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Clinical management and outcomes of acute pancreatitis: Identifying areas for quality improvement in a tertiary Asian setting

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ABSTRACT

Background: This study aims to review the clinical management of patients with acute pancreatitis in a tertiary institute in Singapore, and to identify areas qualiy improvement based on validation against the recommendations in the IAP/APA and the Japanese guidelines.
Methods: 391 patients from a prospective electronic database were included and reviewed for compliance to the International Association of Pancreatology (IAP)/American Pancreatic Association (APA) guidelines (2013) and the Japanase Guidelines (2015).
Results: The 90 day mortality was 8.4% for moderately severe and 11.9% for severe pancreatitis. The accuracy of SIRS in predicting severe acute pancreatitis on admission was 72.1% and at 48 h 80.8%. Only 61.1% patients had ultrasound scan during their admission of whom 32.9% had it within 24 h of admission. 18.3% patients with initial diagnosis of idiopathic pancreatitis had EUS. 50% received Ringer lactate for initial fluid resuscitation. 38.7% received antibiotics as prophylaxis. 21.4% with severe acute pancreatitis had early enteral nutrition. Only 21.4% patients with biliary pancreatitis had index admission cholecystectomy.
Conclusion: The compliance to existing guidelines for management of acute pancreatitis is variable. Identifying gaps and implementing measures to address them allows for continued improvement in the management of patients with acute pancreatitis.

Introduction

Acute pancreatitis is a common gastrointestinal disease that remains a significant management challenge and is a significant healthcare burden [1–3]. There are many published studies from Western countries and relatively few from Asia, where outcomes appear highly variable. The published overall mortality ranges up to 2% in the Western populations [4–6] and up to 7.5% in an Asian population [7]. Although differences in outcome may reflect differences in ethnicity [7], comorbidity [4], and severity [7] and differences in management.

Over the last 20 years there has been a better understanding of the pathophysiology of acute pancreatitis, improvements in management, including advances in imaging and interventional techniques, all of which have led to many practice guidelines [8–12]. With the exception of the Japanese guidelines [12] many of these guidelines are largely based on evidence and experience from centres in the West, with the contribution from Asian centres relatively minor. Achieving compliance with guidelines is important to improving outcomes [13–16], as it identifies areas for improvement and directs the development of standardized evidence based guidelines, important for clinical practice and trials. The aim of this study was to audit the management and outcomes of acute pancreatitis at the National University Hospital in Singapore and to determine the degree of compliance with two current guidelines: the international IAP/APA (5th July 2013) [8] and the Japanese (2015) guidelines [12]. We chose the IAP/APA as it multi-national as against country specific guidelines and the Japanese guidelines as these were the only guidelines developed specific to the Asian setting. The study is a step towards introducing a local evidence based practice guideline to standardize management for quality improvement and better outcomes.

Materials and methods

The study was approved by the National Healthcare Group Domain Specific Review Board (2015/00030). This study involved the review of data from a prospective electronic database including

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patients admitted with the diagnosis of acute pancreatitis to National University Hospital in Singapore over a 3 year period (1/5/2012 to 30/6/2015). Gaps in the data were completed with a retrospective review of the records. The diagnosis of acute pancreatitis was based on the IAP/APA guidelines [8]. This required 2 out of 3 criteria: upper abdominal pain, serum amylase or lipase more than 3 times above the upper limit of normal and/or imaging criteria consistent with acute pancreatitis. Patients were followed up for at least 2 years after they were discharged from their index admission for acute pancreatitis. Patients readmitted after the index admission were included as follow up of index admission and were not registered as a new case of acute pancreatitis. Patients aged below 18 years old were excluded from the study.

Data collection

Data collected included patient demographics, etiologic factors, comorbidities, severity (Revised Atlanta Classification [17]), relevant laboratory tests, imaging tests, outcomes, local and systemic complications, SIRS response, hospital stay, admission to High Dependency Unit (HDU) and Intensive Care Unit (ICU), fluid therapy, nutrition management, antibiotic use, biliary tract management and interventions for pancreatic necrosis. We used the Revised Atlanta Classification to define local complications which included acute peripancreatic fluid collection (APFC), acugte necrotic collection (ANC), pseudocyst and walled-off necrosis (WON). Necrotizing pancreatitis was defined as
pancreatic parenchymal necrosis and/or peripancreatic necrosis on contrast enhanced Computed Tomography (CT) scan using these criteria: 1) lack of pancreatic parenchymal enhancement (patchy or confluent) by intravenous contrast agent and/or 2) presence of findings of peripancreatic collections associated with necrosis, including acute necrotic collections (ANC) and walled-off necrosis (WON) [17]. Acute Cholangitis was defined using the updated Tokyo Guidelines [18]. The diagnosis of hypertension and diabetes was based on the medical records and follow up. Hyperlipidemia was defined as serum cholesterol level more than 6.18 mmol/L and/or serum triglycerides more than 2.25 mmol/L and/or patients on medications for hyperlipidemia based on the medical records. The Charlson comorbidity Index [19] was used to classify comorbidities (Table 1). The admission criteria for HDU included 1) patients needing support for a single failing organ system, requiring non-invasive ventilation but excluding those requiring intubation and mechanical ventilation, 2) patients who could benefit from more intensive observation than can be provided on a general ward and 3) patients no longer needing to be in the ICU but not well enough to be returned to the ward. The admission criteria for ICU include 1) pulse <40 or >150 beats/min, 2) systolic arterial pressure <80 mmHg (<10.7 kPa) or mean arterial pressure <60 mmHg (<8.0 kPa) or diastolic arterial pressure >120 mmHg (>16 kPa), 3) respiratory rate >35 breaths/min, 4) serum sodium <110 mmol/l or >170 mmol/l; 5) serum potassium <2.0 mmol/l or >7.0 mmol/l, 6) paO_2 <50 mmHg (<6.7 kPa), 7) pH < 7.1 or >7.7, 8) serum glucose >800 mg/dl (>44.4 mmol/L), 9) serum calcium > 15 mg/dl (>3.75 mmol/L), 10) anuria, and/or 11) coma, requiring support for one or more organ dysfunctions that could not be managed in HDU.

Compliance

Compliance was determined by comparing the collected data with recommendations from two current evidence based guidelines: IAP/APA (2013) [8] and Japanese (2015) [12]. The IAP/APA recommendations included 12 main topics, incorporating 38 clinical questions and their answers (Table 2). The Japanese recommendations included 17 subject areas, for which 43 recommendations were derived (Table 2). Compliance was calculated by the number/percentage of patients who were managed according to each recommendation.

Table 1
Baseline characteristics of the patient cohort.

