

Development of Scoring System for Prediction of Choledocholithiasis

Danny Amos Tarigan¹, Hafidh Komar^{1*}, Legiran²

¹Department of Surgery, Faculty of Medicine, Universitas Sriwijaya

²Department of Anatomy, Faculty of Medicine, Universitas Sriwijaya

* Correspondence Author Email: editor.bioscmed@gmail.com

Abstract

Introduction. Gallstones (cholelithiasis) and gallbladder stones (choledocholithiasis) are still a public health problem because of the high incidence rate. Management of stones in common bile duct (CBD) is done with history taking about patient complaints and tracking patient history such as yellow appearance, physical examination, laboratory examination, and imaging examination before, during and after surgery. Of the many imaging assessment that can be done, in practice not all can be done because these tests are expensive, complicated, risk of morbidity and mortality. A scoring system that includes many parameters can be very useful for many surgeons to be able to assess the presence of gallbladder stones.

Methods. The study was an analytic observational study with a cross sectional study design carried out in the digestive surgery polyclinic and the inpatient installation of Dr. Moh Husein general hospital, Palembang from September 2018 to May 2019. The sample of this study was all patients suspected of having gallbladder stones that met the inclusion and exclusion criteria.

Results: Receiver operating characteristic (ROC) analysis of scoring on bile duct stone diagnosis had a cut-off of > 4 with a sensitivity value of 100% and a specificity of 75%. In the Fisher's Exact analysis test and it was found that the scoring had a significant relationship to the diagnosis of bile duct stones with an odd ratio (OR) value of 12.52.

Conclusion. The use of a scoring system can predict the incidence of gallbladder stones.

Keywords: scoring system, prediction, choledocholithiasis

Introduction

Gallstones (cholelithiasis) and gallbladder stones (choledocholithiasis) are still a public health problem because of their high incidence rate. In the UK more than 40,000 cholecystectomies are performed annually, in America more than 700,000 cholecystectomies are performed annually. The incidence of gallstones found during or before cholecystectomy is 10-15% .¹ Gallstones and gallstones are commonly found in Western countries, but in Asia and Africa the incidence continues to increase. In Indonesia, there is no official data on the incidence rate of bile duct stones, but this number is thought to be not much different from the figures in other countries in Southeast Asia. Improvements in socioeconomic conditions, changes in diet to the Western style, as well as improvements in diagnostic facilities, especially ultrasonography, have resulted in an increased prevalence of bile diseases in Indonesia. The frequency of choledocholithiasis increases with age. About 25% of elderly patients who undergo cholecystectomy have stones in their bile ducts. More found in women with a ratio of 2: 1.3 In about 12-15% of patients with cholelithiasis there will be migration of stones into the common bile duct (CBD) called secondary stones. Primary stones that occur in the bile duct, usually are pigment stones, which occur in patients with chronic infections or recurrent infections of the hepatobiliary tract, or can also be caused by parasites.²

As with gallbladder stones, bile duct stones can remain asymptomatic for many years and can spontaneously enter the duodenum or often this choledocholithiasis endangers the sufferer because it can cause biliary obstruction resulting in biliary colic, obstructive jaundice, to the point of obstructive jaundice, up to life-threatening conditions, such as ascending cholangitis and pancreatitis.³⁻⁴ Ten percent of patients with choledocholithiasis can progress to pancreatic and biliary malignancy. Therefore, an accurate method to predict the presence of choledocholithiasis before surgery is very useful.⁵

Management of stones in the CBD is done with history taking about patient complaints and tracking patient history such as yellow appearance, physical examination, laboratory examination, and imaging assessment before, during and after surgery. Scanning that can be done is abdominal ultrasonography, endoscopic ultrasonography, Computed Tomography Scan (CT scan), Magnetic Retrograde Cholangiography and pancreaticography (MRCP), Endoscopic Retrograde Cholangiopancreatography (ERCP), and Percutaneous Transhepatic Cholangiography (PTC). Abdominal ultrasonography is a standard diagnostic test for patients with suspected gallstones and

this ultrasound examination must be examined before the patient is operated on.^{6,7} Whereas the gold standard for establishing a diagnosis of choledocholithiasis is cholangiography.^{8,9}

