Published in final edited form as:

J Hepatobiliary Pancreat Sci. 2018 January ; 25(1): 101–108. doi:10.1002/jhbp.493.

Preoperative Predictors of Conversion as Indicators of Local Inflammation in Acute Cholecystitis:

Strategies for Future Studies to Develop Quantitative Predictors

Roheena Z Panni, MD^{*,†} and Steven M Strasberg, MD^{*}

^{*}Division of Hepato-Pancreato-Biliary Surgery, Department of Surgery. Washington University School of Medicine, St Louis, MO

[†]Division of Public Health Sciences, Section of Oncologic Biostatistics, Department of Surgery. Washington University School of Medicine, St Louis, MO

Abstract

Background—Several observational studies have identified risk factors of conversion in laparoscopic cholecystectomy in acute cholecystitis. The aim of this study is to evaluate the reliability of these predictors of conversion and to identify sources of heterogeneity in literature.

Methods—The OVID database was searched for papers published from 1995 to 2016. Studies were considered eligible if they included more than 100 patients. The risk factors for conversion were abstracted from these studies and were categorized by their statistical significance by two independent observers.

Results—11 studies including 9992 patients were evaluated. Inflammation with difficulty in anatomic identification was the most common reason of conversion in 8 out of 11 studies. Age was identified as a significant predictor in 6 studies, followed by maleness and WBC count identified in 4 studies. Significant sources of heterogeneity identified in these studies included the criteria for diagnosis of acute cholecystitis, selection of patients for laparoscopic cholecystectomy, selection of variables and variations in their thresholds.

Conclusion—In patients with acute cholecystitis, severe inflammation is the most common reason for conversion and age, maleness and WBC are identified as common pre-operative predictors of conversion. However, further large scale prospective studies with minimal heterogeneity are needed to establish the validity of predictors of conversion.

Keywords

predictors of conversion; laparoscopic cholecystectomy; acute cholecystitis

Corresponding Author: Steven M. Strasberg MD, Section of HPB Surgery, Washington University in Saint Louis, 4990 Children's Place, Suite 1160, (Campus Box 8109), St Louis MO 63110, USA, Tel: 314 362 7147 FAX: 314 222 6255, strasbergs@wustl.edu.

Conflicts of Interest

RZP and SMS have no relevant conflicts of interest.

Introduction

In laparoscopic cholecystectomy for acute cholecystitis severe local inflammation is associated with increased chance of biliary injury (1–3). Therefore, preoperative assessment of the extent of local inflammation is of importance in guiding surgeons whether to perform early laparoscopic cholecystectomy or an alternative intervention such as cholecystostomy, open early cholecystectomy, or delayed cholecystectomy.

Because severe local inflammation is associated with increased operative difficulty there is increased incidence of conversion from laparoscopic to open cholecystectomy when severe local inflammation is present. Consequently, need for conversion has been equated with presence of severe local inflammation and predictors of conversion have been used as surrogates for predictors of severe local inflammation, although obviously other indications for conversion might be present in these patients as they are in patients without acute cholecystitis. Some of the markers of inflammation used to grade the severity of acute cholecystitis in the Tokyo Guidelines (4) such as white blood cell count (WBC) and duration of symptoms were derived from studies of predictors of conversion.

To evaluate the reliability of current predictors of local inflammation in acute cholecystitis a review was performed of studies that have identified preoperative risk factors for conversion of laparoscopic to open cholecystectomy in patients having early laparoscopic cholecystectomy for acute cholecystitis. First it was asked whether these studies, in fact, support a conclusion that conversion can be used as a marker of severity of local inflammation in acute cholecystitis. Then the preoperatively available risk factors for conversion in this group of studies were analyzed with the intention of determining the strongest and most reliable predictors. However, because of clinical and methodological heterogeneity in these studies a quantitative approach using standard meta-analytic methods was not possible. Therefore, a qualitative analysis of the results of the available studies was performed along with a detailed investigation into the sources of heterogeneity with the ultimate aim of creating a framework and guide for future quantitative studies.