Gender	n	%
Male	224	57.3
Female	167	42.7
Age		
Median (range)	59.0 (18–97)	
Ethnicity		
Chinese	234	59.8
Malay	63	16.1
Indian	63	16.1
Others	31	7.9
Aetiology		
Gallstones	238	60.9
Alcohol	36	9.2
Hypertriglyceridemia	12	3.1
Endoscopic retrograde cholangiopancreatography-induced	11	2.8
Drug-induced	5	1.3
Others (including autoimmune and mumps infection, postoperative)	7	1.7
Idiopathic	82	20.9
Comorbidities		
Charlson Comorbidity Index [19] (median, range)	3.00 (0–14)	
Hypertension	203	51.9
Hyperlipidemia	164	41.9
Type II diabetes mellitus	125	32.0
Chronic pancreatitis	20	5.1
Severity (Revised Atlanta Classification)		
Mild	266	68.0
Moderately severe	83	21.3
Severe	42	10.7

Statistical analysis

All collected data were analysed with SPSS Version 24 (SPSS Inc., Chicago, IL, USA). Categorical data is stated as frequency, percentage and median (range). The association between categorical variables was examined with the Chi-square test and Fisher's exact test Continuous data is stated as mean and standard deviation. The comparison between 3 patient groups was by one-way ANOVA with the Bonferroni adjustment method was used for normally distributed data with homogenous group-wise standard deviation. A p value of <0.05 was considered significant.

Results

Patient charachteristics

Of 400 consecutive patients admitted with acute pancreatitis during the three year period, complete data was available for 391 (97.7%) patients. The overall median age, ethnicity, aetiology, comorbidities and eventual severity are given in Table 1.

Clinical outcomes

The clinical outcomes were examined by severity grade [8] (Table 3). Infected local (pancreatic or peripancreatic) complications occurred in only 8 (2%) patients and all had severe acute pancreatitis. Persistent organ failure occurred in 42 (10.7%) patients, and this defined severe acute pancreatitis. Admission to HDU was required for 79 (20.2%) patients and to ICU for 31 (7.9%). There was a stepwise increase in the duration of hospitalization with increasing severity of acute pancreatitis ($p < 0.001$). There was no

Table 2
IAP/APA guidelines (I).

Indicator	No.	Guideline	Grade and Agreement	Compliance
Diagnosis	1	The definition of acute pancreatitis is based on the fulfillment of '2 out of 3' of the following criteria: clinical (upper abdominal pain), laboratory (serum amylase or lipase >3× upper limit of normal) and/or imaging (CT, MRI, ultrasonography) criteria.	1B strong	100
Aetiology	2	On admission, the aetiology of acute pancreatitis should be determined using detailed personal (i.e. previous acute pancreatitis, known gallstone disease, alcohol intake, medication and drug intake, known hyperlipidemia, trauma, recent invasive procedures such as ERCP) and family history of pancreatic disease, physical examination, laboratory serum tests (i.e. liver enzymes, calcium, triglycerides), and imaging (i.e. right upper quadrant ultrasonography).	1B strong	32.9
	3	In patients considered to have idiopathic acute pancreatitis, after negative routine work-up for biliary aetiology, endoscopic ultrasonography (EUS) is recommended as the first step to assess for occult microlithiasis, neoplasms and chronic pancreatitis. If EUS is negative, (secretin-stimulated) MRCP is advised as a second step to identify rare morphologic abnormalities. CT of the abdomen should be performed. If aetiology remains unidentified, especially after a second attack of idiopathic pancreatitis, genetic counseling (not necessarily genetic testing) should be considered.	2C weak	18.3
Prediction of severity	4	Systemic inflammatory response syndrome (SIRS) is advised to predict severe acute pancreatitis at admission and persistent SIRS at 48 h.	2B weak	100
	5	During admission, a 3-dimension approach is advised to predict outcome of acute pancreatitis combining host risk factors (e.g. age, co-morbidity, body mass index), clinical risk stratification (e.g. persistent SIRS) and monitoring response to initial therapy (e.g. persistent SIRS, blood urea nitrogen, creatinine).(GRADE 2B, strong agreement)	2B strong	100
Imaging	6	The indication for initial CT assessment in acute pancreatitis can be: 1) diagnostic uncertainty, 2) confirmation of severity based on clinical predictors of severe acute pancreatitis, or 3) failure to respond to conservative treatment or in the setting of clinical deterioration. Optimal timing for initial CT assessment is at least 72–96 h after onset of symptoms.	1C strong	100
	7	Follow up CT or MR in acute pancreatitis is indicated when there is a lack of clinical improvement, clinical deterioration, or especially when invasive intervention is considered.	1C strong	NA
	8	It is recommended to perform multidetector CT with thin collimation and slice thickness (i.e. 5 mm or less), 100–150 ml of non-ionic intra-venous contrast material at a rate of 3 mL/s, during the pancreatic and/or portal venous phase (i.e. 50–70 s delay). During follow up only a portal venous phase (monophasic) is generally sufficient. For MR, the recommendation is to perform axial FS-T2 and FS-T1 scanning before and after intravenous gadolinium contrast administration.	1C strong	100
Fluid therapy	9	Ringer's lactate is recommended for initial fluid resuscitation in acute pancreatitis.	1B strong	50
	10a	Goal directed intravenous fluid therapy with 5–10 ml/kg/h should be used initially until resuscitation goals (see Q10b) are reached	1B weak	NA
	10b	The preferred approach to assessing the response to fluid resuscitation should be based on one or more of the following: 1) non-invasive clinical targets of heart rate < 120/min, mean arterial pressure between 65 and 85 mmHg (8.7e11.3 kPa), and urinary output > 0.5e1ml/kg/h, 2) invasive clinical targets of stroke volume variation, and intrathoracic blood volume determination, and 3) biochemical targets of hematocrit 35–44%	2B weak	NA
Intensive care management	11	Patients diagnosed with acute pancreatitis and one or more of the parameters identified at admission as defined by the guidelines of the Society of Critical Care Medicine (SCCM). Furthermore, patients with severe acute pancreatitis as defined by the revised Atlanta Classification (i.e. persistent organ failure) should be treated in an intensive care setting.	1C strong	59.5
	12	Management in, or referral to, a specialist center is necessary for patients with severe acute pancreatitis and for those who may need interventional radiologic, endoscopic, or surgical intervention.	1C strong	NA
	13	A specialist center in the management of acute pancreatitis is defined as a high volume center with up-to-date intensive care facilities including options for organ replacement therapy, and with daily (i.e. 7 days per week) access to interventional radiology, interventional endoscopy with EUS and ERCP assistance as well as surgical expertise in managing necrotizing pancreatitis.	2C weak	NA
	14	Early fluid resuscitation within the first 24 h of admission for acute pancreatitis is associated with decreased rates of persistent SIRS and organ failure.	1C strong	100
Preventing infectious complications	17	Intravenous antibiotic prophylaxis is not recommended for the prevention of infectious complications in acute pancreatitis.	1B strong	63.9
	18		2B weak	0

