

ORIGINAL RESEARCH

Evaluation of The Diagnosis and Treatment of Gallstone Pancreatitis

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Abstract

Introduction. Acute pancreatitis is a major health problem due to the serious complication and mortality. Annual incidence of acute pancreatitis vary from under 10 to 40 per 100.000 person per year. Gallstone and biliary sludge contributes about 30-65% of the cause of acute pancreatitis and usually diagnosed as biliary or gallstone pancreatitis. There is still no data concerning the prevalence, diagnosis and management of gallstone pancreatitis in Indonesia.

Methods. The objective of this study is to know the prevalence and characteristic of diagnosis and management of gallstone pancreatitis in some hospitals in Jakarta. This is a descriptive cross sectional study using the data from medical record of acute pancreatitis and gallstone pancreatitis patients in Cipto Mangunkusumo, Fatmawati, and St Carolus Hospital in 2008-2012.

Results. There were 154 acute pancreatitis patients with only 22 (14,2%) patients diagnosed as having gallstone pancreatitis and 24 (15,5%) patients that met the criteria of gallstone pancreatitis but were not diagnosed as having one. On average, gallstone pancreatitis were diagnosed on the fifth day of hospitalization. Among 46 gallstone pancreatitis patients, only 6 (13%) patients had severity assessment. The most frequent examination used to explore the causes was abdominal ultrasound, performed in 37 (80,4%) patients. One (2,2%) patient had biliary sepsis and underwent internal drainage on day 15th. Only 10 (21,7%) patients underwent cholecystectomy. Three (8,3%) patients died, all before having cholecystectomy. Two (5,6%)

patients that had not undergone cholecystectomy got readmitted to the hospital due to recurrent acute pancreatitis and pancreatic pseudocyst

Conclusion. *From this study we can conclude that the diagnosis and management of gallstone pancreatitis still remain a challenge in Jakarta.*

Keywords: *Gallstone Pancreatitis, biliary cute pancreatitis, cholecystectomy*

Introduction

Acute pancreatitis is a major health problem regarding its serious complication and mortality.¹ The annual incidence of acute pancreatitis vary until up to 40/100.000 population.² About 30-65% of acute pancreatitis cases were caused by gallstone or sludge and termed gallstone pancreatitis.²⁻⁶ About 8-11% of patients with galstone will develop acute gallstone pancreatitis.⁷

The morbidity and mortality of gallstone pancreatitis were 30-40% and 2-20% respectively.^{1,4,7-10} The morbidity of gallstone pancreatitis vary from mild symptoms to systemic inflammatory response, organ failure, and death.^{11,12} The recurrency of pancreatitis and other complications caused by gallstone can cause recurrent hospitalization with longer length of stay if the treating physicians do not recognize the relation between gallstone and acute pancreatitis. In some cases, the clinical appearance of gallstone pancreatitis is similar to acute abdomen that if surgery is performed will increase morbidity and mortality.

The relation between gallstone and acute pancreatitis had been studied since 1901. Obstruction of the pancreatic duct by the impacted gallstone leads to blocked pancreatic secretion and triggers

pancreatitis. Another mechanism of pancreatitis is due to direct inflammation from cholangitis.¹³ On cellular level, there was autodigestion of pancreatic acinar cells by digestive enzymes that was activated by ductal obstruction, hypersecretion, or cellular injury process.^{6,9,10,14}

There are some guidelines of the management of gallstone pancreatitis that are issued by the International Association of Pancreatology with the collaboration of American Pancreatic Association (IAP/APA) and the Japanese (JPN) Guidelines. The guidelines include the diagnostic criteria, laboratory examination, imaging, severity assessment, treatment, biliary drainage, and the role of surgery.^{13,15,16}

This study evaluates the diagnostic and treatment of gallstone pancreatitis in Jakarta compared to the guidelines. Based on the outcome of this study we hope that the physicians, especially surgeons, can refresh the knowledge about the management of gallstone pancreatitis patients, particularly the role of surgery.

Materials and Methods

This is a descriptive cross sectional study. The medical records of all acute pancreatitis and gallstone pancreatitis patients hospitalized in Ciptomangunkusumo, Fatmawati, and St Carolus hospital in 2008-2012 were studied and compared to the guidelines.

Results

There were 154 acute pancreatitis patients in three hospital during 2008-2012, with 22 (14,2%) diagnosed as having gallstone pancreatitis. Twenty four (15,5%) patients fulfilled the criteria of gallstone pancreatitis but were not diagnosed as having one. We found seven (4,5%) patients with post ERCP pancreatitis, four (2,6%) patients with pancreatitis due to alcoholism, and six (4,9%) acute pancreatitis patients due to other causes like trauma and malignancy. There were 57 (36,8%) acute pancreatitis patients with unknown cause and 34 (22%) acute pancreatitis patients with incomplete work up (Fig. 1).