Methods

Literature search

The OVID database was searched for papers published from 1995 to the end of 2016 with key words “laparoscopic cholecystectomy”, “acute cholecystitis” and “conversion” all present in the title. These papers were then searched for references to papers that might be appropriate for inclusion and these papers were also selected for study if they met criteria. Only papers with more than 100 patients were included. Papers with patients having interval (delayed) cholecystectomy in the analysis of results were excluded if the results were not clearly separated from those of patients having early cholecystectomy. Papers examining only one risk factor such as timing of cholecystectomy were excluded. Papers that included a change in management based on a preliminary analysis and then that performed an analysis that included combined data from before and after groups were excluded. One center published four studies from 1997 to 2002. The latest paper using standard multivariable

analysis in methods was selected for inclusion (5). A total of 11 papers were left for analysis.

Data extraction

The following variables were extracted from the selected papers: country, type of hospital(s), year of publication, number of patients, gender, age, number of conversions to open cholecystectomy, percent converted, reasons for conversion, timing of operation in relation to time of onset of symptoms and time of presentation, statistical methods, method of diagnosis of acute cholecystitis, results of univariable or multivariable analysis of risk factors for conversion.

The results of univariable or multivariable analysis of risk factors for conversion were classified as related to history, physical examination, laboratory, and imaging findings. The clinical factors searched for included age, gender, weight, comorbidities including diabetes, prior abdominal surgery, prior attacks of gallbladder pain or cholecystitis, fever at admission, palpable tender gallbladder, ASA score, and timing of cholecystectomy in relation to time of onset of symptoms and time of presentation. Laboratory indicators examined were WBC count, C-Reactive protein (CRP), ESR, serum albumin, AST, ALT, ALP, and bilirubin. Imaging factors that were examined included thickness of gallbladder wall, pericholecystic fluid, size, position or location and impaction of stones and evidence of choledocholithiasis including Common Bile Duct (CBD) diameter. Additionally, imaging characteristics which are already accepted as indicators of marked local inflammation (i.e. gangrene, emphysematous cholecystitis, perforation abscess) were noted.

Relationship between inflammation and need for conversion

Studies were searched for information regarding the reasons for conversion. These were categorized as clearly related to inflammation or not related to inflammation and whether they were common or uncommon reasons for conversion.

Categorization of risk factors for conversion

Some studies performed univariate analyses only and others performed multivariate analyses. Risk factors for conversion were categorized by the variables tested in a study and whether univariate or multivariate methods were used for analysis. Variables were first classified into categories based on whether they were derived from history including demographics, physical examination, laboratory tests, ultrasound or imaging as outlined above. These risk factors were then separated according to the statistical method used (univariate vs multivariate analysis) and the results (significant vs not significant). The results are presented as a heat map.

Sources of Heterogeneity

Sources of heterogeneity in the studies were sought, the purpose of which was to create a framework for future improved studies that might be suitable for systematic review and metaanalysis. Heterogeneity was examined in the following areas: criteria for diagnosis of acute cholecystitis, criteria for selection of patients with acute cholecystitis to undergo

laparoscopic cholecystectomy, thresholds used in evaluating the predictive value of variables and selection of variables to be tested.

Results

Demographics

11 studies published between 2000 and 2015 from 10 countries were evaluated (5–15) (Table 1). In all there were 9992 patients of whom 7242 were from one large database study. In the other 10 studies the mean number of patients was 275 ± 196.12 . 59.3 % of patients were females and 40.6 % were males (Table 1). All studies were conducted at university affiliated hospitals in urban centers.

Conversion rate

The conversion rate varied from 6% to 32% (Table 2). The lowest conversion rate was in the large database study from the USA that included more than 7000 patients (13). Other than that study the conversion rate varied from 14% to 32%. The conversion rate of 6% in the large database study was less than 50% of the next lowest conversion rate in the other 10 studies (mean conversion rate in the 11 studies was 22.75%).

