What is the best score for predicting difficult laparoscopic cholecystectomy? A diagnostic trial study

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What is the best score for predicting difficult laparoscopic cholecystectomy?

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Camilo Ramírez-Giraldo: Study conception and design, acquisition of data, data analysis and interpretation, drafting of manuscript, critical revision of manuscript.

Andrés Isaza-Restrepo: Data analysis and interpretation, drafting of manuscript, critical revision of manuscript.

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Andrea Carolina Castillo-Barbosa: Study conception and design, data acquisition, critical revision of manuscript.

Juan José Rubio-Avilez: Study conception and design, data acquisition, critical revision of manuscript.

Isabella Van-Londoño: Drafting of manuscript, critical revision of manuscript.

Ethical Standards

Ethical compliance with the Helsinki Declaration, current legislation on research Res. 008430-1993 and Res. 2378-2008 (Colombia) and the International Committee of Medical Journal Editors (ICMJE) were ensured under our Ethics and Research Institutional Committee (IRB) approval. Informed consent was obtained from all individual participants included in the study.

Study Design

Diagnostic trial study

Word count: 1990

Abstract

Background: Multiple scores have been created in order to predict difficult cholecystectomy, nonetheless there is not a consensuated standard on which to use. The importance of a predictive score to be able to establish a difficult cholecystectomy would be a relevant instrument in order to better inform the patient, properly call for help when needed, choose the correct staff, and schedule and plan the surgical procedure accordingly.

Methods: A total of 635 patients between 2014-2021 were selected for a diagnostic trial study. All different predictive scores for difficult cholecystectomy were calculated for each patient. The correlation between the preoperative score and cholecystectomies considered as "difficult" were measured estimating the preoperative score's predictive value using a ROC curve in order to predict findings for difficult cholecystectomy.

Results: Selected patients had a mean average age of 55.0 (IQR: 28) and were mostly female (64.25%). Surgical outcomes in this group had statistically significant higher rates of subtotal cholecystectomies, drain usage, complications and reinterventions, prolonged surgical times, and longer hospital stay. When analyzing the predictive value on each of the different scores applied, score 4 had the highest performance for predicting difficult cholecystectomy with an AUC=0.783 (CI 95% 0.745-0.822).

Conclusions: Difficult cholecystectomies are associated to worse surgical outcomes. The standardization and use of predictive scores for difficult cholecystectomy must be implemented in order to improve surgical outcomes as a result of more meticulous planning when scheduling the procedure.

Keywords: Laparoscopic cholecystectomy, cholecystectomy complications, risk factors, difficult cholecystectomy.

Introduction

Laparoscopic cholecystectomy is one of the most common procedures realized in our population and it is the standard treatment for gallstone disease (1). Multiple preoperatory factors - such as age, sex, body mass index, inflammatory status (leukocytes, neutrophiles, reactive protein C), imaging findings related to cholecystitis (gallbladder wall thickening, impacted gallstones in the gallbladder neck, pericholecystic collection, among others), anatomical variations (Moynihan lump, the presence of more than one cystic artery, among others), history of abdominal surgery, surgeon's experience and comorbidities such as cirrhosis, symptom duration, time of cholecystectomy (elective, delayed or emergency procedure), among other factors - have been associated with a higher difficulty for the procedure and may imply adverse surgical outcomes (2–4). It has been proven that it's unlikely that one sole factor is directly responsible for a difficult cholecystectomy, and it's more widely considered that the sum of multiple risk factors are associated with difficult cholecystectomy, therefore the importance of a score which may evaluate multiple factors at one given time (3).

Faced with a grand variety of factors associated with difficult laparoscopic cholecystectomy, multiple studies have designed different predictive scores for difficult cholecystectomy (5,6) in order to establish an instrument which may better inform the patient, choose appropriate staff, call for help when needed, and plan and schedule the surgical procedure accordingly (6). Nonetheless, there is not a generalized consensus on the usage of the scores described nor a comparison between their utility. As a result, the objective of this study is to evaluate the predictive value for each of the different scores available in order to better predict difficult cholecystectomy.

Patients and methods

A diagnostic trial study was performed. Between January 2014 and December 2021 13.132 laparoscopic cholecystectomies were performed in our institution. A simple random sampling was done until the calculated sample size was reached. Different variables were collected on an anonymous database. This study was reviewed and approved by the Universidad del Rosario's (number DVO005 2096-CV1613) ethics committee. We followed STARD guidelines in order to report this study (7).

Patients

Patients under 18 years of age, patients with scheduled open cholecystectomy, patients with diagnosed gallbladder cancer, patients with cholecystectomy associated to other procedures (gastrectomy, pancreatoduodenectomy, among others) and patients whose registry did not include variables of interest were excluded from the study.

Laparoscopic cholecystectomy indications included all cases in which the main motive was biliary cholic, pancreatitis, choledocholithiasis, cholecystitis or a combination of these; and in all cases there was at least one diagnostic image which confirmed biliary disease. Patients diagnosed with cholecystitis were classified according to their severity and treatment was established using Tokyo guidelines (8,9). Additionally, ASGE criteria for risk of choledocholithiasis was established in order to define a management plan; cholecystectomy with no additional studies was defined for the low-risk group, magnetic resonance cholangiography for the intermediate-risk group and endoscopic retrograde cholangiopancreatography (ERCP) for the high-risk group (10). In cases with diagnosis of pancreatitis cholecystectomy was performed once pancreatitis was resolved.

Study design

A literature review was performed in order to find predictive scores for difficult cholecystectomy, findings are reported in **table 1**. Every patient had their preoperative score measured using each of the predictive scores included for difficult cholecystectomy.

Table 1. Scores found in literature for predicting difficult cholecystectomy.

