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INTRAOPERATIVE REASONS FOR CONVERSION OF LAPAROSCOPIC CHOLECYSTECTOMY TO OPEN SURGERY (SYSTEMATIC REVIEW)

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ABSTRACT

Three electronic databases were searched to identify the studies reporting intraoperative risk factors of conversion in laparoscopic cholecystectomy. Primary outcomes were to spot and specify the unpredictable risk factors and identify the most common intraoperative conversion causes. Secondary outcomes were comparing the impact of each group reasons on conversion rate – patient-related factors, surgeon-related factors and equipment-related and other factors of conversion.

Key words: Laparoscopic cholecystectomy, conversion, intraoperative risk factors.

INTRODUCTION

The reasons for conversion have been investigated deeply to reduce the rate of conversion. Authors of many studies in this field mainly focused on the risk factors that can be identified and diagnosed before surgery to prevent the risk of conversion. Advanced age, male gender, high body mass index (BMI), previous upper abdominal surgery, choledocholithiasis, urgent surgery, thicker gallbladder wall, raised white cell count (WCC), and alkaline phosphatase (ALP) was found as a predictor of conversion in laparoscopic cholecystectomy (A.S.Y. Hu et al, 2017 and J.P. Rothman et al, 2016).

There is a clear lack of investigations in the literature for unpredictable causes of conversion in minimally access surgery. Authors of some studies have mentioned some unpredictable risk factors (A. Gangemi et al, 2017 and A.

Licciardello et al, 2014) but they did ignore their importance in practice. Deep knowledge of the epidemiology of intraoperative risk factors for conversion to open surgery allows early identification and recognition of difficult situations and potential reasons for conversion. This gives an opportunity of avoiding unnecessary laparoscopic attempts that increases the risk of further complications that cannot be solved even open approach afterward. Moreover, keeping in mind these factors improves the situation awareness of surgeons and forces them to rethink before making any important step of the procedure that leads to minimization of severe iatrogenic complications. Further, a systematic assessment of such factors improves patients' consent forms for laparoscopic cholecystectomy and allows them to be better informed of the risks before the surgery.

Purpose of the study. The study's main aim was to define the intraoperative reasons for conversion from laparoscopic cholecystectomy to open surgery. Moreover, we aimed to reveal the popularity of each reason among others calculating their proportion within the included studies.

METHODS

Protocol and registration. This review was conducted according to the guidelines set by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) (D. Moher et al, 2009). Before analyzing the factors under consideration within the included studies and data extraction stage, the review was registered on the International Prospective Register of Systematic Reviews (PROSPERO) database (University of York, 2019) with the registration number CRD42019135834.

Eligibility criteria. We found the articles eligible for our study that reported intraoperative reasons or all causes of conversion (where intraoperative factors were mentioned as well) from standard 4-port laparoscopic cholecystectomy to open surgery. In all included studies, indication for surgery had to be gallstone disease and other benign pathologies of gallbladder. Only English language studies were included in the review.