Of the many narrations that can be done, in practice not all can be done because these tests are expensive, complex, risk of morbidity and mortality, cause surgery delay, and not all health facilities have it. Intraoperative cholangiography is a relatively simple examination but can cause prolonged surgery and increase morbidity and not all operating rooms have a C-arm as a support for the examination. Until now there is no laboratory examination that can detect the presence of choledocholithiasis in patients with gallstones. Standard pre-operative examinations are performed by performing liver function tests and abdominal ultrasound which are not accurate enough to diagnose stones in the bile duct. There is no one parameter that can accurately predict the presence of stones in the bile duct in patients with gallstones.

The American Society for Gastrointestinal Endoscopy (ASGE) has proposed a standard method for predicting stones in the bile duct that divides patients into 3 groups: those at low, medium and high risk, ASGE also explained that those at low risk should undergo surgery. cholecystectomy without further investigation, while those at intermediate risk should require preoperative radiological examinations such as ultrasound or MRCP and those at high risk should have preoperative ERCP and stone extraction.⁹

But returning to the limitations of the health facility and the costs involved in carrying out these investigations, a scoring system that includes many parameters can be very useful for many surgeons to be able to assess the presence of gallstones. This is what led many researchers to create scoring systems from various clinical parameters of patients, laboratories, and imaging to help detect choledocholithiasis, for example research by Monreal - Robles (2016), Cohen (2001), Gouveia (2018).¹⁰⁻¹² Most predictive models are made based on a combination of clinical, biochemical and ultrasound findings. The association between clinical, laboratory and ultrasound examination has a sensitivity of 96% - 98% for the diagnosis of gallbladder stones. Multivariate factors have more accurate values than one predictor factor.¹³⁻¹⁵

Al-Jiffry et al in 2016 conducted research to build a scoring system in predicting the presence of gallstones. This scoring system includes several parameters, each of which has been statistically tested so that it has a certain value . The parameters that exist are the age of the patient, the widening of the bile duct and the discovery of stones on ultrasound examination, increase in

liver enzymes (alkaline phosphatase, alanine transaminase, and abnormal serum bilirubin). From the total value of all parameters it can be concluded that the accuracy of the scoring system is 91.7% .⁵

Methods

This research used observational analytic study with cross sectional design to develop a scoring system for the diagnosis of choledocholithiasis, where first the effect of each component of the scoring system was performed on the occurrence of choledocholithiasis. The study was conducted at the clinic and inpatient treatment at Dr. Moh Hoesin general hospital Palembang. This study was approved by the ethics committee of the Faculty of Medicine, Universitas Sriwijaya (No. 211 / kptfkunsri-rsmh / 2017). A total of 30 research subjects met the inclusion and exclusion criteria. The inclusion criteria were patients aged > 18 years with symptoms of bile in the form of jaundice and willing to participate in the study. While the exclusion criteria are patients with malignancy and critical conditions.

The items included in the scoring system are age >50 years with a score of 1, alanine transaminase >220 IU with a score of 1, total levels of abnormal bilirubin with a score of 2, alkaline phosphatase levels > 200 IU with a score of 3, CBD dilation 7-10 mm with a score 4, CBD dilatation > 10 mm with a score of 6, and the stone looks at the CBD when ultrasound with a score of 7. The value of the score 0 means there are no CBD stones, 1-3 means the probability of CBD stones is low, 4-7 means the probability of CBD stones is moderate and > 8 means that the probability of CBD stones is high.

The collected data were processed in coding and tabulating and then entering data into the computer. Data analysis includes descriptive analysis presented categorically in numbers and percentages. Analytically assessed the relationship categorically using Chi-square i. e. age, liver enzymes and ultrasound with a significance limit of $P < 0.05$ with a 95% confidence interval. Then multivariate analysis of age, liver enzymes and ultrasound by logistic regression with a significance limit of $P < 0.05$ and assessing Odds ratio. Data in this study will be presented in tabular form and analyzed using SPSS version 24.