Score	Author	Variables		Points	AUC
Score 1	Gupta, et al (11)	Age (years)	≤50	0	0.86
	Randhawa, et al (12)		>50	1	0.82
	Tongyoo, et al (13)	Sex	Male	1	0.75
	Agrawal, et al. (14)		Female	0	0.87
		History of hospitalization	No	0	
		for acute cholecystitis	Yes	4	
		BMI	<25 kg/m^2	0	
			25 - 27.5 kg/m^2	1	
			>27.5 kg/m^2	2	
		Abdominal scar	No	0	
			Infraumbilical	1	
			Supraumbilical	2	
		Palpable gallbladder	Yes	1	
			No	0	
		Gallbladder wall thickness	<4 mm	0	
			≥4 mm	2	
		Pericholecystic collection	No	0	

			Yes	1	
		Impacted stone	No	0	
			Yes	1	
Score 2	Siddiqui, et al (15)	Gallbladder wall thickness	<4 mm	0	NR
			≥ 4 mm	2	
		Transverse diameter of gallbladder	<5 cm	0	
			≥5 cm	2	
		Presence of impacted stones	No	0	
			Yes	2	
		Common bile duct diameter	≤6 mm	0	
			>6 mm	2	
		Presence of pericholecystic collection	No	0	
			Yes	1	
		Number of stones >1	No	0	
			Yes	1	
		Liver size ≥ 15.5 cm	Yes	1	
Score 3	Kama et al. (16) Bulbuller, et al. (17)	Sex	Male	11	0.83
			Female	0	NR
		Abdominal tenderness	No	0	
			Yes	9	
		Previous upper abdominal operation	No	0	
			Yes	8	
		Thickened gallbladder wall	No	0	
			Yes	13	
		Age (years)	≥60	5	
			<60	0	
		Acute cholecystitis	No	0	
			Yes	15	
		Constant		-20	
Score 4	Tongyoo, et al. (13)	Age (years)	≤50	0	0.82
			>50	1	
		Sex	Male	1	
			Female	0	
		History of previous biliary inflammation and procedure (previous acute cholecystitis, cholangitis, ERCP)	No	0	
			Yes	4	
		BMI	<25 kg/m^2	0	
			25 - 27.5 kg/m^2	1	
			>27.5 kg/m^2	2	
		Abdominal scar	No	0	
			Infraumbilical	1	
			Supraumbilical	2	
		Contracted gallbladder	Yes	1	
			No	0	
		Gallbladder wall thickness	<4 mm	0	
			≥4 mm	2	
		Pericholecystic collection	No	0	
			Yes	1	
		Impacted gallstone	No	0	
			Yes	1	

Score 5	Carrizo, et al. (18)	Age	≤60 years	0	NR
			>60 years	2	
		Sex	Male	1.5	
			Female	0	
		BMI	≤30 kg/m^2	0	
			> 30 kg/m^2	1	
		Previous surgery (upper hemiabdomen)	No	0	
			Yes	2	
		Gallbladder wall thickness	≤3 mm	0	
			>3 mm	2	
		Common bile duct stone	No	0	
			Yes	8	
		Leukocytes	≤10.0x10^3	0	
			>10.0x10^3	2	
Score 6	Nassar, et al. (6) Ramírez-Giraldo, et al. (19)	Age	<40 years	0	0.78 0.88
			≥40 years	1	
		Gender	Male	1	
			Female	0	
		ASA classification	I	0	
			II	1	
			III	2	
			IV-V	7	
		Primary diagnosis	Pancreatitis	0	
			Biliary colic	0	
			CBD stone	1	
			Cholecystitis	4	
		Gallbladder wall thickness	<3 mm	0	
			≥3 mm	2	
		Common bile duct diameter	≤6mm	0	
			>6 mm	1	
		Pre-operative ERCP	No	0	
			Yes	1	
		Admission type	Elective	0	
			Delay	1	
			Emergency	2	
Score 7	Alponat, et al. (20)	Acute cholecystitis	No	0	NR
			Yes	1.1390	
		Gallbladder wall thickness	<3.5 mm	0	
			≥3.5 mm	1.3227	
		Leukocytes	≤11.0x10^3	0	
			>11.0x10^3	1.3063	
		Elevated alkaline phosphatase	No	0	
			Yes	0.8014	
		Constant		- 4.2149	

NR: Not reported.
BMI: Body mass index

Scores containing variables not routinely measured on patients scheduled for laparoscopic cholecystectomy in our institution were excluded from the study, such as one by Bourgouin, et al. which measured fibrinogen, another one by Lipman et al. which measured albumin, one score by

Schrenk, et al. which included the inability to observe the gallbladder in intraoperative cholangiography as one of its variables and a score described by Vivek, et al. which is difficult to calculate due to the amount of variables and the inclusion of intraoperative variables (21–24).

There are multiple other studies in which risk factors have been evaluated, however, none of these studies designed scores from identifiable factors for predicting difficult cholecystectomy, and as a result were excluded from the study (25–33).

We consider as difficult cholecystectomy (reference standard) the presence of at least one of the following conditions: bile duct injury, non-evident anatomical visualization, Mirizzi syndrome, severe inflammation of the Calot triangle, conversion to laparotomy, scleroatrophic gallbladder or pericholecystic abscess. This was defined by a panel of experts with a majority consensus of ≥80% as the presence of any one of these findings (34).

The surgeon that would perform the cholecystectomy was not aware of any of the preoperative score results as these were calculated by the research team in a retrospective manner.

Statistical Analysis

Multiple samples were calculated according to the sensibility and specificity for each of the scores **(table 1)**, out of which the biggest sample size was chosen. The biggest sample size was calculated with a 78% sensibility and 72% specificity as was reported by Kama et al (16) while the prevalence of difficult cholecystectomy previously reported in our population is 51.72% (19).

A description of demographic, clinic, paraclinical, surgical and outcome variables was made using the following parameters: categorical variables were described as ratios and continuous variables as a mean average with a respective interquartile range (IQR). A bivariate analysis was performed with a Chi-squared value on categorical variables and with the Mann-Whitney test on continuous variables in order to compare differences between the variables in respect to difficulty (easy versus difficult), considering a statistically significant $p<0.05$.

We calculated the score for every different predictive score for difficult cholecystectomy on each patient **(table 1)**. The correlation between the preoperative score and cholecystectomies