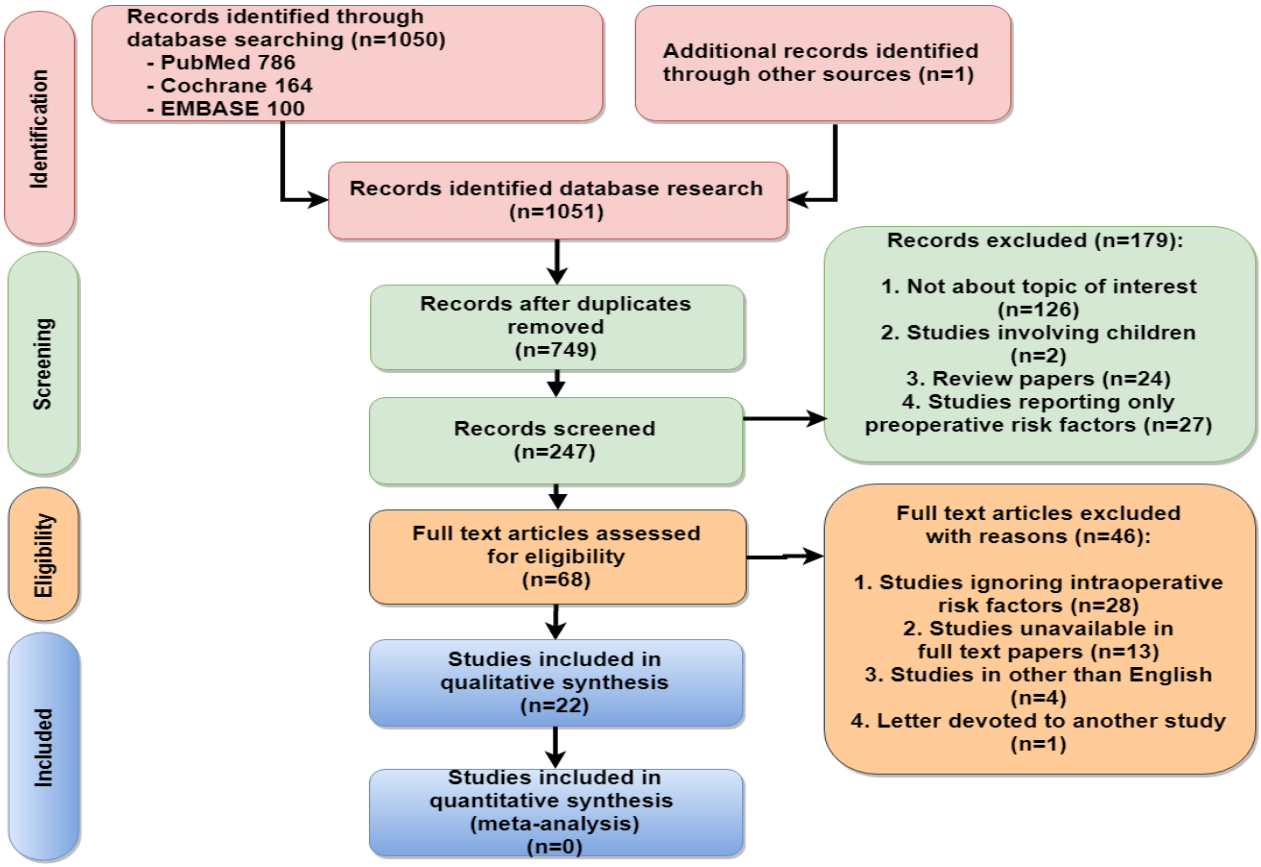
Search strategy and study selection. A systematic search of relevant articles was carried out through the electronic medical literature databases of PubMed, Cochrane, and EMBASE by the first two authors. The search was started on January 21 2019, and refreshed on weekly basis until July 1, 2019. Titles and abstracts of the papers retrieved applying the search tactics mentioned above and those from additional databases were reviewed independently by two study authors (R.K. and J.S.) to identify studies that potentially meet the eligibility criteria. Duplicate papers in all three databases were matched and removed. As soon as a title or abstract of any record fit our eligibility criteria, full texts of the potentially

eligible studies were acquired and evaluated by two review team members in terms of eligibility for the systematic review. Any discrepancies and disagreements were resolved through discussion.

Data collection and data items. A unique modified data extraction form was designed by the first author and employed to systematically collect data from all eligible studies. The form was adjusted for our primary as well as secondary outcomes.

Statistical Analysis. Data were assembled in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). The overall proportion of conversion cases in the eligible studies was calculated using simple mathematic methods to learn the general conversion rate individually. All statistical analyses were accomplished on IBM SPSS Statistics Version 26 (IBM Corporation, Endicott, NY, USA). The total percentage, median, mean with standard deviation (SD), minimum, maximum, and p-value were calculated for each risk factor with an α level of 0.05. In this way, we found out the popularity of each intra-operational risk factor.

