease should be suspected in older women, with history of cholecystitis without jaundice and intraoperative palpable mass in the gallbladder. Therefore, incidentally diagnosed gallbladder cancer represents a predisposing factor for conversion during LC.

Biliary pancreatitis

The most recent systematic review (73) addressed that in cases of mild acute biliary pancreatitis, LC should be offered as definitive treatment during the same admission of the patient and ideally within 7 days from the onset of symptoms. However, studies (74-76) comparing the conversion rate between the early and the delayed LC in mild acute biliary pancreatitis cases concluded that the time of the definitive operation did not influence it. Thus, mild acute biliary pancreatitis should not be considered as a predisposing factor for conversion.

Concomitant CBD stone(s)

Up to 14.7% of the patients with gallstones have concomitant choledocholithiasis (77), while its incidence has been reported as high as 43% in patients older than 80 years (16). However, the role of choledocholithiasis as a predisposing factor for conversion is debatable and contra-dictionary results have been published (78).

For preoperatively known choledocholithiasis, preoperative ERCP followed by LC is the preferable treatment modality both in metropolitan and nonmetropolitan areas (79).

For patients with cholangitis, it is advisable firstly to drain the biliary obstruction by ERCP (80) or by percutaneous transhepatic cholangial drainage (81), followed by LC.

For intraoperatively discovered CBD stone(s), laparoscopic CBD exploration (LCBDE) can be offered to all patients, if local resources and surgical expertise is available (82,83) However, only in 30% of the patients, the LCBDE, was offered (79).

Systematic review (84) and meta-analyses (85,86) concluded that the single-stage approach (LC + LCBDE) has similar and comparable results to the two-stage approach (ERCP + LC) in terms of CBD clearance, postoperative morbidity and incidence of retained stones. Based on the above, current literature addresses that gallstones and concomitant choledocholithiasis can be successfully treated by endoscopic and/or laparoscopic approach in one- or two-stage approach and only exceptionally CBD stones can be considered as predisposing factors for conversion.

Laboratory parameters

C reactive protein (CRP)

Elevated CRP plasma levels reflect the severity of an inflammation and are used for the estimation of the inflammation process in acute cholecystitis cases. Mok *et al.* (87) disclosed that plasma CRP level >200 mg/dL has 100% sensitivity, 87.9% specificity and 100% negative predictive value for gangrenous cholecystitis, proposing CRP >200 mg/dL as an indicator for early/urgent operation. In retrospective studies, multivariate analyses among several factors including CRP, disclosed that CRP >165 mg/dL (88) or CRP >220 mg/dL (89) was significantly associated to conversion. However, aggregation of CRP with other parameters in several predictive scoring systems concluded that CRP either predicted the patients that should be considered as high risk for conversion (88,89) or was unrelated to the rate of conversion or the rate of complication (90). CRP may reflect the severity of the inflammation in acute cholecystitis and the consequences it causes, but only indirectly can be considered as a predisposing factor for conversion.

White blood cell count (WBC)

WBC represents one of the most exhaustively investigated factor which might affect the conversion rate. We should mention however, that the methodology of the studies was not homogenous, since other authors chose as cut-off level the 9×10^3 cells/mm^3 (4), while others set the cut-off level in 10×10^3 (27), 11×10^3 (91), or 12×10^3 (15,51). Other studies (4,21,27,51,91) disclosed elevated WBC as an independent predisposing for conversion factor, while others (5,20,58,92,93) concluded that the levels of WBC were unrelated to the conversion. Currently, the only available evidence-based result is coming from the meta-analysis of Rothman *et al.*, (11) who claimed that WBC was not associated to the conversion.