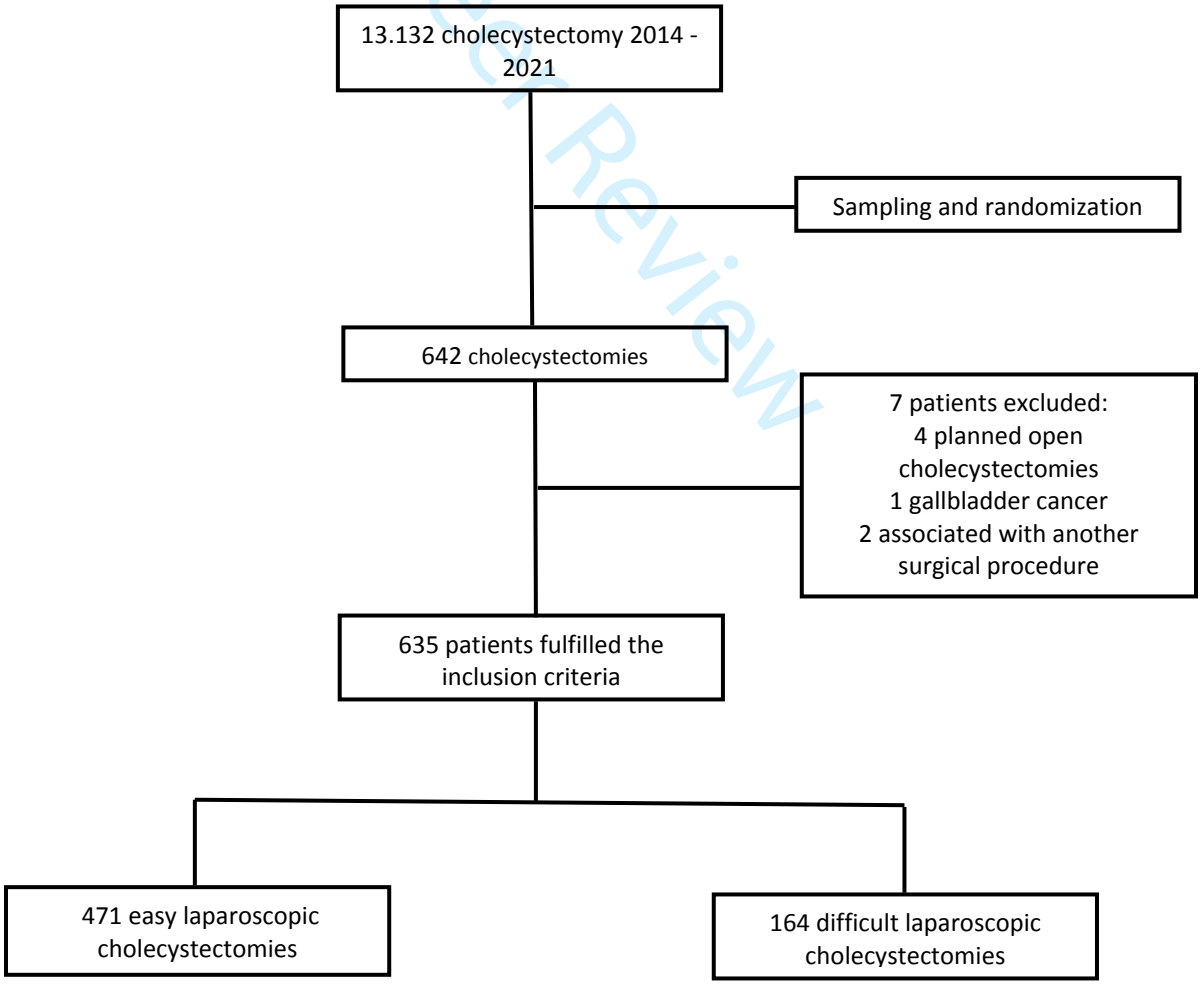
considered as difficult was gauged by means of a ROC curve estimating the preoperative score's predictive value to acknowledge findings defined as difficult cholecystectomy. The area under the curve (AUC) for each of the different predictive scores for difficult cholecystectomy were compared in order to assess if there were statistically significant differences between them.

The entirety of this analysis was executed on SPSS®26, deeming a $p<0.05$ as statistically significant.

Results

A total sum of 635 patients were included in this study. 471 were classified as easy laparoscopic cholecystectomies (74.17%) and 164 were classified as difficult (25.83%). The selection process is shown in the following flowchart **(figure 1)**.

Figure 1. Study selection process flowchart.



Selected patients had a mean age of 55.0 (IQR: 28.0) years and were predominantly female (64.25%). In **table 2** other demographic, clinic and paraclinical aspects in cholecystectomized patients are reported with the difference between these according to cholecystectomy difficulty.

Table 2. Demographic, clinical and surgical characteristics by difficulty.

	N (%)	**Easy (%) n=471**	**Difficult (%) n=164**	**P value**
Age (median)(IQR) years	55.00 (28.00)	51.00 (27.00)	61.5 (23.25)	**<0.001***
Sex				**<0.001**
Female	408 (64.25)	329 (69.85)	79 (48.17)	
Male	227 (35.75)	142 (30.15)	85 (51.83)	
Body mass index	26.40 (5.35)	26.3 (5.309	26.70 (5.30)	0.375*
ASA classification				**0.011**
1	254 (40.00)	192 (40.76)	62 (37.80)	
2	274 (43.15)	213 (45.22)	61 (37.20)	
3	103 (16.22)	63 (13.38)	40 (24.39)	
4 - 5	4 (0.63)	3 (0.64)	1 (0.61)	
Comorbidities				
Diabetes Mellitus	74 (11.65)	48 (10.19)	26 (15.85)	0.052
Arterial hypertension	171 (29.93)	121 (25.69)	50 (30.49)	0.233
Chronic obstructive pulmonary disease	17 (2.68)	11 (2.34)	6 (3.66)	0.366
Chronic kidney disease	11 (1.73)	7 (1.49)	4 (2.44)	0.421
Cardiovascular disease	44 (6.93)	27 (5.73)	17 (10.37)	**0.044**
Liver disease	7 (1.19)	6 (1.27)	1 (0.61)	0.483
History of abdominal surgery				
Supraumbilical	28 (4.41)	19 (4.03)	9 (5.49)	0.435
Infraumbilical	223 (35.12)	173 (36.73)	50 (30.49)	0.149
Previous episodes of cholecystitis	6 (0.94)	5 (1.06)	1 (0.61)	0.606
Abdominal pain	513 (80.79)	363	150 (91.46)	**<0.001**
Palpable gallbladder	8 (1.26)	1 (0.21)	7 (4.27)	**<0.001**
Charlson comorbidity index (median)(IQR) points	1.00 (2.00)	1.00 (2.00)	2.00 (3.00)	**<0.001***
Anticoagulant agents	12 (1.89)	7 (1.49)	5 (3.05)	0.206
Antiplatelet agents	53 (8.35)	33 (7.01)	20 (12.20)	**0.039**
Lab tests (median)(IQR)				
Leukocytes (x10^3)	9.85 (5.59)	9.31 (5.01)	11.95 (5.66)	**<0.001***
Hemoglobin (mg/dL)	14.90 (1.90)	14.80 (1.70)	15.00 (2.00)	**0.008***
Total bilirubin (mg/dL)	0.76 (0.98)	0.71 (0.91)	0.96 (1.24)	0.108*
Alkaline phosphatase (mg/dL)	105.00 (88.00)	105.00 (89.00)	105.50 (87.25)	0.930*
Aspartate aminotransferase (mg/dL)	27.00 (74.75)	27.00 (95.25)	28.00 (39.25)	0.587*
Alanine aminotransferase (mg/dL)	31.00 (104.00)	30.1 (142.50)	34.00 (69.00)	0.938*
Image findings				