RESULTS. Overall, 1050 records were found in all medical electronic databases (please see the PRISMA 2009 Flow Diagram below). One study was identified in the reference list as eligible for the current review. We compared the records within three electronic databases by screening the titles and authors and found 302 identical studies, which were eliminated from the study. Next, 179 records were excluded, 126 of them were out of the topic, two studies involved paediatric content. 24 records were secondary studies and 27 findings were reporting isolated preoperative risk factors to create a prognostic program for safe cholecystectomy. Both types of records were removed from the review. Finally, sixty-eight were derived and read in full text by the first two authors of the study, and 46 papers were subsequently excluded owing to the following reasons: 28 studies ignored intra-operative reasons for conversion from laparoscopic cholecystectomy to open surgery, 13 records were unavailable in full text, four papers due to the language and the last one record was a comment letter for another study. Due to the difference in the style, methods, and outcomes of the studies (heterogeneity) found throughout the databases, we could not perform meta-analysis.



Graph 1. PRISMA 2009 Flow Diagram

Study characteristics

This systematic review included 22 prospective and retrospective observational studies thcovereding 40 315 patients in total (table 1).

Table 1.

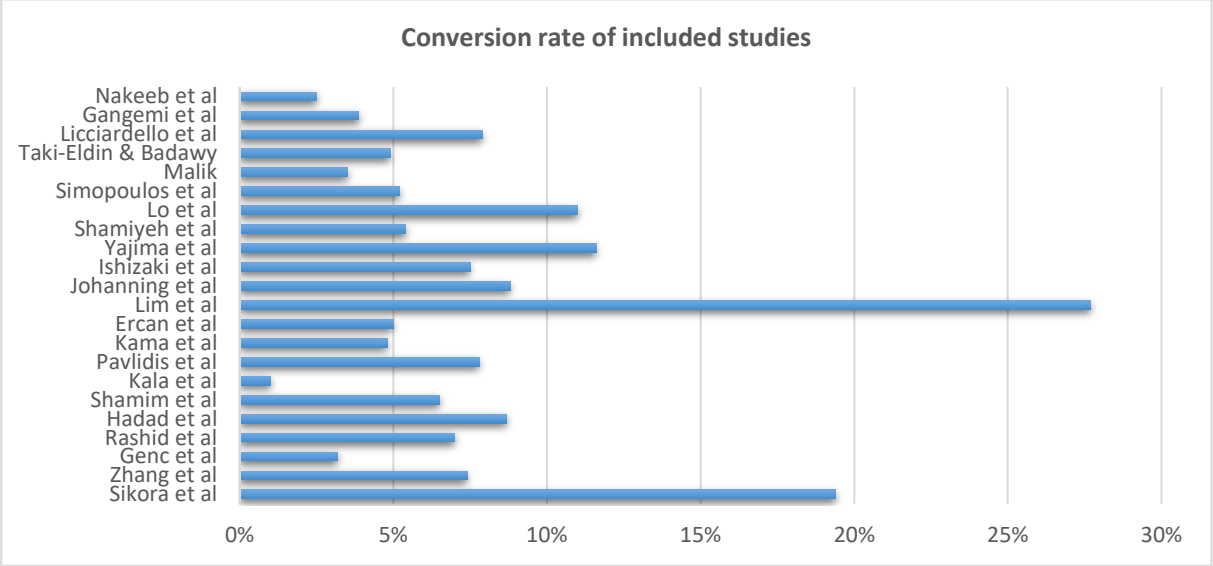
Patients' demographic parameters in the studies