Results

Distribution based on age of bile duct stone diagnosis, there were 56.5% subjects with age > 50 years and 43.5% subjects with age \leq 50 years in the positive diagnosis group, while there were 57.1% subjects with age > 50 years and 42.9% subjects with age \leq 50 years in the negative diagnosis group. Subject distribution based on bilirubin total subjects on diagnosis, there were 8.7% subjects with bilirubin \leq 1.2 g / dl and 91.3% subjects with total bilirubin > 1.2 g / dl in the positive diagnosis group, while there were 100.0% subjects with bilirubin > 1.2 g / dl in the negative diagnosis group. In the distribution of alanine transaminase on the diagnosis of gallbladder stones, there were 100.0% of subjects with alanine transaminase \leq 220 IU and 0.0% of subjects with alanine transaminase > 220 IU in the group with positive diagnosis, while there were 85.7% subjects with alanine transaminase \leq 220 IU and 14.3% of subjects with alanine transaminase > 220 IU in the group with a negative diagnosis. In the distribution of alkali phosphatase on bile duct stone diagnosis, there were 30.4% with alkali phosphatase \leq 200 IU and 69.6% with alkali phosphatase > 200 IU in the group with positive diagnosis, while there were 85.7% subjects with alkali phosphatase \leq 200 IU and 14.3% subjects with alanine transaminase > 200 IU in the negative diagnosis group.

Table 1. Scoring System in Choledocolithiasis

Age	Diagnosis		p_Value
	Positive	Negative	
> 50 years	13 (56.5%)	4 (57.1%)	1.000a
≤ 50 years	10 (43.5%)	3 (42.9%)	
Total Bilirubin			1.000a
≤ 1,2 g/dL	2 (8.7%)	0 (0.0%)	
> 1,2 g/dL	21 (91.3%)	7 (100.0%)	
Alanine Transaminase			0.233a
≤ 220 IU	23 (100.0%)	6 (85.7%)	
> 220 IU	0 (0.0%)	1 (14.3%)	
Alkali Phosphatase			0.025a
≤ 200 IU	7 (30.4%)	6 (85.7%)	
> 200 IU	16 (69.6%)	1 (14.3%)	
CBD Dilatation			0.003a
CBD Dilatation <7 mm	3 (13.0%)	6 (85.7%)	
CBD Dilatation 7 – 10 mm	4 (17.4%)	0 (0.0%)	
CBD Dilatation > 10 mm	12 (52.2%)	1 (14.3%)	
Stone appearance in CBD	4 (17.4%)	0 (0.0%)	

a Fisher Exact Test, p<0,05

In the regression analysis of research variables on diagnosis it is known that only the results of usg and alkali phosphatase are the superior examinations of the diagnosis of gallstones. In the linear regression analysis test research variables on the diagnosis of gallbladder stones, and it was found that the results of USG and alkaline phosphatase are risk factors that can determine the

diagnosis of gallbladder stones with a value of $r = 0.440$ which means the results of USG and alkaline phosphatase play a role in predicting bile ducts by 44.0 %.

In the analysis of ROC scoring of bile duct stone diagnosis, it is known that cut-off scoring in this study lies at > 4 with a sensitivity value of 100% and a specificity of 75%. AUC value was also obtained in this scoring of 0.949 which means that this scoring has a very strong diagnostic ability against the diagnosis of gallbladder stones.