Impacted stone	40 (6.30)	21 (4.46)	19 (11.59)	**0.001**
Pericholecystic collection	81 (12.76)	35 (7.43)	46 (28.05)	**<0.001**
More than one stone	620 (97.64)	461 (97.88)	159 (96.95)	0.501
Scleroatrophic	6 (0.94)	6 (1.27)	0 (0.00)	0.146
Gangrenous/perforated	24 (3.78)	1 (0.21)	23 (14.02)	**<0.001**
Liver >15.5 cm	12 (1.89)	9 (1.91)	3 (1.83)	0.947
Gallbladder wall thickness	2.00 (2.00)	2.00 (2.00)	4.00 (2.00)	**<0.001***
Gallbladder transverse diameter (median)(IQR) cm	3 (0.00)	3 (0.00)	3 (0.00)	0.733*
Bile duct diameter (median)(IQR) mm	3 (0.00)	3 (0.00)	3 (0.00)	0.382*
Primary diagnosis				
Biliary cholic	204 (32.13)	173 (36.73)	31 (18.90)	**<0.001**
Pancreatitis	53 (8.35)	41 (8.70)	12 (7.32)	0.580
Choledocholithiasis	74 (11.65)	48 (10.19)	26 (15.85)	0.052
Cholecystitis	272 (42.83)	150 (31.85)	122 (74.39)	**<0.001**
Tokyo classification				**<0.001**
I	92 (14.49)	69 (14.65)	23 (14.02)	
II	104 (16.8)	59 (12.53)	45 (27.44)	
III	76 (11.97)	22 (4.67)	54 (32.93)	
Preoperative ERCP				**0.001**
No	554 (87.24)	423 (89.81)	131 (81.10)	
Yes	81 (12.76)	48 (10.19)	33 (18.90)	
Type of admission				**<0.001**
Elective	122 (19.21)	108 (22.93)	14 (8.54)	
Delayed	507 (79.84)	362 (76.86)	145 (88.41)	
Emergency	6 (0.94)	1 (0.21)	5 (3.05)	
Previous cholecystostomy	3 (0.47)	2 (0.42)	1 (0.61)	0.766
Time from admission to surgical procedure (median)(IQR) days	3.00 (4.00)	3.00 (4.00)	3.00 (4.00)	0.175

p values were obtained from the Chi-squared test
**p* values were obtained from the Mann–Whitney test
Values in bold indicate statistically significant *p* values ($p < 0.05$)

Surgical outcomes evidenced a statistically significant higher ratio of subtotal cholecystectomies, drain usage, complications and reinterventions, prolonged surgical times and longer hospital stay in the group of patients classified as difficult cholecystectomies. There were also higher mortality rates in the difficult cholecystectomies group, however, the difference was not statistically significant **(Table 3)**.

Table 3. Postoperative cholecystectomy surgical outcomes according to difficulty.

	N (%)	**Easy (%) n=471**	**Difficult (%) n=164**	**P value**
Type of cholecystectomy				**<0.001**

Total	610 (96.06)	469 (99.58)	141 (85.98)	
Subtotal	25 (3.94)	2 (0.42)	23 (14.02)	
Drain usage				**<0.001**
No	601 (94.65)	467 (99.15)	134 (81.71)	
Yes	34 (5.35)	4 (0.85)	30 (18.29)	
Surgical time (median)(IQR) minutes	60.00 (10.00)	60.00 (2.00)	60.00 (60.00)	**<0.001***
Hospital stay (median)(IQR) days	3.00 (4.00)	3.00 (3.00)	5.00 (5.00)	**<0.001***
Complications				
Biliary leak	2 (0.31)	0 (0.00)	2 (1.22)	**0.016**
Bile duct injury	1 (0.16)	0 (0.00)	1 (0.61)	0.090
Intestinal injury	2 (0.31)	1 (0.21)	1 (0.61)	0.434
Surgical site infection	13 (2.05)	7 (1.49)	6 (3.66)	0.091
Perioperative AMI	1 (0.16)	1 (0.21)	0 (0.00)	0.555
Healthcare-associated pneumonia	2 (0.31)	1 (0.21)	1 (0.61)	0.434
Healthcare-associated urinary tract infection	1 (0.16)	1 (0.21)	0 (0.00)	0.555
Pleural effusion	4 (0.63)	2 (0.42)	2 (1.22)	0.268
Reintervention				**<0.001**
No	625 (98.43)	469 (99.58)	156 (95.12)	
Yes	10 (1.57)	2 (0.42)	8 (4.88)	
Clavien-Dindo				**<0.001**
I	22 (3.46)	11 (2.34)	11 (6.71)	
II	12 (1.89)	4 (0.85)	8 (4.88)	
IIIA	12 (1.89)	5 (1.06)	7 (4.27)	
IIIB	6 (0.94)	2 (0.42)	4 (2.44)	
IV	1 (0.16)	0 (0.00)	1 (0.61)	
V	5 (0.79)	2 (0.42)	3 (1.83)	
Mortality				0.080
No	630 (99.21)	469 (99.58)	161 (98.17)	
Yes	5 (0.79)	2 (0.42)	3 (1.83)	

p values were obtained from Chi-squared test
**p* values were obtained from Mann–Whitney test
Values in bold indicate statistically significant *p* values ($p < 0.05$)

When measuring predictive capacity for difficult cholecystectomy with each score we found score 4, described by Tongyoo, et al. (13), as the score with better performance for predicting a difficult cholecystectomy. On the other hand, score 2 which focused exclusively on image findings, reported by Siddiqui, et al. (15) was the one with the lowest predictive performance **(Figure 2 and table 4)**.

Figure 2. ROC curves for scores evaluated.