Factors influencing decision to convert – role of inflammation

Eight of the 11 studies described the reasons for conversion to open cholecystectomy (Tables 3). Table 2 lists comments regarding the degree of inflammation encountered in converted cases. Severe inflammation associated with inflammatory adhesions and difficulty in anatomic identification were described clearly in all 8 studies. Table 3 lists the reasons for conversion by frequency. Inflammation and associated adhesions resulting in difficulty of anatomic identification was responsible for conversion in 75% to 93% of cases, in the 8 studies and these were by far the most common causes. Therefore, conversion was a good marker for operative difficulty caused by inflammation in acute cholecystitis. Less common causes of conversion were concern for malignancy, need for bile duct exploration, inability to create pneumoperitoneum, hypercapnia, choledochoduodenal fistula, spilled stone, atrial fibrillation and perforation of transverse colon.

Preoperative indicators of the need for conversion

Risk factors for conversion are presented in a color coded heat map for ease of comprehension (Figure 1). The map has the advantage that it may be scanned for results within studies and across studies. Four colors were used for coding - dark red, light red, dark green and light green. Dark red indicates significance of a variable in a multivariate analysis and light red indicates significance in a univariate analysis ($p < 0.05$). Dark green indicates non-significance of a variable in a multivariate analysis and light green indicates non-significance in a univariate analysis ($p > 0.05$). In some studies, information that a variable was not significant was present only for the univariate analysis and in that case the information is noted in light green. In most studies the cutoff for including or excluding a variable from the multivariable analysis was not provided. In two the cutoff was $p < 0.1$ (8, 13). Only variables that were tested in two or more studies are included in the analysis shown in Figure 1.

Some variables were evaluated in most studies such as male gender, age and WBC count for which data is available from 10 of 11 studies. Others such as hypertension, comorbidities and CRP level were examined in only 2 or 3 studies.

Age was identified as a significant predictor of conversion on multivariate analysis in six studies (5, 8, 12–15). Both maleness and WBC count were found to be significant predictors in four of these studies (5, 8, 12, 13). So in all, four studies identified the three variables maleness, age, and WBC count to be predictive of conversion in multivariate analysis (5, 8, 12, 13). Additional studies identified these factors in univariate analysis (Figure 1). Notably maleness and age have also been shown to be predictive for conversion in elective cholecystectomy in multiple studies (16–18). Long interval between symptom onset and operation was a positive predictor of conversion in 3 studies in univariate analyses (6, 7, 11). Other variables in which there are at least 3 positive results and in which positive results predominate over negative ones are ASA level and pericholecystic fluid (Figure 1). CRP was tested in only two studies (11, 14) but in one study which evaluated both WBC count and CRP in a multivariate analysis only CRP was predictive (14). Since both are measures of inflammation this raises the possibility that CRP may be the superior predictive variable. Only one study evaluated the physical finding of a palpable gallbladder and that study actually found that *inability* to palpate the gallbladder was a positive predictor of conversion (5). Note that eight variables were found to be significant in the study by Sippey et al. indicating the strength of large numbers of patients to determine predictive variables.

Sources of Heterogeneity and Areas where Heterogeneity May Be Hidden

Criteria for diagnosis of acute cholecystitis—Five studies used a combination of clinical, laboratory, and imaging results, but not pathological findings, to make the diagnosis (7–10, 14). Two of these specifically used the Tokyo guidelines for diagnosis of acute cholecystitis (9, 10). Five other studies accepted the diagnosis of acute cholecystitis only when the diagnosis was confirmed by microscopic examination of the resected gallbladder (5, 6, 11, 12, 15). The histologic criteria for diagnosis were usually not stated. Microscopic findings were used to grade the severity of acute cholecystitis only by Schafer et al (11). In some other studies severity was estimated by a gross finding such as gangrene or perforation (6). In one study the diagnosis was based on ICD-9 codes only (13).