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Table 2 (*continued*)

Indicator	No.	Guideline	Grade and Agreement	Compliance
		Selective gut decontamination has shown some benefits in preventing infectious complications in acute pancreatitis, but further studies are needed.		
	19	Probiotic prophylaxis is not recommended for the prevention of infectious complications in acute pancreatitis.	1B strong	100
Nutritional support	20	Oral feeding in predicted mild pancreatitis can be restarted once abdominal pain is decreasing and inflammatory markers are improving.	2B strong	97.3
	21	Enteral tube feeding should be the primary therapy in patients with predicted severe acute pancreatitis who require nutritional support.	1B strong	21.4
	22	Either elemental or polymeric enteral nutrition formulations can be used in acute pancreatitis.	2B strong	NA
	23	Enteral nutrition in acute pancreatitis can be administered via either the nasojejunal or nasogastric route.	2A strong	21.4
	24	Parenteral nutrition can be administered in acute pancreatitis as second-line therapy if nasojejunal tube feeding is not tolerated and nutritional support is required.	2A strong	NA
Biliary tract management	25a	ERCP is not indicated in predicted mild biliary pancreatitis without cholangitis.	1A strong	92.6
	25b	ERCP is probably not indicated in predicted severe biliary pancreatitis without cholangitis.	1B strong	75
	26	Urgent ERCP (<24 h) is required in patients with acute cholangitis. Currently, there is no evidence regarding the optimal timing of ERCP in patients with biliary pancreatitis without cholangitis.	2C strong	NA
	27	MRCP and EUS may prevent a proportion of ERCPs that would otherwise be performed for suspected common bile duct stones in patients with biliary pancreatitis who do not have cholangitis, without influencing the clinical course. EUS is superior to MRCP in excluding the presence of small (<5 mm) gallstones. MRCP is less invasive, less operator-dependent and probably more widely available than EUS. Therefore, in clinical practice there is no clear superiority for either MRCP or EUS.	2C strong	33.6
Indications for intervention in necrotizing pancreatitis	28	Common indications for intervention (either radiological, endoscopical or surgical) in necrotizing pancreatitis are: 1) Clinical suspicion of, or documented infected necrotizing pancreatitis with clinical deterioration, preferably when the necrosis has become walled-off, 2) In the absence of documented infected necrotizing pancreatitis, ongoing organ failure for several weeks after the onset of acute pancreatitis, preferably when the necrosis has become walled-off.	1C strong	100
	29	Routine percutaneous fine needle aspiration of peripancreatic collections to detect bacteria is not indicated, because clinical signs (i.e. persistent fever, increasing inflammatory markers) and imaging signs (i.e. gas in peripancreatic collections) are accurate predictors of infected necrosis in the majority of patients. Although the diagnosis of infection can be confirmed by fine needle aspiration (FNA), there is a risk of false-negative results.	1C strong	100
	30	Indications for intervention (either radiological, endoscopical or surgical) in sterile necrotizing pancreatitis are: 1) Ongoing gastric outlet, intestinal, or biliary obstruction due to mass effect of walled-off necrosis (i.e. arbitrarily >4–8 weeks after onset of acute pancreatitis), 2) Persistent symptoms (e.g. pain, 'persistent unwellness') in patients with walled-off necrosis without signs of infection (i.e. arbitrarily >8 weeks after onset of acute pancreatitis), 3) Disconnected duct syndrome (i.e. full transection of the pancreatic duct in the presence of pancreatic necrosis) with persisting symptomatic (e.g. pain, obstruction) collection(s) with necrosis without signs of infections (i.e. arbitrarily >8 weeks after onset of acute pancreatitis).	2C strong	100
Timing of intervention in necrotizing pancreatitis	31	For patients with proven or suspected infected necrotizing pancreatitis, invasive intervention (i.e. percutaneous catheter drainage, endoscopic transluminal drainage/necrosectomy, minimally invasive or open necrosectomy) should be delayed where possible until at least 4 weeks after initial presentation to allow the collection to become 'walled-off'.	1C strong	76.9
	32	The best available evidence suggests that surgical necrosectomy should ideally be delayed until collections have become walled-off, typically 4 weeks after the onset of pancreatitis, in all patients with complications of necrosis. No subgroups have been identified that might benefit from earlier or delayed intervention.	1C strong	100
Intervention strategies in necrotizing pancreatitis	33	The optimal interventional strategy for patients with suspected or confirmed infected necrotizing pancreatitis is initial image-guided percutaneous (retroperitoneal) catheter drainage or endoscopic transluminal drainage, followed, if necessary, by endoscopic or surgical necrosectomy.	1A strong	66.7
	34	Percutaneous catheter or endoscopic transmural drainage should be the first step in the treatment of patients with suspected or confirmed (walled-off) infected necrotizing pancreatitis.	1A strong	15.4
	35	There are insufficient data to define subgroups of patients with suspected or confirmed infected necrotizing pancreatitis who would benefit from a different treatment strategy.	2C strong	NA

Table 2 (*continued*)