The IAP/APA guidelines recommend to explore the cause of every acute pancreatitis patients by thorough history taking (e.g. previous episode of acute

pancreatitis, gallstone disease, alcohol consumption, medication, hyperlipidemia, trauma, and recent invasive procedure like ERCP) including the family history of pancreatic disease.¹⁵

Acute pancreatitis was said to be idiopathic if no obvious causes that can be related. Some idiopathic pancreatitis, based on a study, was shown to correlate with gallstone or sludge, therefore idiopathic pancreatitis must be diagnosed after complete work up. If initial examination (repeated right upper abdominal ultrasound) were negative, it is recommended to perform endoscopic ultrasound (EUS) to detect microlithiasis, neoplasm, and chronic pancreatitis. The alternative is to perform microscopic bile analysis which sample is taken by ERCP. The patients were said to have bile sludge if monohydrate crystal cholesterol or calcium bilirubinate granule were found in the sediment. If all the examinations were negative, it is advised to perform MRCP to detect rare morphological anomaly. Computerized tomography scan should be performed as needed. Genetic counseling is considered if the cause remain unknown, especially after second idiopathic pancreatitis episode.^{1,6,10,15}

Among 46 gallstone pancreatitis patients, 24 (52,2%) were female and 22

(47,8%) were male. The youngest patient was 24 years old and the oldest was 86 years old with average of 51,1 years old.

a. Diagnosis

Amongst 48 patients that fulfilled the criteria of gallstone pancreatitis, acute pancreatitis were diagnosed on the first until tenth day of hospitalization, with mean duration of three days after admission. The diagnosis of gallstone pancreatitis could be made on 22 patients on the first until tenth day of hospitalization, with the average was on the fifth day.

National Guidelines in the United Kingdom stated that the diagnosis of gallstone pancreatitis can actually be made within the first 48 hours of admission. An evaluation study was done regarding this guideline revealed that this expectation has been made in 92% of cases.⁸ Indonesia has not had national guideline for gallstone pancreatitis. However, if the UK's guideline is applied here, the expectation is met only for 32% cases as in this study mentioned only 7 out of 22 patients were diagnosed within the first 48 hours after hospital admission. This rapid diagnosis is of prioritised importance because it is pivotal for early management because the disease might evolve progressively.

Most of the patients that were not diagnosed as having gallstone pancreatitis but actually fulfilled the criteria of gallstone pancreatitis, was diagnosed to have acute pancreatitis and gallstones or bile duct stones. Consequently, there was no comprehensive management plan that is appropriate for the gallstone pancreatitis.

The JPN guideline which was published in 2006 stated that clinical diagnosis of acute pancreatitis can be made if there are two out of three criteria after other causes of acute abdomen and other pancreatic disease entities have been excluded. These criteria are¹⁶:

1. Attack of acute abdominal pain and tenderness in the upper abdomen
2. Increased levels of pancreatic enzymes in blood, urine, or ascites
3. Abnormal imaging findings in pancreas associated with acute pancreatitis

Patients having two or more of the above three criteria are diagnosed with acute pancreatitis excluding other pancreatic diseases and acute abdomen.

Signs and symptoms of gallstone pancreatitis are presented on table 1. From 46 patients diagnosed or fulfilled the gallstone pancreatitis criteria, only 22

patients in whom classical signs and symptoms of gallstone diseases were found. The symptoms are vastly varied such as abdominal discomfort or early satiety after eating foods rich in fat, biliary colic, history of jaundice, or history of previous gallstone defined by associated supporting examinations. Patient presenting with upper abdominal pain should be evaluated for signs and symptoms of gallstone diseases to increase the diagnosis accuracy. Other than that, alcoholic beverages consumption was also noted to play a role in gallstone diseases. However, in this study, the question about alcohol consumption was asked only in 12 patients.

Some patients were found to have signs and symptoms mimicking peritonitis. This should arise caution because if pancreatitis was not suspected as one of the differential diagnosis, patients would be managed by unnecessary surgical intervention, even more, causing higher morbidity and mortality. Accordingly, it is stated by JPN guideline that any other cause of acute abdomen, gastrointestinal tract perforation, acute cholecystitis, ileus, mesenteric artery occlusion, and acute aortic dissection have to be excluded from differential diagnosis before making a diagnosis of acute pancreatitis.¹⁶

The laboratory profile of patients with gallstone pancreatitis in this study can be viewed on table 2. The results of radiology examinations and the presence of gallstone or sludge were shown on table 3.