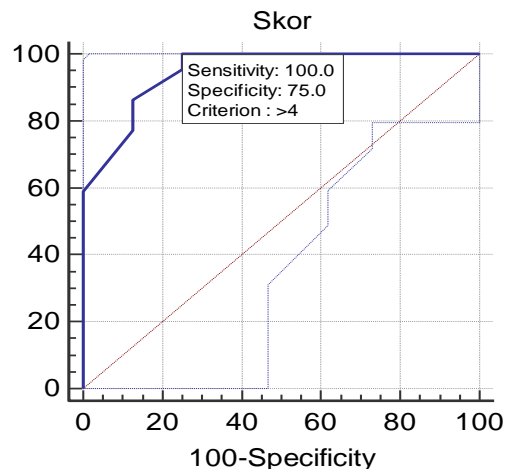


Figure 1. ROC Curve Analysis

In the distribution of subjects based on a scoring system for diagnosis, there were 95.7% subjects with moderate-high probability scoring and 4.3% subjects with low probability scoring in the group with positive diagnoses, while there were 42.9% subjects with moderate-high probability scoring and 57.1% subjects with low probability scoring with negative diagnosis. Fisher's Exact analysis was conducted and it was found that the scoring had a significant relationship to the diagnosis of gallbladder stones with an odd ratio of 12.52.

Table 2. Distribution of Subjects based on a Scoring System for Diagnosis

Scoring	Diagnosis		P Value	OR
	Positive	Negative		
Moderate-high probability	22 (95.7%)	3 (42.9%)	0.006	12.52
Low probability	1 (4.3%)	4 (57.1%)		

Fisher's Exact Test

Discussion

A total of 56.5% subjects > 50 years old and 43.5% subjects > 50 years in the positive diagnosis group, while there were 57.1% subjects > 50 years and 42.9% subjects > 50 years in the negative diagnosis group. Fisher's exact analysis was tested and found that there was no significant relationship between the age group and the diagnosis group. In the distribution of subjects according to the sex of the subject against diagnosis, there were 56.5% of subjects with male sex and 43.5% of subjects with female sex in the positive diagnosis group, while there were 14.3% of subjects with male sex and 85.7% of subjects with the female sex in the negative diagnosis group. Fisher's exact analysis was tested and found that there was no significant relationship between the sex group and the diagnosis group. This is in accordance with several theories which say that the risk of getting gallstones increases with age. Patients with gallstones in young women are found to be 5% - 8%, but increase to 25% - 30% in women aged 50 years. In men, the prevalence of gallstones also increases with age.²¹⁻²⁴

A total of 8.7% subjects with bilirubin \leq 1.2 g / dl and 91.3% subjects with total bilirubin > 1.2 g / dl in the positive diagnosis group, while there were 100.0% subjects with bilirubin > 1.2 g / dl in the diagnosis group negative. Fisher's exact analysis was tested and found that there was no significant relationship between the total bilirubin group and the diagnosis group. There were 100.0% subjects with alanine transaminase \leq 220 IU and 0.0% subjects with alanine transaminase > 220 IU in the group with positive diagnosis, while there were 85.7% subjects with alanine transaminase \leq 220 IU and 14.3% subjects with alanine transaminase > 220 IU in group with negative diagnosis. Fisher's exact analysis was conducted and it was found that there was no

significant relationship between the alanine transaminase group and the diagnosis group. There were 30.4% with alkali phosphatase ≤ 200 IU and 69.6% with alkali phosphatase > 200 IU in the group with positive diagnosis, while there were 85.7% subjects with alkali phosphatase ≤ 200 IU and 14.3% subjects with alanine transaminase > 200 IU in the diagnosis group negative. Fisher's exact test analysis was conducted and found that there was a significant relationship between the alkali phosphatase group and the diagnosis group.

Bilirubin Total subjects on diagnosis, there were mean total bilirubin in the group with positive and negative diagnoses of 6.76 ± 5.91 and 5.59 ± 3.63 . In the distribution of subjects based on Alanine Transaminase against Diagnosis, there was an average of Alanine Transaminase in the positive and negative diagnosis groups of 72.83 ± 36.35 and 104.43 ± 111.93 . In the Mann-Whitney analysis test results, there were no significant mean differences between groups with positive and negative diagnoses.