Included studies	Sample size	Main age	Gender distribution	
			Male	Female
El Nakeeb et al	3269	N/A	933 (28.5%)	2336 (71.5%)
Gangemi et al	960	N/A	244 (25.4%)	716 (74.6%)
Licciardello et al	414	51.7±16.4	169 (40.8%)	245 (59.2%)
Taki-Eldin & Badawy	492	49.35±8.68	106 (21.5%)	386 (78.5%)
Malik	936	39.88±8.66	97 (10.36%)	839 (89.64%)
Simopoulos et al	1804	52.66±14.66	425 (23.6%)	1379 (76.4%)
Lo et al	70	59.9	28 (40%)	42 (60%)
Shamiyeh et al	5049	N/A	N/A	N/A
Yajima et al	407	N/A	183 (45%)	224 (55%)
Ishizaki et al	1339	55±13	600 (50.9%)	579 (49.1%)

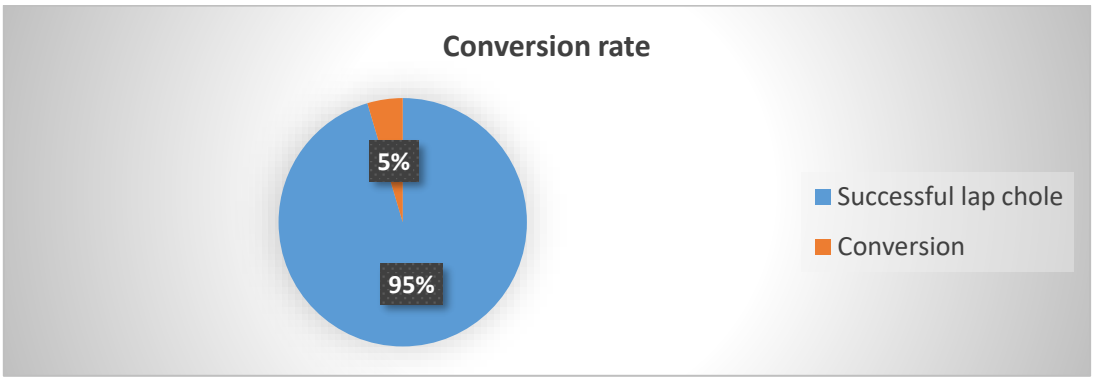
Johanning et al	3247	N/A	N/A	N/A
Lim et al	201	N/A	82 (40.8%)	119 (59.2%)
Ercan et al	2015	Lap – 52.4±13.9* Con – 57.8±13.0*	644 (31.96%)	1371 (68.04%)
Kama et al	1000	43.8	196 (19.6%)	804 (80.4%)
Pavlidis et al	1263	54±15.15	354 (28%)	909 (72%)
Kala et al	8347	38.2	2825 (33.85%)	5522 (66.15%)
Shamim et al	1238	41.25±12	158 (12.76%)	1080 (87.24%)
Hadad et al	1385	N/A	N/A	N/A
Rashid et al	300	42.69	38 (12.67%)	262 (87.33%)
Genc et al	5164	N/A	1570 (30.4%)	3594 (69.6%)
Zhang et al	1265	N/A	430 (34%)	835 (66%)
Sikora et al	150	39±12	36 (24%)	114 (76%)
TOTAL	**40 315**			

*Ercan et al calculated the mean age of the patients separately in two different groups, successful laparoscopic and converted groups

Most of the studies remain under 10 percent in terms of conversion rate (graph 2). This pattern is exceeding a quarter in Lim et al, 2007 and reached up to 20 percent in the study conducted by Sikora et al. (1995). The first group of authors observed patients with acute cholecystitis only. Overall conversion rate was about 5% (graph 3)



Graph 2. The conversion rate of individual studies.



Graph 3. Overall conversion rate of the review

We found 12 patient-related risk factors of conversion in laparoscopic cholecystectomy throughout our eligible studies. Three out of them, dense adhesions/fibrosis of GB & Callot's triangle, unclear anatomy at Calot's triangle, and severe forms of inflammation were the most popular causes of conversion in almost all studies. Most of the authors mentioned those three factors with significantly high numbers (tables 2). In three studies, the proportion of converted patients due to the dense adhesions/fibrosis of GB & Callot's triangle made up over 70 percent (see graph 4). 5 out of 22 eligible studies did not mention this factor as a reason for conversion from laparoscopic cholecystectomy. Other causes for conversion were negligible. Mean of abscess for conversion was 6,35% p=0.260; Mirizzi syndrome - 3,65%, p=0.376; Contracted gallbladder - 2,825%, p=0.04; Dilated cystic duct with unsuccessful cholangiogram – 8.85%, p=0.018; Thickened gallbladder/grasping inability – 6.95%, p=0.278.