Indicator	No.	Guideline	Grade and Agreement	Compliance
Timing of cholecystectomy	36	Cholecystectomy during index admission for mild biliary pancreatitis appears safe and is recommended. Interval cholecystectomy after mild biliary pancreatitis is associated with a substantial risk of readmission for recurrent biliary events, especially recurrent biliary pancreatitis.	1C strong	21
	37	Cholecystectomy should be delayed in patients with peripancreatic collections until the collections either resolve or if they persist beyond 6 weeks, at which time cholecystectomy can be performed safely.	2C strong	100
	38	In patients with biliary pancreatitis who have undergone sphincterotomy and are fit for surgery, cholecystectomy is advised, because ERCP and sphincterotomy prevent recurrence of biliary pancreatitis but not gallstone related gallbladder disease, i.e. biliary colic and cholecystitis.	2B strong	NA
Japanese guidelines (II)				
Indicator	No.	Guideline	Strength and grade	Compliance
Diagnosis	1	The measurement of serum lipase is recommended for the diagnosis of acute pancreatitis. However, when the measurement of lipase is difficult, serum amylase (pancreatic amylase) should be measured.	1B	39.1
	2	Urinary trypsinogen-2 dipstick may be useful for minimally invasive method and rapid diagnosis of acute pancreatitis. However, this is not commercially available in Japan and therefore it cannot be recommended at this time.	Ungraded B	0
Diagnostic imaging	3	When acute pancreatitis is suspected, ultrasonography is recommended.	1C	61.1
	4	CT is recommended for the diagnosis of acute pancreatitis.	1C	27.4
Severity assessment	8	In principle, it is recommended that a severity assessment be made immediately after diagnosis and repeated over time (especially within 48 h of the diagnosis).	1C	100
	9	It is recommended that a scoring system is used for severity assessments.	1B	100
Fluid therapy	12	An extracellular solution (Ringer's Lactate solution, etc.) is recommended as the initial infusion solution for acute pancreatitis.	1C	50
	13	For patients in shock or with dehydration in the early phases of acute pancreatitis, short-time rapid fluid resuscitation (150–600 mL/h: depending on the presence of shock and the dehydration level) is recommended. However, this should be carried out with great care in order to avoid excessive fluid infusion. For patients without dehydration, they should be monitored closely with an appropriate amount of fluid infusion (130–150 mL/h). Particularly for patients with comorbidities such as cardiac or renal failure, the circulating blood volume should be careful evaluated to determine the rate of fluid infusion.	1C	NA
	14	If a mean arterial pressure of 65 mmHg or more and a urine output of 0.5 mL/kg per h or more has been secured in patients with acute pancreatitis, rapid fluid infusion should be discontinued and a reduction of the rate of fluid infusion is suggested. The volume of infusion should be adjusted to maintain these levels.	2C	100
Nasogastric tube	15	No remedial effect of nasogastric tube insertion has been observed for mild acute pancreatitis. Therefore, the routine use of nasogastric suction tubes is not required.	1A	97.3
Pain control	16	Pain associated with acute pancreatitis is severe and persistent, raising the need of sufficient pain control.	1A	NA
Antibiotics prophylaxis	17a	The prophylactic administration of antibiotics is not necessary in mild acute pancreatitis, since the incidence and mortality rates of infectious complications from mild acute pancreatitis are low.	1A	48.9
	17b	The prophylactic administration of antibiotics in severe acute pancreatitis and necrotizing pancreatitis may improve the prognosis, if carried out in the early phases of pancreatitis (within 72 h of onset).	2B	76.8
	18	No remedial effect of the prophylactic administration of antifungal agents for acute pancreatitis has been observed. Therefore, routine administration is not recommended.	1C	100
Protease inhibitor	19	The effectiveness of intravenous administration of protease inhibitor (gabexate mesilate) for improving the life prognosis and the rate of complications of acute pancreatitis has not been clearly proven. Further consideration of the efficacy of continuous high-dose intravenous administration for severe cases is required.	Ungraded B	0
Nutritional support	20	Intravenous hyperalimentation is not recommended for mild cases.	1B	100
	21a	Total parenteral nutrition (not performed with oral or enteral nutrition) should be avoided if possible.	1B	100
	21b	In severe cases, it is more significant as a measure to prevent infection rather than as a route of nutrition support. It can be applied and implemented for severe cases which do not have accompanying intestinal complications.	1A	21.4
	22	If initiated in the early phase, enteral nutrition can reduce the incidence of complications and can contribute to an increased rate of survival. Therefore, it is desirable that it be started within at least 48 h of admission.	2A	21.4
	23	In principle, it is recommended that enteral feeding tubes be inserted into the jejunum through the Treitz ligament. However, if a feeding tube cannot	2B	100

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Table 2 (*continued*)

Indicator	No.	Guideline	Grade and Agreement	Compliance
		be inserted into the jejunum, nutrients can be infused into the duodenum or stomach instead.		
	24	The initiation of oral administration should be determined using indicators such as the subsidence of abdominal pain and the serum pancreatic enzyme (especially serum lipase) level, etc.	2B	NA
Intensive care	25	No life-saving effect has been observed from peritoneal lavage for acute pancreatitis, and therefore it is not recommended.	2B	100
	26a	For severe cases where circulation dynamics are not stable with anuria even after sufficient initial fluid infusion or cases with abdominal compartment syndrome (ACS), CHF/CHDF should be introduced.	1C	NA
	26b	The efficacy of CHF/CHDF in cases of severe acute pancreatitis not mentioned above is uncertain. Therefore, routine use is not recommended.	2C	100
	27	Continuous Regional Arterial Infusion therapy is reported to be effective in reducing pancreatic infection and mortality rates for severe acute pancreatitis and acute necrotizing pancreatitis, but its efficacy has not been confirmed.	Ungraded B	0
Management of biliary pancreatitis	28	Early ERCP/ES should be performed in gallstone-induced acute pancreatitis when complications of cholangitis or prolonged passage disorder of the biliary tract are suspected.	1A	42.8
	29	To prevent the recurrence of gallstone-induced acute pancreatitis, cholecystectomy is recommended for cases where such surgery is possible.	1B	59.7
	30	A cholecystectomy should be performed as soon as gallstone-induced acute pancreatitis has been resolved.	1B	59.7
Management of abdominal compartment syndrome	31	The sequential measurement of IAP is recommended for cases with excessive fluid infusion, high severity, renal and respiratory complications, and fluid accumulation in multiple areas as observed by CT, since the onset of ACS increases the mortality rate in such cases.	2C	NA
	32	When there is persistent or recurrent IAP≧12 mmHg, conservative treatment (gastrointestinal decompression, intra-abdominal decompression, improvement of abdominal wall compliance, appropriate fluid infusion and circulation management) should be initiated. The goal should be to manage for IAP≦15 mmHg. Surgical decompression should be considered only when internal treatment is not effective for patients with IAP>20 mmHg and where the additional complication of organ failure is of concern.	2D	NA
Interventions for the local complications	33	In principle, conservative treatment should first be performed for necrotizing pancreatitis. The best indication for intervention is applied to cases of infected pancreatic necrosis with suspected or confirmed infection accompanying an aggravated general condition.	1C	100
	34	Infected pancreatic necrosis should be suspected when clinical symptoms and blood test findings deteriorate. Routine use of FNA is not required for diagnosis, and clinical signs and CT should be used for a comprehensive determination. If an aggravated general condition is observed, percutaneous drainage or endoscopic drainage should be given for diagnosis and treatment.	1C	100
	35	If possible, therapeutic intervention for infected pancreatic necrosis should be performed after 4 weeks of onset, when the necrosis has been sufficiently walled off, or in other words, during WON period.	2C	76.9
	36	During therapeutic intervention for infected pancreatic necrosis, percutaneous (retroperitoneal) drainage or endoscopic transluminal drainage should be first given, and if no improvement is achieved, necrosectomy should then be performed. Necrosectomy by endoscopic or retroperitoneal approach is recommended.	2B	66.7
Post-ERCP pancreatitis	37a	Prophylactic temporary pancreatic stent placement is useful as an effective endoscopic procedure for the prevention of post-ERCP pancreatitis. This should only be performed in the high-risk groups for post-ERCP pancreatitis given the risks and cost.	2A	NA
	37b	The guidewire method is very likely to reduce the incidence of post-ERCP pancreatitis.	2A	100
	38	For the prevention of post-ERCP pancreatitis, the intrarectal administration of NSAIDs should be carried out for all cases undergoing ERCP with no contraindications.	2A	0
Clinical indicators (Pancreatitis Bundles 2015)	39	A high rate of implementation of the pancreatitis bundles may contribute to improving prognosis of patients with severe acute pancreatitis.	1C	0

NA: Not assessed.

difference in mean duration of HDU stay ($p = 0.262$), ICU stay ($p = 0.368$) based on severity grade, but the number of patients admitted to HDU ($p = 0.003$) and ICU ($p = 0.003$) was higher with increasing severity. The overall 90-day mortality was 4.1%, and it was 8.4% and 11.9% for moderately severe and severe acute pancreatitis respectively ($p = 0.001$).