Based on Al-Jiffry's research in 2016, it was stated that total Bilirubin, alanine transaminase and alkaline phosphatase had an accuracy of 63%, 69.7%, 62% respectively, while in a study conducted by Tozatti in 2015 found that patients with choledocholithiasis had an accuracy of 63%, 69.7%, 62%, whereas in a study conducted by Tozatti in 2015 found that patients with choledocholithiasis had higher total bilirubin, alanine transaminase and alkaline transaminase are higher than in patients without choledocholithiasis. Devin in 2019, said that the total bilirubin levels at presentation, averaged more than 24 hours and an average of more than 48 hours (3.74 mg / dl vs 2.29 mg / dl, $p = 0.005$; 3.72 mg / dl vs 2.40 mg / dl, $p = 0.009$; 2.41 mg / dl vs 1.47 mg / dl, $p < 0.001$) respectively, all higher in those with choledocholithiasis.²³⁻²⁶ This can be different due to the different number of samples.

In the process of cholestasis, there is a failure of bile transport to the duodenum and causes accumulation of bile (including bilirubin) in the biliary canaliculi. This accumulation eventually reaches the tight boundary between loose hepatocytes and bile transfer from biliary canaliculi to liver sinusoidal blood. Necrosis and apoptosis of hepatocytes that occur in cholestasis also causes the entry of bile into the liver sinusoid. In cholestasis there are also changes in transport proteins in the hepatocyte membrane and result in the diversion of bile flow into the sinusoid (MRP2 sinusoidal membrane). Here it can be concluded that the severity of liver damage appears in total and direct bilirubin levels in serum.^{28,29}

Increased levels of serum enzymes are used as indicators of liver toxicity while increases in total bilirubin and conjugation levels are used to measure overall liver function. An increase in transaminase levels followed by an increase in bilirubin levels to 2 times normal is called a typical marker of hepatotoxicity. Estimates of serum bilirubin, urine bilirubin, and urobilinogen levels can be used to determine liver capacity in organic anion transport and drug / xenobiotic metabolism. Increased bilirubin levels with little or no increase in alanine transaminase (ALT) indicate cholestasis. In acute liver damage, total bilirubin is a good indicator to determine the severity of liver damage compared to ALT.^{30,31}

Increased levels of serum enzymes are used as indicators of liver toxicity while increases in total bilirubin and conjugation levels are used to measure overall liver function. An increase in transaminase levels followed by an increase in bilirubin levels to 2 times normal is called a typical marker of hepatotoxicity. Estimates of serum bilirubin, urine bilirubin, and urobilinogen levels can be used to determine liver capacity in organic anion transport and drug / xenobiotic metabolism. Increased bilirubin levels with little or no increase in alanine transaminase (ALT) indicate cholestasis. In acute liver damage, total bilirubin is a good indicator to determine the severity of liver damage compared to ALT.^{30,31}

Bilirubin test is also used as a marker of various cholestatic diseases. In a clinical trial bilirubin test was obtained as a sensitive test to see the prognosis and progression of primary biliary sclerosis. Patients with lower levels of biochemical markers (bilirubin, alkalie phosphatase, and aspartate aminotransferase) have a better 10-year-free transplanted prognosis than patients with higher biochemical marker levels.³²⁻³⁴

In the Al-Jifri study, it was found that among 272 patients who met the inclusion criteria, PPV values for CBD diameters <7 mm, 7-10 mm, and > 10 mm were 28%, 84.3%, and 93%. 5 Ultrasound examination has a high degree of specificity and sensitivity for detecting gallbladder stones and widening of intrahepatic or extra hepatic bile ducts. With ultrasound can also be seen thickened gallbladder wall due to fibrosis or edema caused by inflammation or other causes. Stones found in the distal choledochal duct are sometimes difficult to detect because they are blocked by air in the intestine. With ultrasound punctum the maximum pain in the gallbladder is more pronounced than with ordinary palpation.²⁸ Endoscopic ultrasonography (EUS) is now also

frequently used and has very high sensitivity and specificity. However, this examination is invasive.^{9,35}