Liver function tests (LFTs)

Total bilirubin, alkaline phosphatase (ALP) and γ-glutamyltransferase (γGT) have been studied as factors predisposing to conversion. For bilirubin, other studies (20,59,93) did not conclude in any association, while others

(94,95) found that an increased bilirubin can increase the risk for conversion up to three-fold. For alkaline phosphatase, the majority of the studies (20,52,59,93,94) did not find any association, while others (4,21,92) disclosed ALP as a predisposing factor for conversion. Finally, γGT has been disclosed as a strong predisposing factor for conversion (96). In a prediction model (97), in which duration of LC for more than 60min was encountered as a "difficult" one, fact indirectly predisposing to conversion, LFTs was disclosed as an independent predisposing factor for conversion. However, other authors (20,78) did not support this finding. The role of LFTs in conversion should be investigated further.

Serum albumin

Severe inflammation, as in cases of acute cholecystitis, results in decreased albumin synthesis, while hypoalbuminemia can also be the result of protein-calorie malnutrition or reduced hepatic synthetic secondary to cirrhosis or other hepatic diseases (95). Since, low serum albumin level has been shown to predict postoperative complications in general, hypoalbuminemia has been studied as a risk factor for conversion and several reports (21,95,96) disclosed it as a strong and independent variance for conversion.

Surgeon's related factors

Surgeons experience

Studies from Western countries (98-101) clearly stated that in general, the conversions rates are lower among the well-trained high-volume laparoscopic surgeons, compared either to the general surgeons or to the inexperienced laparoscopic ones. On the other hand, the finding of increased conversion rates among the more experienced surgeons (102,103), probably reflects the fact that more likely an experienced surgeon will be involved in a difficult LC in high risk surgical patients: patients who otherwise might had been treated either open from the beginning or might had been converted at an earlier stage of the procedure by less experienced surgeons.

From the technical point of view, Tang *et al.* (104) identified the dissection at Calot's triangle as the task in which most errors were committed (the hazard zone of LC) and 97% of these errors were related to surgeon's visual perceptual illusion. They also observed that the use of different dissecting instruments was associated with different error probabilities. However, surgical experience leads to standardization of the method, fact probably affecting the conversion rates (101). Based on the above,

it is postulated that well-structured educational models can guarantee high safety profile (102). Early resident involvement in laparoscopic procedures (105), as well as advanced laparoscopic fellowship training, decrease conversion rates of LC for acute cholecystitis (106,107) thus the patients experienced shorter hospitalizations, fact which may influence the overall morbidity and the cost (97,105).

Serious intraoperative complications

The most common intraoperative complication leading to conversion is the intraoperative bleeding, followed by the suspicion for bile duct injury (53). Complications such as duodenal injury, life-threatening intraabdominal bleeding from puncture of the inferior vena cava or the external iliac artery by a trocar, injury to the right portal vein branches, uncontrollable bleeding from the liver bed and small bowel injury caused by the blind insertion of the umbilical trocar, have been described as factors which can enforce a surgeon to convert the LC (58,108).

Conclusions

The conversion of a LC to an open procedure seems to be multifactorial, be affected by factors related to the patient, the gallbladder's pathology and the surgeon.

Among the more than twenty parameters which have been studied as possible predisposing factors for conversion, current literature addresses that: a male patient, above 65 years old, with ASA score ≥3, suffering from acute cholecystitis, with a thickened gallbladder's wall on preoperative CT and an impacted stone in infundibulum or Mirizzi syndrome as intraoperative finding, who was operated on more than 72 hours from the onset of symptoms, by a non-laparoscopic surgeon, represents the most likely candidate for conversion from LC to open surgery. The probability increases further in the presence of malnutrition and/or cirrhosis. The proposed predictive scores for conversion have not yet found worldwide acceptance and their use is limited to theoretical or training purposes. Even patients with maximum predictive score, do not have a 100% probability for conversion. An experienced surgeon can complete a difficult LC successfully in high-risk surgical patient using the subtotal LC.

The need for conversion to laparotomy should be considered as neither a failure nor a complication, but as an attempt to be avoided intra- or post-operative complications. The present review attempts to present the most recent knowledge on the field "conversion from LC to open surgery".

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