Peripheral blood examination has multiple roles; for making the diagnosis of acute pancreatitis, predicting the presence of gallstone as the underlying cause, for severity grading, and also for clinical monitoring. Furthermore, the laboratory examination result can estimate the presence of persistent common bile duct stone, according to the previous studies.^{6,13,15}

To establish the diagnosis of acute pancreatitis based on the JPN guidelines, the level of pancreatic enzymes such as amylase and lipase need to be examined.¹⁶ The mean level of amylase in this study was 923,6 U/L. A study conducted by Tabone et al found mean value of blood amylase concentration of 2.184 U/L while a different study by Sanjay et al found that the median was 1.155 U/L.^{4,17} The mean level of lipase in this study was 1.426,6 U/L, which was much lower than 3.366 U/L, a mean lipase level found in a study directed by Tabone et al.¹⁷ The lower average level of pancreatic enzymes found in this study were caused by the lower cut-off value used for diagnosing acute pancreatitis compared to other studies.

The presence of gallstones as the underlying cause can be predicted by AST, ALT, bilirubin, and alkaline phosphatase concentration. According to the JPN guideline 2010 for gallstone pancreatitis, the ALT concentration of more than 150 IU/L of patients with acute pancreatitis was associated with gallstone origin.¹³ The mean ALT concentration in this study was higher than 150 IU/L. Thus, the majority of gallstone pancreatitis cases in this study have ALT level in conjunction with gallstone or sludge as the cause.

Several studies have been done to evaluate the timing and appropriate examinations to predict persistent common bile duct stones. One of them was done by Telem et al which found that the blood level of alkaline phosphatase ≥ 250 U/L, Gamma GT ≥ 350 U/L, total bilirubin ≥ 3 mg/dL, and direct bilirubin ≥ 2 mg/dL combined with common bile duct width of ≥ 9 mm on ultrasound were essential for the prediction of persistent common bile duct stone.¹⁸ In this study, there were two patients found to have common bile duct stone on ERCP. Both of them fulfilled three out of four laboratory criteria suggested by Telem et al and found to have common bile duct dilatation on ultrasonography. Radiology examination of

gallstone pancreatitis patients was performed to detect the presence of gallstone or sludge either in the gallbladder or in the duct. Inflammation of the pancreas can also be shown. According to gallstone pancreatitis management by JPN, both laboratory and ultrasound examinations are needed to conclude whether the gallstone is present.¹³ In this study, ultrasound was performed in only 37 (80,4 %) patients, followed by CT scan, MRCP, and ERCP. A study in UK found that all patients with gallstone pancreatitis were detected to have gallstone by merely using ultrasound.⁸ EUS was not done in this study.

Among 46 patients having gallstone pancreatitis, only six patients that were evaluated for the degree of severity. The scoring system APACHE II was used in three patients while three others using Ranson score. The severity grading was established on the first day of admission in five patients while in the other one was on the 8th day.

Based on the national guideline for pancreatitis in the UK, the severity grading should be established during the first 48 hours of hospitalisation.⁸ This target was met only in 10,9 % of cases in this study. Moreover, re-evaluation of the severity has not been done at all. This is essential

because even mild to moderate pancreatitis can progress into more severe disease. Consequently, re-evaluation every 2 days is highly suggested.

There are two scoring systems most commonly used; Ranson and APACHE II. The time needed to apply Ranson and Glasgow criteria is 48 hours. However, APACHE II is even more complicated to be used routinely. One study found that BISAP score (Table 4) can be suggested for routine use due to its simplicity because it requires less supporting examinations. The study evaluated that BISAP is as accurate as APACHE II for severity grading.¹⁹ In the end, the choice of scoring system is based on each institution's policy which is further tailored by physician preferences. However, it is crucial to use the same scoring scheme when re-evaluating the patient.

We retrospectively evaluated the degree of severity for pancreas inflammation according to the corresponding CT-scan result using Balthazar scoring system in 12 patients. One patient was categorized into Balthazar A, one patient was Balthazar B, four patients were Balthazar C, five patients were Balthazar D, and one patient was Balthazar E. Only one patient who had already been evaluated for Balthazar score by the treating physician. Balthazar score as

an aid in evaluating acute pancreatitis severity has not gained its popularity among treating physicians in hospitals in which this study was conducted.

b. Management

There are three indications for surgical intervention in gallstone pancreatitis; severe inflammation of pancreatic tissue (infected necrotizing pancreatitis or pancreatic abscess), biliary drainage in acute cholangitis or biliary sepsis (endoscopic or percutaneous), and gallstone extraction as a definitive treatment (cholecystectomy with/without common bile duct exploration).^{13,16}

Surgical intervention for severe inflammation of pancreas tissue was not done in these hospitals because there was no patient presenting with infected necrotizing pancreatitis or pancreatic abscess.