Diagnosis and aetiology

Amylase alone was used in 238 (60.9%) patients to make the diagnosis, amylase and lipase in 152 (38.8%), and lipase alone in 1 (0.3%) patient. The Japanese guidelines recommends the use of serum lipase alone, rather than amylase. The compliance with IAP/

Table 3
Outcomes of patients admitted with acute pancreatitis based on severity grade.

Outcome	Units	Overall (391)		Mild (266)		Mod severe (83)		Severe (42)		p-value
		n	%	n	%	n	%	n	%	
Infected local complications	patients	8	2.1	0	0.0	0	0.0	8	19.1	<0.001
Transient organ failure	patients	39	10.0	0	0.0	39	47.0	0	0.0	<0.001
Persistent organ failure (total)	patients	42	10.7	0	0.0	0	0.0	42	100.0	<0.001
Persistent organ failure (single organ)	patients	31	7.9	0	0.0	0	0.0	31	73.8	<0.001
Persistent organ failure (multiple organ)	patients	11	2.8	0	0.0	0	0.0	11	26.2	<0.001
HDU admission	patients	79	20.2	26	9.8	28	35.4	25	59.5	0.003
HDU duration mean ± SD (range)	days	5.00 ± 3.83 (1–21)		4.12 ± 1.75 (2–9)		5.07 ± 5.11 (1–21)		5.91 ± 3.72 (2–15)		0.262
ICU admission	patients	31	7.9	3	1.1	11	13.2	17	40.5	0.003
ICU duration mean ± SD (range)	days	11.13 ± 9.67 (3–30)		4.00 ± 1.00 (3–5)		12.00 ± 9.08 (4–29)		13.83 ± 11.77 (4–30)		0.368
Hospital stay Mean ± SD (range)	days	8.79 ± 14.11 (1–171)		6.74 ± 11.87 (1–171)		11.31 ± 17.69 (2–120)		16.74 ± 15.83 (3–76)		<0.001
Mortality (90day)	patients	16	4.1	4	1.5	7	8.4	5	11.9	0.001
Fluid therapy	Units	Overall (391)		Mild (266)		Moderately severe (83)		Severe (42)		p-value
Mean rate of fluid resuscitation ± SD (range)	ml/kg/hr	1.50 ± 0.85 (0.19–7.64)		1.46 ± 0.69 (0.26–4.05)		1.39 ± 0.64 (0.19–2.88)		1.87 ± 1.50 (0.24–7.64)		0.240
Antibiotics		n	%	n	%	n	%	n	%	
Patients receiving antibiotics		232	59.3	136	51.1	58	69.9	38	90.5	<0.001
Patients who did not receive antibiotics		159	40.7	130	48.9	25	30.1	4	9.5	
Nutrition		n	%	n	%	n	%	n	%	
Oral feeding	patients	362	92.6	259	97.3	71	85.6	32	76.2	
Enteral nutrition	patients	25	6.4	6	2.3	10	12.0	9	21.4	<0.001
Biliary pancreatitis		n	%	n	%	n	%	n	%	
Cholestasis										
Without cholangitis	patients	98	41.2	68	42	22	44	8	30.8	0.507
ERCP performed	patients	9	9.2	5	7.4	2	9.1	2	7.6	0.732
MRCP performed	patients	7	7.1	4	5.9	3	13.6	0	0.0	
EUS performed	patients	26	26.5	18	26.5	7	31.8	1	12.5	
Cholangitis										
With cholangitis	patients	140	58.8	94	58	28	56	18	69	0.5
ERCP performed	patients	60	42.9	40	42.5	10	35.7	10	55.5	0.38
Cholecystectomy		n	%	n	%	n	%	n	%	
Cholecystectomy in index admission	patients	51	21.4	34	21.0	13	26.0	4	15.4	0.123
Cholecystectomy in interval admission (>4 weeks)	patients	91	38.2	70	43.2	16	32.0	5	19.2	0.108

APA guideline was 100% and with Japanese guideline 0.2%. In patients considered to have idiopathic acute pancreatitis, after negative routine work-up for biliary aetiology, endoscopic ultrasonography (EUS) is recommended as the first step to assess for occult microlithiasis, neoplasms and chronic pancreatitis [IAP/APA guideline 3]. Only 15/82 (18.3%) patients with initial diagnosis of idiopathic pancreatitis had EUS and 10/82 (12.2%) had magnetic resonance cholangio-pancreatography (MRCP).

Prediction of severity

The modified Glasgow criteria were used to predict severity in all 391 patients. The sensitivity, specificity and accuracy of Glasgows score on admission and at 48 h is shown in Table 4A. The accuracy of predicting severe acute pancreatitis on admission was 70.9% and at 48 h it was 77.5%. This approach is not recommended by either Guideline.

The IAP/APA guideline [4] recommends using 'SIRS' is used to predict severity on admission and 'persistent SIRS' at 48 h. SIRS was positive (2 or more criteria) in 145/391 (37%) patients on admission and 107/391 (27.3%) patients at 48 h. The sensitivity, specificity and accuracy of predicting severity is shown in Table 4B. The accuracy of predicting severe acute pancreatitis on admission was 72.1% and at 48 h it was 80.8%.

The Japanese guideline [9] recommends that Japanese Scoing system is used. Compliance was 0%. CRP is a part of the scoring system it was measured on admission in 135 (34.5%) patients and at 48 h in 123 (31.5%) patients.

Imaging

Only 239 (61.1%) patients had ultrasound scan of the hepatobiliary system (US) performed during their admission (Table 5) of whom 129 (32.9%) had the US scan performed within 24 h of admission. A significant proportion (107/152, 70.4%) of the patients who did not have an US scan had a CT scan, and 26/152 (17.1%) had an US prior to admission. Complicance with the IAP/APA [2] and Japanese [3] guidelines is 32.9%.

In this study a CT scan was performed in 182 (46.5%) patients, although the indications were not always apparent. Both guidelines recommend a CT scan if there is diagnostic uncertainty and to investigate for local complications. The Japanese guidelines state that the optimal timing for a CT scan is at least 72–96 h after symptom onset. Note that only 38/182 (20.8%) patients had a CT scan after 72 h of admission (Table 5). There were 36.4% patients with mild acute pancreatitis that had a CT scan, which increased to 69.8% and 64.2% for moderately severe and severe patients respectively.