Table 2.

Intraoperative patient-related risk factors of conversion from laparoscopic surgery to open surgery.

Authors	Conversion	Patient-related factors of conversion				
		Dense adhesions/fibrosis of GB & Callot's triangle	Unclear anatomy	Severe inflammation	Biliodigestive fistula	Mirizzi syndrome
El Nakeeb et al	83 (2.5%)	35 (42.2%)	29 (34.9%)		2 (2.4%)	
Gangemi et al	11 (3.87%)	2 (18.2%)	1 (9.1%)	2 (18.2%)		
Licciardello et al	33 (7.9%)	14 (42.4%)		12 (36.3%)	1 (3%)	2 (6%)
Taki-Eldin & Badawy	24 (4.9%)		4 (16.7%)	11 (45.8%)		-
Malik	33 (3.52%)	25 (75.7%)		5 (15.1%)		
Simopoulos et al	94 (5.2%)		70 (74.4%)		6 (6.4%)	1 (1%)

Lo et al	8 (11%)	6 (75%)			1 (12.5%)	
Shamiyeh et al	245 (5.4%)	35 (14.3%)	42 (17.1%)	72 (29.4%)	7 (2.95)	3 (1.2%)
Yajima et al	47 (11.6%)	15 (31.9%)		8 (17%)		-
Ishizaki et al	89 (7.5%)		55 (62%)			4 (4%)
Johanning et al	234 (8.8%)	51 (21.8%)	39 (16.7%)	61 (26.1%)		
Lim et al	56 (27.7%)	20 (35.8%)	26 (46.4%)			
Ercan et al	101 (5%)	58 (57.4%)	20 (19.8%)		3 (3%)	
Kama et al	48 (4.8%)		34 (3.4%)			
Pavlidis et al	98 (7.8%)	37 (37.7%)	1 (1%)	20 (20.4%)	2 (2%)	3 (3%)
Kala et al	82 (1%)	7 (8.5%)		38 (46.3%)	1 (1.2%)	10 (12.2%)
Shamim et al	81 (6.5%)	4 (5%)	44 (54.3%)		1 (1.2%)	
Hadad et al	109 (8.7%)	32 (29.3%)	2 (1.8%)	4 (3.6%)		
Rashid et al	21 (7%)	8 (38.1%)	5 (23.8%)			
Genc et al	163 (3.2%)	118 (76.3%)			4 (2.4%)	1 (0.6%)
Zhang et al	94 (7.4%)	26 (27.75%)	52 (55.3%)			5 (5.3%)
Sikora et al	29 (19.4%)		9 (31%)	9 (31%)		
Total	1783/40 315 (4.6%)	493 (27.6%)	433 (24.3%)	242 (13.5%)	28 (1.5%)	29 (1.6%)
Mean±SD (%)	7,758±5,88 23	37,491±22, 450	29,231±23,0 27	26,29±13,1 895	3,705±3,41 6	4,175±3,75 7
Median (%)	6,75	35,8	21,8	26,1	2,675	3,5
Minimum (%)	1	5	1	3.6	1.2	0.6
Maximum (%)	27.7	76.3	74.4	46.3	12,5	12.2
***p* value**	<0.001*	<0.001*	<0.001*	<0.001*	0,008*	0.016*

**Statistically significant result (p<0.05)*

Overall, 11 surgeon-related risk factors of conversion were identified including bile duct injury (4.24%, p=<0.001), uncontrollable bleeding (10.06%, p<0.001), duodenal injury (3.41%, p=0.06), colonic injury (0.9%, p=0.2), bile leakage (4.65%, p=0.193), spilled stones of the gallbladder into the abdominal cavity (2.35%, p=0.053), common bile duct exploration due to large CBD stone (3.7%, p=0.01), torn cystic duct (3.4%), failed insertion of trocar or initial laparoscopy failure (4.8%, p=0.36), anesthesia (4.8%) and respiratory disturbances (2.1%) (tables 3).