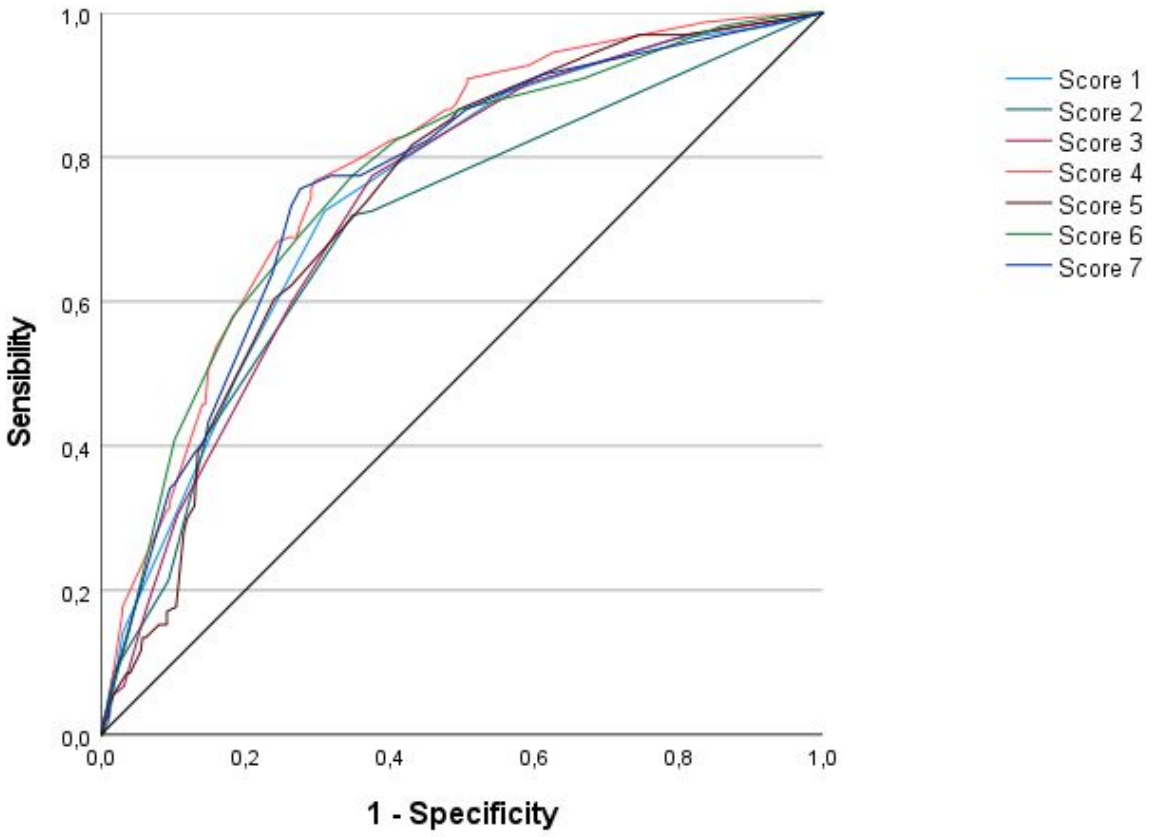


Table 4. AUC for each score.

Score	AUC	CI95%
Score 1	0.747	0.704 – 0.789
Score 2	0.703	0.655 – 0.750
Score 3	0.736	0.694 – 0.778
Score 4	0.783	0.745 – 0.822
Score 5	0.740	0.699 – 0.781
Score 6	0.768	0.726 – 0.809
Score 7	0.761	0.719 – 0.803

Finally, we made a comparison between each score's AUC, in which we can evidence score 4, which had the best performance, was statistically significantly superior to scores 1, 2, 3 and 5. And despite score 4 having a superior value to scores 6 and 7, there was not a statistically significant difference between them **(Table 5)**.

Table 5. AUC differences between each score.

	AUC difference	p value
Score 1 – Score 2	0.044	**0.018**
Score 1 – Score 3	0.011	0.383

Score 1 – Score 4	0.037	**0.022**
Score 1 – Score 5	0.007	0.755
Score 1 – Score 6	0.021	0.269
Score 1 – Score 7	0.015	0.438
Score 2 – Score 3	0.033	0.114
Score 2 – Score 4	0.081	**<0.001**
Score 2 – Score 5	0.038	0.127
Score 2 – Score 6	0.065	**0.001**
Score 2 – Score 7	0.059	**0.001**
Score 3 – Score 4	0.047	**0.010**
Score 3 – Score 5	0.004	0.800
Score 3 – Score 6	0.032	0.088
Score 3 – Score 7	0.026	0.222
Score 4 – Score 5	0.043	**0.017**
Score 4 – Score 6	0.016	0.121
Score 4 – Score 7	0.022	0.100
Score 5 – Score 6	0.028	0.138
Score 5 – Score 7	0.021	0.274
Score 6 – Score 7	0.006	0.668
Measured by a non-parametric estimate Values in bold indicate statistically significant *p* values ($p < 0.05$)		

Discussion

This study identified that cases considered as difficult cholecystectomy are associated to higher rates of subtotal cholecystectomy, complications and reinterventions, thus the importance in being able to predict difficult cholecystectomy. Out of the 7 scores for predicting a difficult cholecystectomy evaluated, score 4 (AUC 0.783) had the highest performance. This scale is based on a scale designed by Randhawa (score 1) in which the criteria “palpable gallbladder” was modified for “contracted gallbladder” and “history of hospitalization for acute cholecystitis” was modified to “history of previous biliary inflammation and procedure (previous acute cholecystitis, cholangitis, ERCP)”. The scores reported by Nassar and Alponat had lower performances compared to score 4 but the difference was not statistically significant (6,13,20).

That preoperative identification of difficult cholecystectomy may imply a greater surgical risk has been a relevant topic of discussion in recent years. Risk assessment before surgical intervention allows for better preparation for the procedure, a more accurate measurement of surgical times, adequate planning for different services not available 24 hours (availability of a hepatobiliary surgeon, intraoperative imaging, among others), and counseling and risk breakdown are more proper and realistic for the patient when signing informed consent (14).

Traditionally, the approach to difficult cholecystectomy differs depending on the surgeon. The wide array of surgical techniques available are mainly based on surgeon experience and different strategies have been devised to guide professionals on an individualized management (35). On the other hand, the term “difficult” is not standardized; some authors define difficulty on surgical time while others determine it as the need of conversion to open procedure and further intraoperative findings; and as a result, each of the scores yield to different reference standards (26,35,36). In this review, in order to establish a reference point on the definition of difficult cholecystectomy we employed a consensus recently published by an expert surgeon panel in Spain which considers clinical aspects, imaging features and intraoperative findings (34). These multiple definitions for difficult cholecystectomy limit the implementation of a specific score to predict difficulty and act as a barrier when trying to reach a unanimous standard.

Out of multiple scores created for the assessment of difficult cholecystectomy, few have been frequently used in a clinical setting due to the complexity and difficult applicability of some variables (37). Even though Vivek et al. published a score with a high AUC (0.956), the 22 variables required to adequately measure it (including an intraoperative variable) pose a challenge when trying to assess difficulty on an everyday basis (23). Moreover, other scores consider variables which are not routinely measured and are difficult to obtain, such as preoperative fibrinogen and intraoperative cholangiography (21,22).