Ultrasound and Alkaline Phosphatase are the leading examinations of the diagnosis of gallstones. In the distribution of subjects based on a scoring system for diagnosis, there were 95.7% subjects with moderate-high probability scoring and 4.3% subjects with low probability scoring in the group with positive diagnoses, while there were 42.9% subjects with moderate-high probability scoring and 57.1% subjects with low probability scoring with negative diagnosis. Fisher's Exact analysis was performed and it was found that the scoring had a significant relationship to the diagnosis of gallstone and OR 12.52. In the multivariate regression analysis test, it was found that the examination of USG and alkaline phosphatase was the most significant examination among other scoring variables with a value of $R = 0.440$ which means that the examination of USG and alkaline phosphatase became a risk factor of 44.0% for the diagnosis of choledocholithiasis. From the analysis of the ROC curve it was found that the scoring had a sensitivity of 100% and a specificity of 75% with a cut-off value > 4 .

In 2016, Al-Jiffry obtained from 155 research subjects that common bile duct diameter, alkaline phosphatase ≥ 200 IU, increased bilirubin levels, alanine transaminase ≥ 220 IU, and male age ≥ 50 years were significantly associated with choledocholithiasis and included in the rating system. 90 subjects (35%) had a score of ≥ 8 (high risk), 86 patients (32%) had a score of 4-7 (medium risk), and 27 patients (10%) had a score of 1-3 (low risk). In the validation group, the positive predictive value for the score ≥ 8 is 91.7%, and the scoring system has an area under the curve of 0.896. A score of ≥ 8 is highly correlated with choledocholithiasis in the developmental and validation groups, which suggests that this scoring system might be useful in predicting the need for ERCP therapy. However, prospective validation in large multicenter cohorts is needed to fully understand the benefits of the system.

Study by Adams et al. In the United States, 179 patients with high risk ASGE criteria were analyzed retrospectively and 99 (56.3%) patients had stones or sludge on investigations that had been performed, but nearly 50% of these patients still had ERCPs that actually did not is required. The accuracy of this guideline is 62.1% (sensitivity 47.4%, specificity 73%)^{.36} In Spain, a prospective study was conducted on 256 patients suspected of having CBD stones. Of 208 patients with high risk probability, 124 (59.6%) patients had stones / sludge on ERCP so this study said the

accuracy of the ASGE guidelines was 29.3% (sensitivity 85.5%, specificity 24.3%). Another 48 patients had moderate probability and only 21 (43.8%) found stones on ERCP (accuracy 41%, sensitivity 14.4%, specificity 75.6%).³⁷ Studies by He in 2017 in China, conducted a study involving 1171 patients at high risk, and definitive tests (MRCP, EUS, IOFC, and ERCP) were carried out. The results showed CBD stones were found in 1076 (40%) patients (70% sensitivity, specificity 74.3%).³⁸ A retrospective study by Suarez et al in 2016 analyzed 71 patients who met the high risk criteria for developing CBD stones, only 39 patients (54%) which is proven to have stones when ERCP. This study states the accuracy of ASGE is 63% (sensitivity 54.9%, specificity 68.6%).³⁹ Another study by Sethi, et al in 2016 involving 336 patients suspected of having CBD stones, 244 patients had a high risk; 185 patients (78.5%) were found to have CBD stones at ERCP (accuracy 69.05%). Of 92 patients at moderate risk, 45 patients (48.9%) found CBD stones during ERCP (accuracy 39.95%).⁴⁰

Conclusion

Item-based scoring systems > 50 years old, alanine transaminase > 220 IU, abnormal bilirubin levels, alkaline phosphatase levels > 200 IU and CBD dilatation have significant potential to be used as scoring for diagnosis of choledocholithiasis.