Table 4A
Prediction of severity based on Glasgow score on admission and at 48 h.

Glasgow score on admission	Actual Severity of AP (Revised Atlanta Classification)							
	Overall (391)		Mild (266)		Moderately severe (83)		Severe (42)	
	n	%	n	%	n	%	n	%
<3	263	67.3	204	76.7	43	51.8	16	38.1
≥3	128	32.7	62	23.3	40	48.2	26	61.9
Sensitivity			76.7		48		61.9	
Specificity			52.8		71.4		70.8	
Accuracy			69		66.9		70.9	
Glasgow score at 48 h	n	%	n	%	n	%	n	%
<3	305	78.0	224	84.2	59	71.1	22	52.4
≥3	86	22.0	42	15.8	24	28.9	20	47.6
Sensitivity			84.2		28.9		47.6	
Specificity			35.2		79.9		81.9	
Accuracy			68.5		69.1		77.5	

Table 4B
Prediction of severity based on SIRS on admission and persistent SIRS at 48 h.

SIRS	Actual Severity of AP (Revised Atlanta Classification)			
	Overall (391)	Mild (266)	Moderately severe (83)	Severe (42)
SIRS on admission				
Number with 2 or more positive criteria (%)	145	55	51	39
Sensitivity		20.7 (79.3)*	61.4	92.8
Specificity		28 (72)*	69.5	69.6
Accuracy		23 (76.9)*	67.8	72.1
Persistent SIRS at 48 h				
Number with 2 or more positive criteria (%)	107	22	48	37
Sensitivity		8.3 (91.7)*	57.8	88.1
Specificity		32 (68)*	80.8	79.9
Accuracy		15.9 (84.1)*	75.9	80.8

* Values in parenthesis – sensitivity/specificity and accuracy in absence of SIRS for mild acute pancreatitis.

Fluid therapy

Data on fluid therapy was available on only 204/391 (52.2%) patients. Normal Saline (38.8%), Ringer Lactate (23%) were the most common crystalloids used. Lactated Ringer's was used alone or in combination with other fluids in 102 (50%) patients. The overall mean rate of fluid resuscitation was mean 1.5 ± 0.85 SD ml/kg/hour in the first 24 h. For the 42 patients with severe acute pancreatitis, the mean rate of fluid resuscitation was mean 1.87 ± 1.5 SD ml/kg/hr (range 0.24–7.64). There was significantly different in the rate based on severity of acute pancreatitis ($p = 0.24$). Only 2/42 (4.8%) patients with severe pancreatitis received 5 ml/kg/hour or more of intravenous fluids within the first 24 h from admission. Ringer's lactate is recommended as the initial fluid of choice for resuscitation in the IAP/APA guideline [9] and Japanese guideline [12] and was used alone or in combination in 102/204 patients, with 50% compliance.

Table 5
Imaging by ultrasonography (US) and Computed Tomography (CT) scanning.

	n	%
Timing of US (n = 239)		
Within 24 h from admission	129	54.0
25–48 h after admission	52	21.8
49–72 h after admission	34	14.2
More than 72 h after admission	24	10.0
Reasons for not doing US		
CT scan was performed instead	107	70.4
US was performed previously	26	17.1
MRI scan was performed	4	2.6
Unknown	15	9.9
Timing of CT (n = 182)		
Within 72 h from symptom onset	144	79.1
72–96 h after symptom onset	8	4.4
More than 96 h after symptom onset	30	16.5
Overall CT frequency by severity (RAC)		
Mild	97/266	36.4
Moderately severe	58/83	69.8
Severe	26/42	64.2

Intensive care management

Of the patients with moderately severe acute pancreatitis 28/83 (33.7%) and 11/83 (13.24%) patients were admitted to the HDU and ICU respectively. Of the patients with severe acute pancreatitis, 25/42 (59.5%) and 17 (40.5%) patients were admitted to the HDU and the ICU, respectively (Table 3). The IAP/PAPA guideline [11] recommends that patients with severe acute pancreatitis, as defined by RAC, should be transferred to an intensive care setting, which gives a compliance of 40.5%. Compliance to HDU admission was 33.7% for patients with moderately severe pancreatitis. The Japanese guidelines do not make recommendations for admission to HDU or ICU but mentions that severe cases should be treated immediately at a `facility' capable of providing treatment for severe acute pancreatitis (based on the Japanese Scoring System). The Japanese guideline [25] recommends against peritoneal lavage and [26b] against routine hemofiltration/dialysis. The compliance to Japanese guideline [25 and 26b] was 100%.

Antibiotic use

Of the 232/391 (59.3%) patients who received antibiotics, 142/232 (61.2%) had this for the treatment of suspected or proven infection, including cholangitis and infected pancreatic necrosis. This meant that 90/232 (38.7%) received antibiotics as prophylaxis when there were no suspicion or proven infection (Table 6). There were 136/266 (51.1%) patients with mild acute pancreatitis group that received antibiotics. There were 96/125 (76.8%) patients with moderately severe and severe pancreatitis that received antibiotics (Table 3). The antibiotics prescribed were ceftriaxone and metronidazole (n = 177), imipenem (n = 27) or meropenem (n = 28).

IAP/APA guideline [17] states intravenous antibiotics are not recommended for the prevention of infectious complications in acute pancreatitis. Japanese guideline [17] states antibiotics are not recommended in mild acute pancreatitis but states that prophylactic administration of antibiotics in severe acute pancreatitis and necrotizing pancreatitis may improve the prognosis, if carried out in the early phases of pancreatitis (within 72 h of onset). The compliance to IAP/APA guidline [17] was 63.7% and Japanese guideline [17] was 48.9% for mild pancreatits and 76.8% for moderately severe and severe pancreatitis.

Nutritional support

Only 29/391 (7.4%) patients were given any form of additional nutrition support. Oral feeding was permitted in the majority (362/391, 92.6%) of patients with mild (259/266, 97.3%), moderately severe (71/83, 85.6%) and severe acute pancreatitis (32/42, 76.2%). Enteral nutrition was given to 10/83(12%) patients with moderately severe acute pancreatitis and 9/42 (21.4%) patients with severe acute pancreatitis. Only 4/391 (1%) patients were given parenteral nutrition (Table 3). The IAP/APA guideline [21] recommends enteral feeding as primary nutritional therapy for patients with predicted severe acute pancreatitis. Japanese guidelines [21, 22] recommend early enteral nutrition in severe acute pancreatits. The compliance with both guidelines for severe acute pancreatitis was 21.4%.

Management of biliary pancreatitis

There were 238/391 (60.9%) patients diagnosed with biliary acute pancreatitis (Table 1) and ERCP was performed in 69/238 (30%) of these patients. With regards to the management of the bile duct, a distinction was made between patients with cholestasis without cholangitis (98/238, 41.2%) and those with cholestasis and cholangitis (140/238, 58.8%) (Table 3).