In our review aspects related to difficult cholecystectomy included age, male sex, ASA classification, antiplatelet agents, history of cardiovascular disease, palpable gallbladder, leukocytosis, image findings consistent with cholecystitis, pericholecystic collection, gangrenous or perforated gallbladder, impacted stone, patients with Tokyo III score and urgent surgery; variables which were included in various scores. Previous ERCP was recognized as significant and was included in scores 4 and 6, which yielded the highest diagnostic capabilities. In a propensity matching score study performed on 621 patients, patients taken to laparoscopic cholecystectomy with no previous ERCP were compared to patients with previous ERCP, longer surgical times and higher risk of conversion to open procedure were found in the second group (38). In addition to this, Da Costa and Ishizaki reported preoperative ERCP as a strong predictive value for difficult cholecystectomy (27,29).

Our recommendation in order to improve surgical outcomes is the application of a score for predicting difficult cholecystectomy; counting this study's results into account the employment of scores 4, 6 and 7 would yield higher performances when predicting difficult cholecystectomy and are proven to be useful due to their simple implementation and widely available variables.

The 2020 WSES guidelines for the detection and management of bile duct injury during cholecystectomy recommend an exhaustive preoperative work-up prior to cholecystectomy to detect at-risk conditions, choose the best surgical approach, and discuss the risks/benefits ratio of the procedure (39), which can be done more accurately using a scale.

Limitations in this study include its retrospective nature and the fact that it was only done in one institution. Furthermore, another limitation which wasn't considered was the absence of variables not included in the scores employed and it remains unbeknownst if they could've had an impact on surgical difficulty.

Conclusions

Difficult cholecystectomies are associated with worse surgical and clinical outcomes. The standardization and use of predictive scores for difficult cholecystectomy must be implemented in order to improve surgical outcomes as a result of more meticulous planning when scheduling the procedure.

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Table 1. Scores found in literature for predicting difficult cholecystectomy.

Score	Author	Variables		Points	AUC
Score 1	Gupta, et al (11)	Age (years)	≤50	0	0.86
	Randhawa, et al (12)		>50	1	0.82
	Tongyoo, et al (13)	Sex	Male	1	0.75
	Agrawal, et al. (14)		Female	0	0.87
		History of hospitalization	No	0	
		for acute cholecystitis	Yes	4	
		BMI	<25 kg/m^2	0	
			25 - 27.5 kg/m^2	1	
			>27.5 kg/m^2	2	
		Abdominal scar	No	0	
			Infraumbilical	1	
			Supraumbilical	2	
		Palpable gallbladder	Yes	1	
			No	0	
		Gallbladder wall thickness	<4 mm	0	
			≥4 mm	2	
		Pericholecystic collection	No	0	
			Yes	1	
		Impacted stone	No	0	
			Yes	1	
Score 2	Siddiqui, et al (15)	Gallbladder wall thickness	<4 mm	0	NR
			≥ 4 mm	2	
		Transverse diameter of	<5 cm	0	
		gallbladder	≥5 cm	2	
		Presence of impacted	No	0	
		stones	Yes	2	
		Common bile duct	≤6 mm	0	
		diameter	>6 mm	2	
			No	0	
		Presence of pericholecystic	Yes	1	
		collection	No	0	
		Number of stones >1	Yes	1	
			No	0	
		Liver size ≥ 15.5 cm	Yes	1	
Score 3	Kama et al. (16)	Sex	Male	11	0.83
	Bulbuller, et al. (17)		Female	0	NR
		Abdominal tenderness	No	0	
			Yes	9	
		Previous upper abdominal	No	0	
		operation	Yes	8	
		Thickened gallbladder wall	No	0	
			Yes	13	
		Age (years)	≥60	5	
			<60	0	
		Acute cholecystitis	No	0	
			Yes	15	
		Constant		-20	
Score 4	Tongyoo, et al. (13)	Age (years)	≤50	0	0.82
			>50	1	
		Sex	Male	1	

			Female	0	
		History of previous biliary inflammation and procedure (previous acute cholecystitis, cholangitis, ERCP)	No	0	
			Yes	4	
		BMI	<25 kg/m^2	0	
			25 - 27.5 kg/m^2	1	
			>27.5 kg/m^2	2	
		Abdominal scar	No	0	
			Infraumbilical	1	
			Supraumbilical	2	
		Contracted gallbladder	Yes	1	
			No	0	
		Gallbladder wall thickness	<4 mm	0	
			≥4 mm	2	
		Pericholecystic collection	No	0	
			Yes	1	
		Impacted gallstone	No	0	
			Yes	1	
Score 5	Carrizo, et al. (18)	Age	≤60 years	0	NR
			>60 years	2	
		Sex	Male	1.5	
			Female	0	
		BMI	≤30 kg/m^2	0	
			> 30 kg/m^2	1	
		Previous surgery (upper hemiabdomen)	No	0	
			Yes	2	
		Gallbladder wall thickness	≤3 mm	0	
			>3 mm	2	
		Common bile duct stone	No	0	
			Yes	8	
		Leukocytes	≤10.0x10^3	0	
			>10.0x10^3	2	
Score 6	Nassar, et al. (6) Ramírez-Giraldo, et al. (19)	Age	<40 years	0	0.78
			≥40 years	1	0.88
		Gender	Male	1	
			Female	0	
		ASA classification	I	0	
			II	1	
			III	2	
			IV-V	7	
		Primary diagnosis	Pancreatitis	0	
			Biliary colic	0	
			CBD stone	1	
			Cholecystitis	4	
		Gallbladder wall thickness	<3 mm	0	
			≥3 mm	2	
		Common bile duct diameter	≤6mm	0	
			>6 mm	1	
		Pre-operative ERCP	No	0	
			Yes	1	
		Admission type	Elective	0	

			Delay Emergency	1 2	
Score 7	Alponat, et al. (20)	Acute cholecystitis Gallbladder wall thickness Leukocytes Elevated alkaline phosphatase Constant	No Yes <3.5 mm ≥3.5 mm ≤11.0x10^3 >11.0x10^3 No Yes	0 1.1390 0 1.3227 0 1.3063 0 0.8014 - 4.2149	NR
NR: Not reported. BMI: Body mass index					

Table 2. Demographic, clinical and surgical characteristics by difficulty.