Criteria for selecting laparoscopic cholecystectomy as treatment—When patients present with acute cholecystitis only some undergo early laparoscopic cholecystectomy while others are selected for treatments, for example open cholecystectomy or delayed laparoscopic cholecystectomy. Preoperative perceived operative difficulty can lead to variations in streaming into different management options from center to center. This might affect the composition of the patient population who have early laparoscopic cholecystectomy from study to study. In order to evaluate this, the disposition of the entire population of patients presenting with acute cholecystitis during the study period is needed. Most papers gave little or no information regarding criteria for selection of early laparoscopic cholecystectomy or the disposition of patients that were not selected for laparoscopic cholecystectomy. Specifically only a few papers provided (5, 6, 9, 11, 15) any information on the number or per cent of patients treated by early open cholecystectomy

versus, subtotal cholecystectomy, cholecystostomy, or non-invasive means in the early period followed by interval cholecystectomy. Only one study provided detailed information about cases selected for early open cholecystectomy (11). This study compared the risk factors and outcomes of patients who underwent laparoscopic cholecystectomy, lap converted to open and early open cholecystectomy (11). It should be noted that the problem in this area is not only heterogeneity but the inability to evaluate whether heterogeneity is present.

Heterogeneity due to variations in thresholds (Figure 1)—The extent to which a variable is able to predict conversion may depend upon the threshold selected. The threshold for WBC count is a good example. In these studies, the threshold for WBC count being predictive of conversion has been set as low as any value greater than normal, 12k/mm^3 , 15k/mm^3 and 18k/mm^3 . Similarly the threshold for age varied from 60-70 years and that for bilirubin from 1mg/dl to 2mg/dl. ASA was also affected by this problem. However, equally problematic was the fact that in some cases such as age thresholds were not given. Thus again the problem is the inability to examine for heterogeneity.

Heterogeneity due to variables tested—Some studies do not include variables that are logically associated with conversion with the potential result that other variables which are covariate with the excluded variable are identified as significant. WBC count and CRP is a good example. To allow testing of all logically associated variables the number of patients in the study needs to be large.

Discussion

Conversion, Inflammation and Prediction of Operative Difficulty

This study has shown that when performing laparoscopic cholecystectomy for acute cholecystitis the chief reason for conversion from laparoscopic cholecystectomy is inflammation. While other causes for conversion exist, inflammation and its consequences are the reason for conversion in the large majority of cases. Therefore, it can be concluded that conversion is a good marker for operative difficulty due to inflammation in laparoscopic cholecystectomy for acute cholecystitis. It may also be concluded that in patients with acute cholecystitis, preoperative identification of risk factors predictive of conversion will also predict operative difficulty due to inflammation. In the past this has largely been assumed but now it is shown explicitly. This is of importance since such risk factors have been used to build severity grading systems for acute cholecystitis such as The Tokyo Guidelines (19, 20).

Identification of Factors Predictive for Conversion

The original intent of this study was to perform a synthesis of studies that have identified predictors of conversion of laparoscopic to open cholecystectomy in patients having laparoscopic cholecystectomy for acute cholecystitis. This was in conjunction with the program to revise the Tokyo 2013 Guidelines. However the original aim was unattainable because of heterogeneity among studies and importantly the inability to determine whether heterogeneity was present. As a result the aim of the study was changed to identify a range of potential predictors and design a definitive study to fulfill the original purpose. Despite