There was one biliary sepsis case but drainage using ERCP was done after 15 days. Based on the guideline from IAP/APA, ERCP is actually suggested to be done within the first 24 hours after the diagnosis of cholangitis with impending biliary sepsis was established.¹⁵ Other alternative for drainage are PTBD or open-cholecystectomy.

There were eleven patients undergoing invasive interventions and surgery. Among

seven patients who had been known to have only gallstones, six patients underwent cholecystectomy, while the other one discharged due to personal demand.

Characteristic of four patients proven to have stones or sludge in their gallbladder and biliary duct and subsequently underwent ERCP can be viewed on table 5. One patient did not have any surgical intervention after ERCP because he refused further examinations. There was no ERCP done after laparoscopic cholecystectomy procedure.

Several guidelines have suggested alternative intervention to manage gallstone pancreatitis with common bile duct stone. According to one study, laparoscopic cholecystectomy with intraoperative cholangiography is suggested and intra- or postoperative stone extraction was only done if the cholangiography revealed stones. Intraoperative stone extraction can be done through laparoscopy or laparotomy while postoperative stone extraction is done through ERCP. This approach is thought to be the most cost-effective.¹⁷ However, in this study we only performed ERCP followed by cholecystectomy.

There were only 10 (21,7%) patients underwent cholecystectomy in this study (Table 6) while the national guideline in UK

stated that all (100%) gallstone pancreatitis patients has to undergo this procedure.⁸ The fact showed us that gallstone pancreatitis definitive treatment was still far from the suggested standard.

Nine patients had cholecystectomy during the same hospitalisation period with the first acute pancreatitis onset while one patient had this on the subsequent hospitalisation period. In a patient undergoing interval cholecystectomy, the surgical intervention was done 1,5 months after acute pancreatitis onset, 12 days after being discharged from the initial hospitalization. The patient presented with signs and symptoms of acute pancreatitis and was proven to have pancreatic pseudocyst. Therefore, open cholecystectomy and internal drainage was performed. This is in accordance with a study conducted by Nguyen et al which concluded that an ERCP and cholecystectomy during the first hospitalisation period after diagnosis of acute pancreatitis was made is associated with decreased readmission due to acute gallstone pancreatitis.²⁰

In this study no patient undertook either intraoperative cholangiography or common bile duct exploration through laparoscopy.

c. Outcome

There were three patients (8,3%) died, all of them died before cholecystectomy was performed. One patient died due to multiple organ failure as necrotizing pancreatitis complication. This patient had underwent pancreatic debridement at another hospital which then referred the patient for postoperative care. The pathologic report of the pancreas specimen revealed suppurative inflammation. Two others died because of severe comorbidities such as chronic renal failure and cerebrovascular disease. The mortality rate in this study is in agreement with other studies which stated that gallstone pancreatitis mortality rate was ranging from 2 to 17%.^{1,8-10} No patient died after cholecystectomy was performed.

Among the patients who did not undergo cholecystectomy during the first hospitalisation period, two (5,6%) patients were readmitted due to recurrent acute pancreatitis and pancreatic pseudocyst. Rate of recurrence in this study is lower than other studies which found that the recurrence risk of untreated gallstone pancreatitis was 23-61%.^{9,11,21}

Conclusion

The percentage of take and graft revascularization is better with the VAC method compared to the standard tie-over method.

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Table 1. Test of Data Normality

		<i>Shapiro-Wilk</i>	
		P	Data Distribution
Amount of Vascularization	<i>Tie-Over</i>	0,272	Normal
	VAC	0,248	Normal

Table 2 “Take” Distribution of Graft

Methods (Take)	Amount
VAC	
100 %	9
Standard	
80 %	2
100 %	7

Table 3. Comparison of Graft Vascularization

Sample number	Blood Vessel / View	Mean (SD)	t-test P
Group A (<i>tie-over</i>)			
1	12	7.1	
2	5	(4,2)	
3	2		
4	7		
5	14		
6	5		
7	5		
8	3		
9	11		
Group B (VAC)			
1	11	12.6	0,0045
2	17	(3,6)	
3	15		
4	8		
5	17		
6	10		
7	8		
8	15		
9	12		