References

1. Al-Jiffry BO, Elfateh A, Chundeigar T, Othman B, Almalki O, Rayza F, et al. Non-invasive assessment of choledocholithiasis in patients with gallstones and abnormal liver function. *World J Gastroenterol* 2013;19:5877-6882.
2. Nuhadi M. Perbedaan Komposisi Batu Kandung Empedu Dengan Batu Saluran Empedu pada Penderita yang dilakukan Eksplorasi Saluran Empedu. Universitas Padjajaran. RS Hasan Sadikin Bandung. 2011.
3. Diehl AK. Epidemiology and natural history of gallstone disease. *Gastroenterology Clinics of North America* 1991;20(1):1-19.
4. Hassan L, Sadiq T, Naveed MR. Positive predictive value of raised serum alkaline phosphatase in predicting choledocholithiasis taking operative findings as gold standard. *PJMHS* 2018;12(4):1560-62.

5. Al-Jiffry BO, Khayat S, Abdeen E, Hussain T, Yassin M. A scoring system for the prediction of choledocholithiasis: a prospective cohort study. *Ann Saudi Med* 2016;36(1):57-36.
6. Sarli L, Costi R, Gobbi S, Iusco D, Sgobba G, Roncoroni L. Scoring system to predict asymptomatic choledocholithiasis before laparoscopic cholecystectomy. *Surg endos* 2003;17:1396-1403.
7. Canena J. Once upon a time a guideline was used for the evaluation of suspected choledocholithiasis: a fairy tale or a nightmare. 2018. *Port J Gastroenterol*;25:6-9.
8. Khoury T, Adileh M, Imam A, Azraq Y Bilitzky-Kopit A, Massarwa M, dkk. Parameters suggesting spontaneous passage of stones from common bile duct: a retrospective study. 2019. *Canadian Journal of Gastroenterology and Hepatology*:1-5.
9. Committee ASoP, American Society for Gastrointestinal Endoscopy. The role of endoscopy in the evaluation of suspected choledocholithiasis. 2010. *Gastrointestinal endoscopy*;71(1):1-9.
10. Monreal-Robles R, Gonzales-Gonzalez JA. Accuracy of scoring systems for the suspected choledocholithiasis: A 5-variable score system versus ASGE clinical guidelines. *Surgery*. 2016;160(6):1715-6.
11. Cohen ME, Slezak L, Wells CK, et al. Prediction of bile duct stones and complications in gallstone pancreatitis using early laboratory trends. *Am J Gastroenterol* 2001;96:3305-11.
12. Gouveia C, Loureiro R, Ferreira R, Ferreira AO, Santos AA, Santos MPC, et al. Performance of the choledocholithiasis diagnostic score in patients with acute cholecystitis. *Port J Gastroenterol*.2018;25:24-9.
13. Topal B, Van de Moortel M, Fieuws S, Vanbeckevoort D, Van Steenberghe W, Aerts R, dkk. The value of magnetic resonance cholangiopancreatography in predicting common bile duct stones in patients with gallstone disease. *British journal of surgery* 2003;90:42-47.
14. Costi R, Gnocchi A, Di Mario F, Sarli L. Diagnosis and management of choledocholithiasis in the golden age of imaging, endoscopy, and laparoscopy. *World J Gastroenterol* 2014;20(37):13382-13401.