Table 3. Intraoperative surgeon-related risk factors of conversion from laparoscopic surgery to open surgery

Authors	**Conversion**	**Surgeon-related factors of conversion**				
		Bile duct injury	**Bleeding**	**Duodenal injury (perforation)**	**Common bile duct exploration (due to large CBD stone)**	**Bile leakage**
El Nakeeb et al	83 (2.5%)	2 (2.4%)	6 (7.2%)			
Gangemi et al	11 (3.87%)					

Licciardello et al	33 (7.9%)	2 (6%)	2 (6%)			
Taki-Eldin & Badawy	24 (4.9%)		9 (37.5%)			
Malik	33 (3.52%)	1 (3%)	1 (3%)	3 (9%)		
Simopoulos et al	94 (5.2%)	2 (2.1%)	3 (3.2%)			
Lo et al	8 (11%)					1 (12.5%)
Shamiyeh et al	245 (5.4%)	8 (3.3%)	22 (8.9%)	3 (1.2%)	9 (3.7%)	2 (0.8%)
Yajima et al	47 (11.6%)	5 (10.6%)	8 (17%)	1 (2.1%)		
Ishizaki et al	89 (7.5%)	11 (12%)	15 (17%)		4 (4%)	
Johanning et al	234 (8.8%)		32 (13.7%)			
Lim et al	56 (27.7%)		10 (17%)			
Ercan et al	101 (5%)	9 (8.9%)	10 (9.9%)			
Kama et al	48 (4.8%)	5 (0.5%)	2 (0.2%)	3 (0.3%)	1 (0.1%)	
Pavlidis et al	98 (7.8%)	2 (2%)	10 (10.2%)		4 (4%)	
Kala et al	82 (1%)	5 (6.1%)	6 (7.3%)			
Shamim et al	81 (6.5%)		6 (7.4%)	1 (1.2%)	5 (6.1%)	
Hadad et al	109 (8.7%)	3 (2.7%)	1 (0.9%)			
Rashid et al	21 (7%)	1 (4.7%)	2 (9.5%)	2 (9.5%)		1 (4.7%)
Genc et al	163 (3.2%)	6 (3.7%)	14 (8.5%)	1 (0.6%)	1 (0.6%)	1 (0.6%)
Zhang et al	94 (7.4%)	4 (4.3%)	-		7 (7.4%)	
Sikora et al	29 (19.4%)	1 (3.4%)	4 (13.8%)			
Total	1783/40315 (4.6%)	119 (6.6%)	163 (9.1%)	14 (0.7%)	31 (1.7%)	5 (0.2%)
Mean±SD (%)	7,758±5,8823	4,246±2,695	10,066±8,394	3,414±4,028	3,7±2,652	4,650±5,563
Median (%)	6,75	3,40	8,70	1,20	4	2,750
Minimum (%)	1	0.5	0.2	0.3	0.1	0.6
Maximum (%)	27.7	10.6	37.5	9.5	7.4	12.5
***p* value**	<0.001*	<0.001*	<0.001*	0,06	0.01*	0,193

**Statistically significant result ($p<0.05$)*

Regarding the equipment-related factors of conversion in laparoscopic surgery, 6 studies had technical issues with a small number of patients when they had to convert the surgery to open cholecystectomy. Other reasons related to this category are rare and insignificant.