	N (%)	Easy (%) n=471	Difficult (%) n=164	P value
Age (median)(IQR) years	55.00 (28.00)	51.00 (27.00)	61.5 (23.25)	**<0.001***
Sex				**<0.001**
Female	408 (64.25)	329 (69.85)	79 (48.17)	
Male	227 (35.75)	142 (30.15)	85 (51.83)	
Body mass index	26.40 (5.35)	26.3 (5.309	26.70 (5.30)	0.375*
ASA classification				**0.011**
1	254 (40.00)	192 (40.76)	62 (37.80)	
2	274 (43.15)	213 (45.22)	61 (37.20)	
3	103 (16.22)	63 (13.38)	40 (24.39)	
4 - 5	4 (0.63)	3 (0.64)	1 (0.61)	
Comorbidities				
Diabetes Mellitus	74 (11.65)	48 (10.19)	26 (15.85)	0.052
Arterial hypertension	171 (29.93)	121 (25.69)	50 (30.49)	0.233
Chronic obstructive pulmonary disease	17 (2.68)	11 (2.34)	6 (3.66)	0.366
Chronic kidney disease	11 (1.73)	7 (1.49)	4 (2.44)	0.421
Cardiovascular disease	44 (6.93)	27 (5.73)	17 (10.37)	**0.044**
Liver disease	7 (1.19)	6 (1.27)	1 (0.61)	0.483
History of abdominal surgery				
Supraumbilical	28 (4.41)	19 (4.03)	9 (5.49)	0.435
Infraumbilical	223 (35.12)	173 (36.73)	50 (30.49)	0.149
Previous episodes of cholecystitis	6 (0.94)	5 (1.06)	1 (0.61)	0.606
Abdominal pain	513 (80.79)	363	150 (91.46)	**<0.001**
Palpable gallbladder	8 (1.26)	1 (0.21)	7 (4.27)	**<0.001**
Charlson comorbidity index (median)(IQR) points	1.00 (2.00)	1.00 (2.00)	2.00 (3.00)	**<0.001***
Anticoagulant agents	12 (1.89)	7 (1.49)	5 (3.05)	0.206
Antiplatelet agents	53 (8.35)	33 (7.01)	20 (12.20)	**0.039**
Lab tests (median)(IQR)				
Leukocytes (x10^3)	9.85 (5.59)	9.31 (5.01)	11.95 (5.66)	**<0.001***
Hemoglobin (mg/dL)	14.90 (1.90)	14.80 (1.70)	15.00 (2.00)	**0.008***
Total bilirubin (mg/dL)	0.76 (0.98)	0.71 (0.91)	0.96 (1.24)	0.108*
Alkaline phosphatase (mg/dL)	105.00 (88.00)	105.00 (89.00)	105.50 (87.25)	0.930*
Aspartate aminotransferase (mg/dL)	27.00 (74.75)	27.00 (95.25)	28.00 (39.25)	0.587*
Alanine aminotransferase (mg/dL)	31.00 (104.00)	30.1 (142.50)	34.00 (69.00)	0.938*
Image findings				
Impacted stone	40 (6.30)	21 (4.46)	19 (11.59)	**0.001**
Pericholecystic collection	81 (12.76)	35 (7.43)	46 (28.05)	**<0.001**
More than one stone	620 (97.64)	461 (97.88)	159 (96.95)	0.501
Scleroatrophic	6 (0.94)	6 (1.27)	0 (0.00)	0.146
Gangrenous/perforated	24 (3.78)	1 (0.21)	23 (14.02)	**<0.001**

Liver >15.5 cm	12 (1.89)	9 (1.91)	3 (1.83)	0.947
Gallbladder wall thickness	2.00 (2.00)	2.00 (2.00)	4.00 (2.00)	**<0.001***
Gallbladder transverse diameter (median)(IQR) cm	3 (0.00)	3 (0.00)	3 (0.00)	0.733*
Bile duct diameter (median)(IQR) mm	3 (0.00)	3 (0.00)	3 (0.00)	0.382*
Primary diagnosis				
Biliary cholic	204 (32.13)	173 (36.73)	31 (18.90)	**<0.001**
Pancreatitis	53 (8.35)	41 (8.70)	12 (7.32)	0.580
Choledocholithiasis	74 (11.65)	48 (10.19)	26 (15.85)	0.052
Cholecystitis	272 (42.83)	150 (31.85)	122 (74.39)	**<0.001**
Tokyo classification				**<0.001**
I	92 (14.49)	69 (14.65)	23 (14.02)	
II	104 (16.8)	59 (12.53)	45 (27.44)	
III	76 (11.97)	22 (4.67)	54 (32.93)	
Preoperative ERCP				**0.001**
No	554 (87.24)	423 (89.81)	131 (81.10)	
Yes	81 (12.76)	48 (10.19)	33 (18.90)	
Type of admission				**<0.001**
Elective	122 (19.21)	108 (22.93)	14 (8.54)	
Delayed	507 (79.84)	362 (76.86)	145 (88.41)	
Emergency	6 (0.94)	1 (0.21)	5 (3.05)	
Previous cholecystostomy	3 (0.47)	2 (0.42)	1 (0.61)	0.766
Time from admission to surgical procedure (median)(IQR) days	3.00 (4.00)	3.00 (4.00)	3.00 (4.00)	0.175

p values were obtained from the Chi-squared test
**p* values were obtained from the Mann–Whitney test
Values in bold indicate statistically significant *p* values ($p < 0.05$)

Table 3. Postoperative cholecystectomy surgical outcomes according to difficulty.

	N (%)	**Easy (%) n=471**	**Difficult (%) n=164**	**P value**
Type of cholecystectomy				**<0.001**
Total	610 (96.06)	469 (99.58)	141 (85.98)	
Subtotal	25 (3.94)	2 (0.42)	23 (14.02)	
Drain usage				**<0.001**
No	601 (94.65)	467 (99.15)	134 (81.71)	
Yes	34 (5.35)	4 (0.85)	30 (18.29)	
Surgical time (median)(IQR) minutes	60.00 (10.00)	60.00 (2.00)	60.00 (60.00)	**<0.001***
Hospital stay (median)(IQR) days	3.00 (4.00)	3.00 (3.00)	5.00 (5.00)	**<0.001***
Complications				
Biliary leak	2 (0.31)	0 (0.00)	2 (1.22)	**0.016**
Bile duct injury	1 (0.16)	0 (0.00)	1 (0.61)	0.090
Intestinal injury	2 (0.31)	1 (0.21)	1 (0.61)	0.434
Surgical site infection	13 (2.05)	7 (1.49)	6 (3.66)	0.091
Perioperative AMI	1 (0.16)	1 (0.21)	0 (0.00)	0.555
Healthcare-associated pneumonia	2 (0.31)	1 (0.21)	1 (0.61)	0.434
Healthcare-associated urinary tract infection	1 (0.16)	1 (0.21)	0 (0.00)	0.555
Pleural effusion	4 (0.63)	2 (0.42)	2 (1.22)	0.268
Reintervention				**<0.001**
No	625 (98.43)	469 (99.58)	156 (95.12)	
Yes	10 (1.57)	2 (0.42)	8 (4.88)	
Clavien-Dindo				**<0.001**
I	22 (3.46)	11 (2.34)	11 (6.71)	
II	12 (1.89)	4 (0.85)	8 (4.88)	
IIIA	12 (1.89)	5 (1.06)	7 (4.27)	
IIIB	6 (0.94)	2 (0.42)	4 (2.44)	
IV	1 (0.16)	0 (0.00)	1 (0.61)	
V	5 (0.79)	2 (0.42)	3 (1.83)	
Mortality				0.080
No	630 (99.21)	469 (99.58)	161 (98.17)	
Yes	5 (0.79)	2 (0.42)	3 (1.83)	