the considerable heterogeneity among studies three variables maleness, age, and elevated white blood cell count repeatedly stand out as independent predictors for conversion in multivariate analyses. Interval over 72 hours from onset of symptoms to operation has been shown to be related to conversion in the past (21) and is a predictor in the Tokyo Guidelines. In this study it was a significant but less strong predictor. It was significant in 3 studies using univariate analysis (6, 7, 11). It would not be surprising if interval is found to be a strong independent predictor in multivariate analyses since logically it is predictive of the onset of a more vascular and woody type of acute inflammation that is not predicted by other independent variables, however that study needs to be done. ASA like Interval was positive in several univariate analyses. It was also positive in one multivariate analysis. Pericholecystic fluid, thick gallbladder wall, CRP and serum bilirubin level were studied less frequently than other variables. Pericholecystic fluid and thickened gallbladder wall are useful diagnostically in acute cholecystitis but whether they are independent predictors of conversion is unclear. One study made the interesting observation that wall thickness over 5mm predicted conversion but milder degrees did not (6). Therefore “wall thickness >5mm” as opposed to “any increased wall thickness” may be an important predictor. The same might be said of pericholecystic fluid. CRP already is used as a diagnostic variable in the Tokyo guidelines and as noted above may actually be superior to WBC count but just has not been tested against it sufficiently in multivariate analyses to make that determination. Bilirubin levels may rise in acute cholecystitis due to impingement of the inflamed gallbladder on the bile duct and also as an effect of sepsis on the liver. Elevated WBC count, interval, pericholecystic fluid, thickened gallbladder wall and CRP are all effects of inflammation. Large multivariate studies in which all these variables are included will be needed to determine the strength of these variables as independent predictors of conversion. It should be noted that “palpable gallbladder” was not a predictor in any of these studies and that in one study the predictor was actually the absence of ability to palpate a gallbladder (5). All of these variables are potential predictors for conversion due to increased inflammation and should be included in future studies to delineate which are the strongest independent predictors.

Chronic Inflammation in Gallbladder with Acute Cholecystitis

If maleness and age were predictors of conversion just because they predicted acute inflammation it would be expected that one or both of these variables would fall out sometimes in multivariate analyses that contain the variable “elevated white blood cell count” since WBC count is a more direct measure of acute inflammation, but this was not the case. In all 4 studies in which elevated WBC count was significant in a multivariate analysis, maleness and age were also significant and therefore independent predictors of conversion. One clue to the probable explanation lies in the fact that both maleness and age have been repeatedly shown to be risk factors for conversion in elective cholecystectomy i.e. in circumstances in which the diagnosis is not acute cholecystitis (16–18). A second clue is that some of the statements regarding inflammation given in Table 3 referring to contraction of the gallbladder (10) and adhesions (6, 9–11, 15) are appropriate descriptors for chronic inflammation. These are good reasons for considering that maleness and age are predictors for circumstances in which significant chronic inflammation as well as acute inflammation are present and this contributes to the technical difficulty of the procedure. It is well known

that attacks of acute inflammation of the gallbladder may occur on a background of prior attacks of inflammation that scar the gallbladder and these may be more common in older males.

Toward a Definitive Study

Eleven surgical studies were identified that attempted to answer the same question – what are the predictors for conversion in laparoscopic cholecystectomy done for acute cholecystitis? The reason why the question cannot be answered definitively is related to the presence of heterogeneity and importantly to the inability to evaluate the degree of clinical heterogeneity among studies. The inability to evaluate whether heterogeneity is present is actually a greater problem than heterogeneity itself, since heterogeneity can be measured and risk adjusted.