The incidence of cholangitis was not significantly different between the grades of severity (ANOVA p = 0.5) with the diagnosis made in 94/162 (67.1%) with mild, 28/50 (56%) with moderately severe and 18/26 (69%) with severe acute pancreatitis (Table 3). ERCP was performed in only 60/140 (42.8%) of these patients and this was not related to the severity of acute pancreatitis (ANOVA p = 0.38): ERCP was perfomed in 40/162 (24.7%) of mild, 10/50 (20%) moderately severe and 10/26 (38.4%) severe patients. The reasons for not performing ERCP in those diagnosed with cholangitis (80/140), included improving liver function tests (n = 34), normalised liver function tests (n = 29) and no stones identified in the common bile duct by endoscopic ultrasonography (EUS) or magnetic resonance cholangiopancreatography (MRCP) (n = 17).

The incidence of cholestatic liver dysfunction without cholangitis was 98/238 (41.2%) and this was not significantly different between the grades of severity (ANOVA, p = 507): 68/98 (69.4%) with mild, 22/50 (44%) with moderately severe and 8/26 (30.7%) with severe acute pancreatitis (Table 3). ERCP was performed in only 9/98 (9.1%) of these patients and this was not related to the grade of severity (ANOVA p = 0.732) (Table 3). Of these patients with cholestasis alone, 7/98 (7.1%) were investigated with MRCP and 26/98 (26.5%) with EUS (Table 3).

The IAP/APA guideline [25] does not recommend ERCP for predicted mild biliary pancreatitis without cholangitis and it probably not indicated in predicted severe biliary pancreatitis without cholangitis. ERCP is indicated in patients with biliary pancreatitis and cholangitis. ERCP was not performed in 63/68 (92.6%) of patients with mild biliary pancreatitis without cholestasis and cholangitis [IAP/APA guideline 25a]. ERCP was not performed in 6/8 (75%) patients with severe biliary pancreatitis and no cholangitis [IAP/APA guideline 25b]. MRCP or EUS were performed in 33/98 (33.6%) patients with cholestasis and no cholangitis as an alternative to ERCP [IAP/APA guideline 27]. ERCP was performed in 60/140 (42.8%) patients with biliary pancreatitis and cholangitis [IA/APA guideline 25d]. Japanese guideline [28] recommends early ERCP/ES should be performed in gallstone-induced acute pancreatitis. Only 60/140 (42.8%) patients had early ERCP/ES for suspected cholangitis, which is the level of compliance.

Interventions and timing in necrotizing pancreatitis

There were only 14/391 (3.6%) patients with the diagnosis of necrotizing pancreatitis. Nine of these patients were managed conservatively and 5/14 (35.7%) had an intervention. Image-guided percutaneous catheter drainage was performed in 2 patients at 8.0 days and 31.0 days after admission. Minimally invasive necrosectomy was performed in 2 patients at 10.0 days and 42.0 days after admission. Open necrosectomy has performed in one patient after 3 weeks from the onset of symptoms, 2 (66.7%) of whom had prior percutaneous drainage. Of the 9 patients managed conservatively, 8 developed walled off necrosis, 4 of whom were managed with endoscopic cyst-gastrostomy and 4 with surgical cyst-gastrostomy.

The IAP/AP guideline [31] and the Japanese guideline [35] recommend that invasive or therapeutic intervention for infected pancreatic necrosis should be delayed for 4 or more weeks after onset of symptoms and this occurred in 10/13 (76.9%) patients. A step-up strategy with initial percutaneous drainage followed by necrosectomy is recommended in IAP/APA Guideline [33] and this was done in 2/3 (66.7%) patients.

Table 6
Antibiotic usage, both for treatment and prophylaxis.

	Number of patients who received antibiotics (n = 232)		Number of patients who did not receive antibiotics (n = 159)		Total (n = 391)	
	n	%	n	%	n	%
Patients who required antibiotics for suspected or proven infection	142	61.2	0	0.0	142	36.3
Patients who did NOT require antibiotics for suspected or proven infection	90	38.7	159	100	249	63.7

Timing of cholecystectomy

Only 51/238 (21.4%) patients with biliary pancreatitis had a cholecystectomy during their index admission and 91/238 patients (38.2%) had an interval cholecystectomy after an interval of 4 weeks–12 weeks. The proportion of patients who had an index cholecystectomy was not related to the grade of severity (Table 3). There were 96/238 (40.3%) patients who did not have a cholecystectomy at National University Hospital of Singapore, and either did not have a cholecystectomy at all during the study period or had it done elsewhere. 14/91 (15.4%) patients who had delayed cholecystectomy had a relapse of pancreatitis prior to the cholecystectomy.

The IAP/APA guideline [36] recommends cholecystectomy during index admission for mild acute biliary pancreatitis and this recommendation was followed in 34/162 (21%) patients. The Japanese guideline [30] recommends cholecystectomy should be performed as soon as gallstone-induced acute pancreatitis has been resolved, and this occurred in 142/238 (59.7%) patients.

Discussion

This study identifies several aspects of the management of acute pancreatitis where there are compliance issues in relation to the IAP/APA and the Japanese guidelines. While this has the potential to change patient outcomes and treatment costs, it is has not been shown whether the guidelines are relevant to a mixed Singapore population. The overall mortality in this series of 391 patients was 4.1% and for severe acute pancreatitis is was 11.9%. Despite variable practice and compliance, this compares favourably with the published mortality rate for severe acute pancreatitis ranges of 8.5% [20] to 25% [21].

Serum lipase alone was used only one patient, despite being readily available in Singapore [22,23]. In determining biliary aetiology there was a marked under-utilization of ultrasonography (61.1% overall and 32.9% within 24 h), MRCP (12%) and EUS (18%). This is probably because informal bedside ultrasound scan is available in the Emergency Department, the easy availability of cross-sectional imaging, and the lack of dedicated ultrasound support over weekends. It has been shown that clinicians can be formally trained in the use of bedside ultrasonography, and this will also promote compliance to the existing guidelines. There is also highly variable utilization and timing of CT and MR scanning, and it is not clear if it is being used to make the diagnosis of acute pancreatitis, assess severity or identify local complications. An early CT scan has limited value [24,25], but this study found that 79% of CT scans were done within 72 h of admission. This is an area for quality improvement.

In the present study the prediction of severity was almost entirely based on the modified Glasgow criteria [26–28], which is no longer recommended, and has an accuracy with a significant risk of mis-stratification. And while CRP has been shown to be useful in predicting a worse outcome in patients with acute pancreatitis [29–31]. and is recommended by the Japanese guidelines, it was only used after 48 h in 31% of patients. The IAP/APA guidelines [8] recommend using 'SIRS' is used to predict severity on admission and 'persistent SIRS' at 48 h and the Japanese guidelines [12] recommend that a scoring system is used to predict severity, without recommending any particular one. In the present study, SIRS at admission and at 48 h was marginally more accurate than the modified Glasgow score. Despite the plethora of severity scoring systems there is still scope for refining the severity prediction. The harmless acute pancreatitis score (HAPS) [32] which can typically be calculated within 30 min of admission and takes into account three parameters (lack of rebound tenderness or guarding, normal hematocrit, and normal serum creatinine) identifies 98% patients who will have an uncomplicated disease course, and this has potential to decrease hospital stay by aiding discharge planning.