15. Scientific Committee of European Association for Endoscopic Surgery. Diagnosis and treatment of common bile duct stones (CBDS). Result of a consensus development conference. *Surg endo* 1998;12:856-64.
16. Cynthia W Ko, Sum P Lee. Epidemiology and natural history of common bile duct stones and prediction of disease. *Gastrointestinal endoscopy* 2002;56(6S):S165
17. James YW, Yuk Tong Lee, Joseph Sung. Choledocholithiasis. *Elsevier* 2013: Bab 43: 410-420.
18. Ruhl CE, Everhart JE. Gallstone disease is associated with increased mortality in the united states. 2012. *Gastroenterology*;140(2):508-16.
19. Drake RL, Vogl W, Mitchell AWM. *Gray's Anatomy for Students*. Elsevier: 2007.
20. Brunicaudi FC, Andersen DK, Billiar, TR, Dunn DL. *Schwartz principles of surgery*. Ed ke-9. Philadelphia: McGraw-Hills. 2010.
21. Guyton AC. *Textbook of Medical Physiology, 11th edition*. Elsevier: 2006.
22. Laurentius L. Penyakit Batu Empedu. *Buku Ajar Ilmu Penyakit Dalam* ed. 4. Jakarta. 2006 : 479-481
23. Tozatti J, Parizi AL, Frazon O. Predictor Factors for Choledocholithiasis. 2015 : 109-112.
24. Henry V. 2005. Independent risk factor for gallstone formation in a region with high cholelithiasis prevalence. *Digestion*;71:97-105.
25. Cuevas A MD. Review Diet as Risk Factor for Cholesterol Gallstone disease. *Journal of American College of Nutrition*. 2004 : vol 23 : 187-196.
26. Debas Haile T. Biliary Tract In: *Pathophysiology and Management*. Springer-Verlaag. 2004 : chapter 7 : 198-224
27. Garden OJ, Parks RW. *Hepatobiliary and Pancreatic Surgery*. 5th ed. Saunders Elsevier. Chapter 10 : 174-192.
28. Yekeler E, Akyol Y. 2004. Cholelithiasis. *NEJM*;35(122):2318-2321.
29. Baron RL, Tublin ME, Peterson MS. 2002. Imaging the spectrum of biliary tract disease. *Radiol Clin ort Am*;40(6):1325-54.
30. Crawford MJ. *The Biliary Tract. Robin & Cotran Pathologic Basis of Disease*. Philadelphia : Saunders. 2010.

31. Schwartz SI. *Manifestations of Gastrointestinal Disease*. Dalam : Principles of Surgery fifth edition, editor : Schwartz, Shires, Spencer. Singapore : McGraw-Hill, 1989. 1091-1099.
32. Anderson MA, Fisher L, Jain R, et al. Complications of ERCP. *Gastrointest Endosc* 2012;75:467-73.
33. Narvaez-Rivera RM, Gonzalez-Gonzalez JA, Monreal-Robles R, Garcia-Compean D, Paz-Delgadillo J, Garza-Galindo AA, dkk. Accuracy of ASGE criteria for the prediction of choledocholithiasis. *Rev Esp Enferm Dig*. 2016;1008(6):309-14.
34. Caddy GR, Tham TC. Gallstone disease: epidemiology, pathogenesis and classification of biliary stones(common and intrahepatic). *Best Pract Research Clini Gastroenterol* 2006;20:1075-83.
35. Pejovic T, Stojadinovic MM. Scoring system development and validation for prediction choledocholithiasis before open cholecystectomy. *Srp Arh Celok Lek*. 2015;143(11-12):681-7.
36. Adams AMA, Hosmer AE, Wamsteker EJ, Wamsteker EJ, Anderson MA, Elta GH, dkk. 2015. Predicting the likelihood of a persistent bile duct stone in patients with suspected choldocholithiasis: accuracy of existing guidelines and the impact of laboratory trends. *Gastrointest Endosc*;82:88-93.
37. Narvaez-Rivera RM, Gonzales-Gonzalez JA, Monreal-Robles R, dkk. 2016. Accuracy of ASGE criteria for the prediction of choledocholithiasis. *Rev Esp Enferm Dig*;108:309-314.
38. He H, Tan C, Wu J, Dai N, Hu W, Zhang Y, dkk. 2017. Accuracy of ASGE high-risk criteria in evaluation of patients with suspected common bile duct stones. *Gastrointest Endosc*;86:525-532.
39. Suarez AL, LaBarre NT, Cotton B, ayne KM, Cote GA, Elmunzer BJ. 2016. An assessment of existing risk stratification of patients with suspected choledocholithiasis. *Surg Endosc*;30:4613-4618.
40. Sethi S, Wang F, Korson AS, Krishnan S,, Berzin TM, Chuttani R, dkk. Rospective assessment of consensus criteria for evaluation of patients with suspected choledocholithiasis. 2016. *Dig Endosc*; 28:75-82.