The ideal study would have the following characteristics

- 1) The study should be large enough to evaluate at least 20 variables. If the predicted conversion rate is 10% and ten events (conversions) are needed per variable then 2000 patients would be required. This would require a large multiinstitutional registry.
- 2) For study purposes the diagnosis of acute cholecystitis must be secure. Only histological diagnosis is really adequate to eliminate the heterogeneity in diagnosis. Using clinical diagnostic criteria is less secure and ICD code is even less secure. In the USA there is a bias toward making a clinical diagnosis of acute cholecystitis over biliary colic as the former results in higher leveling and therefore access to acute care facilities such as operating time. Obviously including patients in a study group who have biliary colic rather than acute cholecystitis would tend to reduce conversion rates in that group
- 3) The severity of acute inflammation should be graded e.g. as by the classification proposed by Schafer (11). Then predictors can be evaluated as to their ability to predict inflammation as well as conversion.
- 4) The severity of chronic inflammation should be graded histologically by extent of fibrosis.
- 5) The entire cohort of patients presenting with acute cholecystitis should be presented along with their routing to various treatments. Lack of such information is a form of potentially hidden heterogeneity. Note that laparoscopic bailouts such as laparoscopic subtotal cholecystectomies are becoming more common and for study purposes are very similar to conversions.
- 6) The data should be evaluated by multivariate analysis. Importantly for purposes of meta analyses non-significant odds ratio as well as significant odds ratios should be given.
- 7) Reporting certain variables e.g. WBC count as a continuous variable is more informative than dichotomizing and specifying thresholds, which results in loss of information. One argument for this categorization is that it simplifies the

interpretation of results but assessment of continuous variables across their entire range provides much more information to detect any relation between a predictor variable and outcome.

- 8) The reasons for conversion should be described under categories that equate to acute and chronic inflammation.

In summary, severity grading of acute cholecystitis by examination of predictors of conversion has provided guidance to the formation of guidelines. A quantitative analysis is not yet possible due to heterogeneity and the inability to generate heterogeneity however the available studies provide clues to potentially valuable predictors and a pathway to future studies.

Acknowledgments

RZP was supported by funding from National Institutes of Health (NIH) grant number (NIH 5T32CA00962128).

References

1. Davidoff AM, Pappas TN, Murray EA, Hilleren DJ, Johnson RD, Baker ME, et al. Mechanisms of major biliary injury during laparoscopic cholecystectomy. *Ann Surg.* 1992; 215(3):196–202. [PubMed: 1531913]
2. Strasberg SM, Eagon CJ, Drebin JA. The “hidden cystic duct” syndrome and the infundibular technique of laparoscopic cholecystectomy—the danger of the false infundibulum. *J Am Coll Surg.* 2000; 191(6):661–7. [PubMed: 11129816]
3. Tornqvist B, Waage A, Zheng Z, Ye W, Nilsson M. Severity of Acute Cholecystitis and Risk of Iatrogenic Bile Duct Injury During Cholecystectomy, a Population-Based Case-Control Study. *World J Surg.* 2016; 40(5):1060–7. [PubMed: 26669783]
4. Hirota M, Takada T, Kawarada Y, Nimura Y, Miura F, Hirata K, et al. Diagnostic criteria and severity assessment of acute cholecystitis: Tokyo Guidelines. *J Hepatobiliary Pancreat Surg.* 2007; 14(1):78–82. [PubMed: 17252300]
5. Halachmi S, DiCastro N, Matter I, Cohen A, Sabo E, Mogilner JG, et al. Laparoscopic cholecystectomy for acute cholecystitis: how do fever and leucocytosis relate to conversion and complications? *Eur J Surg.* 2000; 166(2):136–40. [PubMed: 10724491]
6. Cwik G, Skoczylas T, Wyroslak-Najs J, Wallner G. The value of percutaneous ultrasound in predicting conversion from laparoscopic to open cholecystectomy due to acute cholecystitis. *Surg Endosc.* 2013; 27(7):2561–8. [PubMed: 23371022]
7. Del Rio P, Dell’Abate P, Soliani P, Sivelli R, Sianesi M. Videolaparoscopic cholecystectomy for acute cholecystitis: analyzing conversion risk factors. *J Laparoendosc Adv Surg Tech A.* 2006; 16(2):105–7. [PubMed: 16646697]
8. Dominguez LC, Rivera A, Bermudez C, Herrera W. Analysis of factors for conversion of laparoscopic to open cholecystectomy: a prospective study of 703 patients with acute cholecystitis. *Cir Esp.* 2011; 89(5):300–6. [PubMed: 21397899]
9. Fuks D, Mouly C, Robert B, Hajji H, Yzet T, Regimbeau JM. Acute cholecystitis: preoperative CT can help the surgeon consider conversion from laparoscopic to open cholecystectomy. *Radiology.* 2012; 263(1):128–38. [PubMed: 22332066]
10. Oymaci E, Ucar AD, Aydogan S, Sari E, Erkan N, Yildirim M. Evaluation of affecting factors for conversion to open cholecystectomy in acute cholecystitis. *Prz Gastroenterol.* 2014; 9(6):336–41. [PubMed: 25653728]
11. Schafer M, Krahenbuhl L, Buchler MW. Predictive factors for the type of surgery in acute cholecystitis. *Am J Surg.* 2001; 182(3):291–7. [PubMed: 11587696]