DISCUSSION. A total of 22 studies were included in this systematic review. Overall, 40 315 patients were observed in those researches. During this review, we found dense adhesions or fibrosis at Calot's triangle and around GB, unclear anatomy at Calot's triangle, and severe destructive forms of inflammation including empyema, gangrene, and abscess as the most common intraoperative patient-related reasons for conversion from laparoscopic cholecystectomy to open surgery. Furthermore, bile duct injury and uncontrollable bleeding were the most popular intraoperative surgeon-related causes of conversion in laparoscopic cholecystectomy. Equipment-related and other factors of intraoperative conversion from laparoscopy to open surgery were negligible and insignificant according to the results of this review.

There is a significant number of studies in the literature investigating preoperative or predictable risk factors of conversion from laparoscopic cholecystectomy to open surgery. Most of these studies are focused on revealing the predictable reasons for conversion and attempted to offer their prediction models of the conversion risk factors in laparoscopic cholecystectomy. Some authors of the studies offered the Tokyo Guideline 2013 as a perfect prediction model to prevent unwanted conversion (M. Bouassida et al, 2017 M. Yokoe et al, 2013). Another team of authors of the research advocated their version of the prediction model (M.S. Kim et al, 2014).

Yet, there is an obvious lack of papers in the literature that reports on the importance of intraoperative or unpredictable causes of conversion from laparoscopic cholecystectomy to open surgery. This lack is even more serious regarding the secondary studies on this topic. Similar to primary studies, the results of some systematic reviews and meta-analyses have analyzed the papers devoted to the predictable factors of conversion of laparoscopic cholecystectomy. For instance, A.S.Y. Hu et al 2017 focused on body mass index, gall bladder wall thickness, previous history of abdominal surgery, presence of choledocholithiasis, patients' age, patient settings (emergency, elective), blood tests for acute inflammation (alkaline phosphate, white blood cell count, etc.), total bilirubin and other risk factors. This review excluded intraoperative findings and conditions that may lead to conversion to open surgery.

Many studies reported that inflammation, symptomatic gallstones, and fibrosis are significantly more extensive in male genders than in females (S. Yol et al, 2006, A. Gangemi et al, 2017, C. Simopoulos et al, 2005). This is the main reason for the higher conversion rate of laparoscopic cholecystectomy among males. Likewise, in patients with acute gallbladder disease, the rate of conversion

is significantly high due to challenging dissection at thickened and densely adherent structures at Calot's triangle.

This review identified several intraoperative risk factors of conversion that have not been investigated by many secondary studies. These factors include bilio-digestive fistula, spilled gallstones into the abdominal cavity, torn cystic duct, and other uncommon causes of conversion.

Limitations of the review. The review included the papers published in English only. There might be studies reporting intraoperative risk factors of conversion in other languages that were not identified by the authors of this research owing to the language filter. Some studies with very interesting titles and abstracts were not available in full texts. Due to the heterogeneity of included studies in the review, we could not accomplish a meta-analysis.

CONCLUSION. We found a wide range of unpredictable risk factors of conversion in laparoscopic cholecystectomy reported in included studies. Some of those factors are vitally important and very common in surgical practice. Further investigations into the reasons for those risk factors can be most helpful and effective tool for minimization the complications and unwanted conversion in laparoscopic surgery.

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IMPROVING THE TREATMENT OF CORONAVIRUS INFECTION COVID-19

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ABSTRACT

This article provides data on a new method of treating coronavirus infection COVID-19 with a mixture of Ganoderma Lucidum and Alhadai. When performing PCR diagnostics, 110 copies / ml were found in the blood of rats on days 5-6, which indicates high levels of the virus in the respiratory tract. The viral RNA detection rate was 95%. Ganoderma Lucidum contains a large number of amino acids, both essential and non-essential, which bind to the protease domain of ACE 2 or to the S-protein of SARS CoV-2 and prevent the two substances from binding. Thus, there is no excessive accumulation of angiotensin II, which, through the activation of AT1R (angiotensin II receptor type I), leads to acute lung injury.

Key words: coronavirus; PCR test; Ganoderma Lucidum; Alhadaya; type II alveolocytes; SARS CoV-2; acute respiratory distress syndrome.