Fluid resuscitation is the mainstay of the early treatment of acute pancreatitis and Ringer's lactate is recommended as the preferred fluid by the IAP/APA [9] and Japanese [12] guidelines. More evidence is needed on the choice of fluid, the rate of fluid administration and the best rescuscitation monitoring methods and parameters. The compliance to use of Ringer lactate as a choice of fluid resuscitation was 50%. In this study full data was not available because the fluids data is captured in different softwares in ICU, High dependency unit, emergency department and the wards and remains a limitation of the study. Goal directed intravenous fluid therapy at 5–10 ml/kg/h is recommended until resuscitation goals are reached [8]. The mean volume fluid resuscitation in severe pancreatitis was 1.87 ± 1.5 ml/kg/hr within the first 24 h from admission. The rate of fluid resuscitation till the resuscitation goals were reached was not studied. Whether this restrictive strategy is related to the outcomes will require further study.

In this study there was a relatively low admission rate to HDU (59%) and ICU (40%) for patients with severe acute pancreatitis, as defined by the Revised Atlanta Classification. Respiratory failure was managed with oxygen support on the ward and renal failure was managed by the Renal Unit. Patients with moderately severe pancreatitis included those with local pancreatic complications, and were usually managed on the ward. Overall there were only 42 patients with persistent organ failure, and these were all managed in HDU/ICU, with a mean hospital stay of 16.7 ± 15.8 days and a mortality rate of 11.9%.

The use of prophylactic antibiotics has been contentious, but both the IAP/APA and the Japanese guidelines recommend against intravenous antibiotic prophylaxis except in cases of suspected or confirmed infected pancreatic necrosis. A meta-analysis has also suggested that there is no evidence to support the routine usage of antibiotics in severe acute pancreatitis [33], although it remains common practice [34–37]. In the present study prophylactic antibiotics were administered in 36% of patients, highlighting the need for better antibiotic stewardship.

Early enteral nutrition has been demonstrated to decrease morbidity and mortality in severe pancreatitis and is thus recommended over parenteral nutrition [38,39]. In this study, only 21% of patients with severe acute pancreatitis received enteral feeding. In our hospital oral feeding with solids or calorie-rich liquid diets is instituted early in patients with acute pancreatitis. Patients who do not tolerate oral feeding are fed either with a nasogastric or a nasojejunal tube. Parenteral nutrition is administered only if enteral feeding is not tolerated. The data from this study demonstrates that almost 80% of patients with moderately severe and severe acute pancreatitis were able to tolerate oral feeding. The question whether there is additional clinical benefit with routine enteral tube feeding, actively chasing nutritional targets were met, remains unanswered. This study did not specifically look at the nutritional outcomes and whether the caloric requirements were met with on demand oral feeding which majority of the patients received.

In patients with biliary acute pancreatitis, a Cochrane meta-analysis [40] supported the use of ERCP in patients with cholangitis and/or co-existing biliary obstruction. In this study, less than half the patients with the diagnosis of cholangitis had an ERCP and sphincterotomy. The reasons for not proceeding with biliary intervention included improving liver function tests and/or no proven choledocholithiasis on EUS or MRCP. For patients with severe biliary acute pancreatitis without cholangitis, there is some

evidence that sphincterotomy is helpful [41] but this is still a matter of debate and not routinely recommended. There is no evidence that ERCP in mild biliary pancreatitis improves outcomes [42]. One of the clinical challenges is distinguishing patients with cholangitis and those with cholestatic liver function tests and SIRS. It is also remains a challenge to reliable predict which patients have or have not passed their ductal stone(s). A randomized controlled trial of EUS and ERCP in biliary pancreatitis showed that in selected patients EUS could safely replace diagnostic ERCP. It was useful for selecting patients with choledocholithiasis for therapeutic ERCP because of a higher sensitivity for detecting ductal stones, without increasing the morbidity rate [43]. Future guidelines will need to provide more specific recommendations about the role of EUS in the management of biliary pancreatitis, and it is likely to further reduce the number of ERCP's required.

Index admission cholecystectomy is recommended in all patients with mild and moderately severe biliary acute pancreatitis, but it was done in only a fifth of the patients in this study. There are many potential reasons for this, including patient preference, patient fitness, availability of theatre, biliary sphincterotomy being considered an adequate prevention strategy, and having surgery at another hospital. However, it is known that there is risk of recurrent biliary and pancreatic complications in those awaiting cholecystectomy [44,45] and cholecystectomy during index admission has been shown to be safe, technically feasible, more cost-effective and a better overall treatment strategy [46,47]. This is an area for quality improvement.

There are a number of limitations with this study. Firstly, some of the gaps in the prospective database were completed retrospectively, risking recall bias. Secondly, as this is a single-center study, it is not representative of the practices of pancreatic surgeons in other institutions in Singapore, or elsewhere. Lastly, we have restricted this study to 2012 to 2015, and it is likely that some of the areas for quality improvement have already been addressed, and therefore compliance to evidence-based guidelines may be different.

This study demonstrated areas where there can be improvement in compliance with current guideline recommendations. This provides the basis for introducing a number of changes in the management of acute pancreatitis. But this study has identified a number of areas where the guidelines might change with further evidence. In the light of the good outcomes for patients in this study the question arises as to whether the current guideline recommendations are too liberal in regards fluid resuscitation rate, indications for ERCP sphincterotomy, requirements for enteral tube feeding, and admission criteria to HDU/ICU. These have significant implications for cost savings.

There are many published clinical guidelines for acute pancreatitis [8,11,12]' and the implementation of recommendations is variable. The impact of implementing guideline recommendations in AP has not been well studied. We have established a guide with recommended standards in managing pancreatitis which is available to the clinicians through the intranet. However presence guidelines doesn't improve compliance. A review revealed the key elements for successful guideline implementation was dissemination, education and training, social interaction, decision support systems and standing orders [48]. While altering the behaviour of clinicians remains a challenge, a recent electronic tool that alerted clinicians to management recommendations did change clinician behaviour and shortened hospital length of stay (LOS) in patients with acute pancreatitis [49]. It is likely that machine learning tools [50] will have an important role to play in ensuring compliance with recommendations for improvements in service delivery and outcomes. This compliance study is an important step towards this and has identified a number of areas for quality improvement that will require ongoing study, including the impact of implementation and cost-effectiveness.

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