12. Simopoulos C, Botaitis S, Polychronidis A, Tripsianis G, Karayiannakis AJ. Risk factors for conversion of laparoscopic cholecystectomy to open cholecystectomy. *Surg Endosc*. 2005; 19(7): 905–9. [PubMed: 15868267]
13. Sippey M, Grzybowski M, Manwaring ML, Kasten KR, Chapman WH, Pofahl WE, et al. Acute cholecystitis: risk factors for conversion to an open procedure. *J Surg Res*. 2015; 199(2):357–61. [PubMed: 26092215]
14. Wevers KP, van Westreenen HL, Patijn GA. Laparoscopic cholecystectomy in acute cholecystitis: C-reactive protein level combined with age predicts conversion. *Surg Laparosc Endosc Percutan Tech*. 2013; 23(2):163–6. [PubMed: 23579511]
15. Yetkin G, Uludag M, Citgez B, Akgun I, Karakoc S. Predictive factors for conversion of laparoscopic cholecystectomy in patients with acute cholecystitis. *Bratisl Lek Listy*. 2009; 110(11):688–91. [PubMed: 20120435]
16. Fried GM, Barkun JS, Sigman HH, Joseph L, Clas D, Garzon J, et al. Factors determining conversion to laparotomy in patients undergoing laparoscopic cholecystectomy. *Am J Surg*. 1994; 167(1):35–9. discussion 9–41. [PubMed: 8311138]
17. Ibrahim S, Hean TK, Ho LS, Ravintharan T, Chye TN, Chee CH. Risk factors for conversion to open surgery in patients undergoing laparoscopic cholecystectomy. *World J Surg*. 2006; 30(9): 1698–704. [PubMed: 16927065]
18. Sanabria JR, Gallinger S, Croxford R, Strasberg SM. Risk factors in elective laparoscopic cholecystectomy for conversion to open cholecystectomy. *J Am Coll Surg*. 1994; 179(6):696–704. [PubMed: 7952482]
19. Takada T, Kawarada Y, Nimura Y, Yoshida M, Mayumi T, Sekimoto M, et al. Background: Tokyo Guidelines for the management of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Surg*. 2007; 14(1):1–10.
20. Takada T, Strasberg SM, Solomkin JS, Pitt HA, Gomi H, Yoshida M, et al. TG13: Updated Tokyo Guidelines for the management of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci*. 2013; 20(1):1–7. [PubMed: 23307006]
21. Hadad SM, Vaidya JS, Baker L, Koh HC, Heron TP, Hussain K, et al. Delay from symptom onset increases the conversion rate in laparoscopic cholecystectomy for acute cholecystitis. *World J Surg*. 2007; 31(6):1298–01. discussion 302–3. [PubMed: 17483986]

Figure 1.

Heat map of variables tested for relation to conversion in patients having laparoscopic cholecystectomy for acute cholecystitis in 11 studies. "Interval" is the time between onset of symptoms and cholecystectomy. CRP= C - reactive protein. PC fluid = pericholecystic fluid.

Table 1

Patient characteristics in included studies.