p values were obtained from Chi-squared test
**p* values were obtained from Mann–Whitney test
Values in bold indicate statistically significant *p* values ($p < 0.05$)

Table 4. AUC for each score.

Score	AUC	CI95%
Score 1	0.747	0.704 – 0.789
Score 2	0.703	0.655 – 0.750
Score 3	0.736	0.694 – 0.778
Score 4	0.783	0.745 – 0.822
Score 5	0.740	0.699 – 0.781
Score 6	0.768	0.726 – 0.809
Score 7	0.761	0.719 – 0.803

Table 5. AUC differences between each score.

	AUC difference	p value
Score 1 – Score 2	0.044	**0.018**
Score 1 – Score 3	0.011	0.383
Score 1 – Score 4	0.037	**0.022**
Score 1 – Score 5	0.007	0.755
Score 1 – Score 6	0.021	0.269
Score 1 – Score 7	0.015	0.438
Score 2 – Score 3	0.033	0.114
Score 2 – Score 4	0.081	**<0.001**
Score 2 – Score 5	0.038	0.127
Score 2 – Score 6	0.065	**0.001**
Score 2 – Score 7	0.059	**0.001**
Score 3 – Score 4	0.047	**0.010**
Score 3 – Score 5	0.004	0.800
Score 3 – Score 6	0.032	0.088
Score 3 – Score 7	0.026	0.222
Score 4 – Score 5	0.043	**0.017**
Score 4 – Score 6	0.016	0.121
Score 4 – Score 7	0.022	0.100
Score 5 – Score 6	0.028	0.138
Score 5 – Score 7	0.021	0.274
Score 6 – Score 7	0.006	0.668
Measured by a non-parametric estimate Values in bold indicate statistically significant p values ($p < 0.05$)		

Figure 1. Study selection process flowchart.

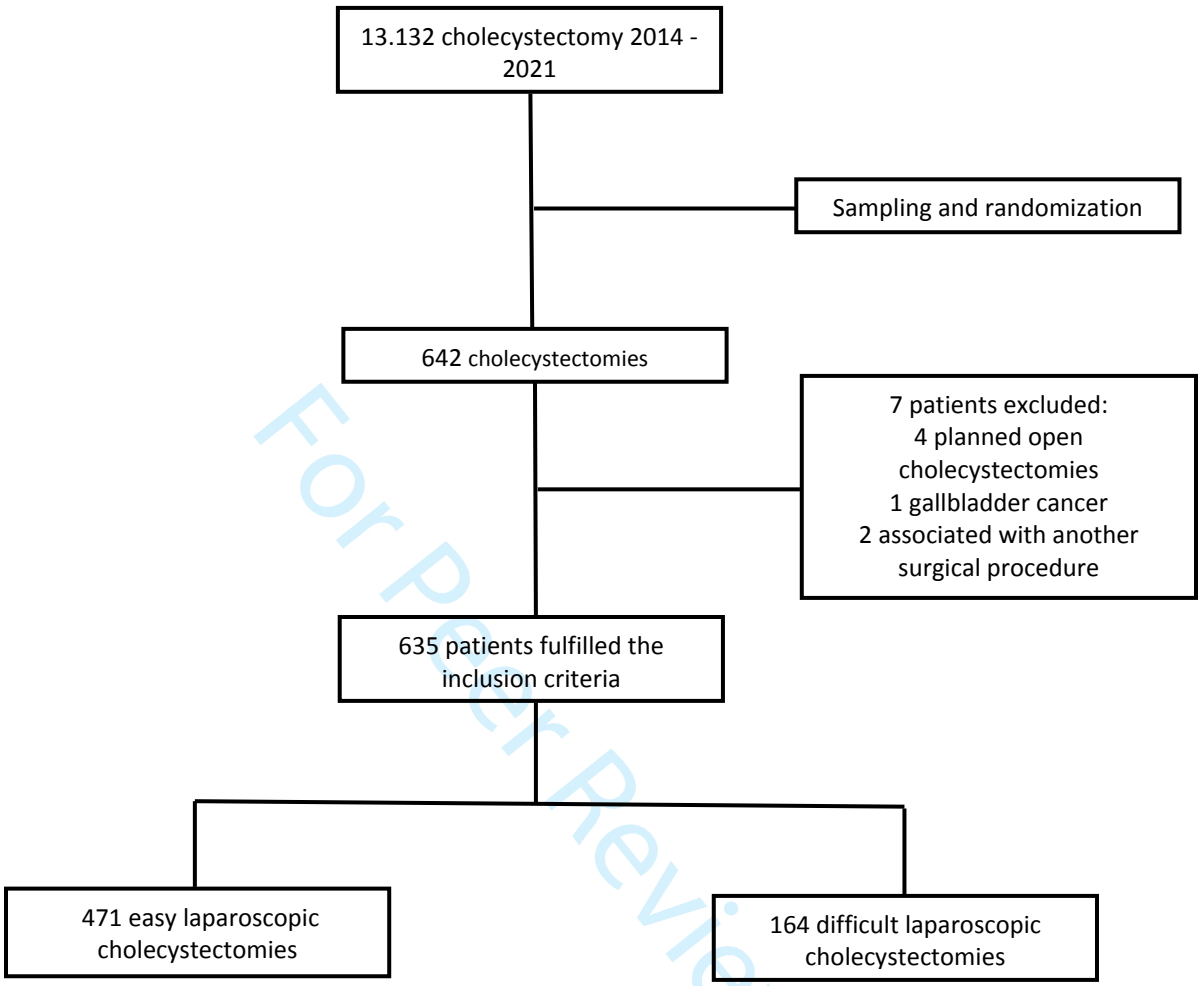

Figure 2. ROC curves for scores evaluated.