Authors	Year	Country	No. of patients (n)	Mean age (years)	% Female	Conversion Rate (%)
Halachmi et al. (6)	2000	Israel	256	55.0	56.6	20.0
Schafer et al. (12)	2001	Switzerland	159	61.4	*	27.6
Simopoulos et al. (13)	2005	Greece	272	52.7	68.4	18.3
Del Rio et al. (8)	2006	Italy	176	61.7	*	32.3
Yetkin et al. (16)	2009	Turkey	108	50.0	63.0	17.6
Dominguez et al. (9)	2011	Colombia	703	47.8	64.4	13.8
Fuks et al. (10)	2012	France	108	58.0	43.5	22.0
Cwik et al. (7)	2013	Poland	542	*	*	24.0
Wevers et al. (15)	2013	Netherlands	261	59.5	59.4	24.0
Oymaci et al. (11)	2014	Turkey	165	52.4	67.9	27.9
Sippey et al. (14)	2015	USA	7242	56.1	58.6	6.0

* Information missing

Table 2

Chief comments regarding reason for conversion in eight studies

Study	Comments
Schafer et al.(12)	The anatomy of Calot's triangle was either severely distorted by the advanced inflammatory reaction or hidden by adhesions, thus making the dissection hazardous.
Simopoulos et al. (13)	Inability to define anatomy in triangle of Calot 11 times more frequent in AC than in elective cholecystectomy.
Yetkin et al. (16)	Inability to display anatomy safely due to severe inflammation and dense adhesions.
Dominguez et al. (9)	Severe inflammation.
Fuks et al. (10)	The two main reasons were: (a) difficulty in dissecting the biliary pedicle due to inflammation with gangrenous acute cholecystitis and (b) adhesions resulting from local inflammation.
Cwik et al. (7)	Impossible identification of the cystic duct. Massive inflammatory or post-operative adhesions.
Wevers et al. (15)	Inability to reach the critical view of safety due to inflammatory changes.
Oymaci et al. (11)	Difficulty identifying anatomy (inflammation, biliary or vascular anomalies) inability to define anatomy including contracted or fibrotic gallbladder and cystic duct; dense adhesions of the gallbladder to either the duodenum or the common bile duct.

Table 3

Reasons for conversion identified in eight studies.

	Schafer et al. (12)	Simopoulos et al. (13)	Yetkin et al. (16)	Dominguez et al. (9)	Fuks et al. (10)	Cwik et al. (7)	Wevers et al. (15)	Oymaci et al. (11)
Sample size	159	272	108	703	108	542	261	165
Conversion rate (%)	27.6	18.3	17.6	13.8	22.0	24.0	24.0	27.9
Reasons for conversion	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Severe inflammation	38 (86.4)	70 (74.5)	15 (78.9)	90 (92.8)	21 (87.5)	109 (83.8)	54 (87.1)	42 (91.3)
Hemorrhage	1 (2.3)	3 (3.2)	4 (21.1)	4 (4.1)	2 (8.3)	11 (8.5)	5 (8.1)	3 (6.5)
Suspected bile duct injury	-	2 (2.1)	-	3 (3.1)	1 (4.2)	3 (2.3)	2 (3.2)	1 (2.2)
Concern for malignancy	-	2 (2.1)	-	-	-	-	1 (1.6)	-
Need for bile duct exploration	1 (2.3)	-	-	-	-	7 (5.4)	-	-
Inability to create pneumoperitoneum	-	9 (9.6)	-	-	-	-	-	-
Choledochoduodenal fistula	-	6 (6.4)	-	-	-	-	-	-
Spilled stone	-	2 (2.1)	-	-	-	-	-	-
Perforation of transverse colon	2 (4.5)	-	-	-	-	-	-	-
Atrial fibrillation	1 (2.3)	-	-	-	-	-	-	-
Hypertcapnia	1 (2.3)	-	-	-	-	-	-	-