MEDDOCS Open Access Publisher

Annals of Gastroenterology and the Digestive System

Open Access | Review Article

Current trends in management of acute pancreatitis: A review

Eduardo Esteban-Zubero[1]*; Estefanía Cabrera-Falcón[2]; Sara Ribagorda-Tejedor[3]; Moisés Alejandro Alatorre-Jiménez[4]; Carlos Arturo López-García[5]; Alejandro Marín-Medina[6]; Rocío Villeda-González[7]; Sara Anabel Alonso-Barragán[8]; José Juan Gómez-Ramos[9]

[1]Emergency Department of Hospital San Pedro, Spain

[2]Primary Care Resident in Cascajos Health Center, Spain

[3]Department of Radiodiagnosis of Hospital San Pedro, Spain

[4]Department of Neurosciences, Mexican Institute of Social Security, Mexico

[5]Mission Regional Medical Center, USA

[6]Department of Genetics, Mexican Institute of Social Security, Mexico

[7]Research Department, Asociación Mexicana de Atrofia Muscular Espinal (AMAME), Mexico

[8]Department of Genetics, University of Guadalajara, México

[9]Emergency Department of Instituto Mexicano de la Seguridad Social, Mexico

***Corresponding Author(s): Eduardo Esteban-Zubero**

Emergency Department of Hospital San Pedro, Logroño, Spain.

Tel: +34-65-412-3994, Email: eezubero@gmail.com

Received: Mar 29, 2018

Accepted: Jun 05, 2018

Published Online: Jun 12, 2018

Journal: Annals of Gastroenterology and the Digestive System
Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Abstract

The incidence of acute pancreatitis has been increased recently with an important mortality rate. Due to that, an adequate management of this pathology is required. Prognosis scales is a useful tool to adequate the treatment. Treatment is based in fluid resuscitation as well as adequate feeding without delay of enteral feeding. Broad spectrum antibiotics should be provided only if another source of infection is clinically suspected and for treatment of fluid collections and necrosis before percutaneous drainage of infectious zone. Necrotic collections are usually monomicrobial and may be produced by gram-negative rods, enterobacter species, or gram-positive organisms. Fever, leukocytosis, and increasing abdominal pain suggest infection of the necrotic tissue. Diagnosis is confirmed by computered tomography scan, which may reveals air bubbles in the necrotic cavity. If debridement is required, it may be realized via minimally invasive techniques, including percutaneous, endoscopic, laparoscopic, and retroperitoneal approaches.

The purpose of this review is to summarize the initial management of acute pancreatitis, especially in the Emergency Department.

Cite this article: Esteban-Zubero E, Cabrera-Falcón E, Ribagorda-Tejedor S, Alatorre-Jiménez MA, López-García CA, et al. Current trends in management of acute pancreatitis: A review. Ann Gastroenterol Dig Syst. 2018; 2: 1006.

Introduction

Acute pancreatitis may range from a mild, self-limiting disease that requires no more than supportive measures to severe disease with life-threatening complications. Due to that, this entity has been associated with significant morbidity, mortality, and hospitalization costs [1]. The incidence of acute pancreatitis has been increased recently (5-11 cases per 100,000), representing the 3rd cause of admission in Gastroenterology Units in the United States and the 5th cause of death due to non malignant diseases. Mortality rate estimated is 5%, which may be as high as 30% in the most severe cases [2].

The most common causes of acute pancreatitis are gallstones and binge alcohol consumption [3]. Atlanta classification divides acute pancreatitis into mild and severe types [4]. Mild acute pancreatitis is characterized by pancreatic inflammation without necrosis or organ failure. This entity is known as interstitial edematous pancreatitis, which is usually self-limiting and resolves in about one week. On the other hand, severe pancreatitis (20% of cases), is related with local complications such as pancreatic necrosis, abscess formation, and pseudocysts. Severe pancreatitis is subdivided further into moderate and severe depending on the presence and duration (> 48 hours) of organ failure.

The purpose of this review is to summarize the initial management of acute pancreatitis, especially in the Emergency Department.

Etiology

Gallstones and binge alcohol consumption are the most common causes of acute pancreatitis [5]. Table 1 summarizes the main causes of acute pancreatitis. The incidence of biliary lithiasis most frequently observed in elderly populations, women patients, in certain races (some groups of Native Americans), pregnancy, obese patients, patients which decrease his weight quickly, intake of certain drugs (estrogen, clofibrate, parenteral nutrition, ceftriaxone or octreotide), and in certain diseases (hypertriglyceridemia, cirrhosis, hemolytic anemia). The development of acute pancreatitis depends on the lithiasis, usually formed in the gallbladder. Lithiasis which causes acute pancreatitis is of a size less than 5 mm [6,7].

Alcohol is the second most common cause of acute pancreatitis. Prolonged alcohol use (four to five drinks daily over a period of more than 5 years) is required for alcohol-associated pancreatitis [8]. Frequently, acute clinical presentation represents a flare superimposed on chronic pancreatitis. The incidence is increased in men and the type of alcohol ingested does not affect risk [9].

Attending to drugs, the drugs most strongly associated with acute pancreatitis are azathioprine, 6-mercaptopurine, didanosine, valproic acid, angiotensin-converting–enzyme inhibitors, and mesalamine. Pancreatitis caused by drugs is usually mild [10]. In addition, in the literature is also observed case reports of acute pancreatitis secondary to pesticides, including organophosphorus poisoning [11].

Finally, about 10% of cases of acute pancreatitis are thought to be caused by infectious microorganisms. These microorganisms include viruses (e.g. mumps, Coxsackie B, and hepatitis), bacteria (e.g. *Mycoplasma pneumoniae* and leptospirosis), and parasites (e.g. Ascaris lumbricoides, Fasciola hepatica, and hydatid disease). The incidence rate of mumps among patients of acute pancreatitis was found to be about 5.1% of patients hospitalized for mumps in the United States. This incidence has been observed to be decreased following the use of the MMR vaccine in children [12].

Diagnosis and prediction of severity

Diagnosis of acute pancreatitis requires at least two of the following three diagnostic features [4]: abdominal pain consistent with acute pancreatitis, serum lipase or amylase levels that are at least 3 times the upper limit of the normal range, and findings of acute pancreatitis on cross-sectional imaging (Computed Tomography (CT) or Magnetic Resonance Imaging (MRI)). Endoscopic ultrasonography (EUS) has been also observed to play an important role in the diagnosis of acute pancreatitis. In fact, EUS sensitivity to diagnose chronic pancreatitis is greater than Endoscopic Retrograde Cholangio Pancreatography (ERCP) and CT, but using EUS-guided Fine Needle Aspiration (EUS-FNA) is not diagnostic. In acute biliary pancreatitis, EUS is superior to CT and to Magnetic Resonance Cholangio Pancreatography (MRCP) for detection of microlithiasis [13].

Classifications of moderately severe pancreatitis and severe pancreatitis are defined by the presence of complications that are systemic, local, or both. Systemic complications include failure of an organ system and exacerbation of a preexisting disorder. Local complications include peripancreatic fluid collections or pseudocysts and pancreatic or peripancreatic necrosis [4,6]. Persistent failure of an organ system is related with a poor outcome, increasing the mortality rate from 5% (overall acute pancreatitis) to 30% [6].

Attending to blood tests, amylase increases its values 2-12 hours after the beginning of acute pancreatitis and decreases its values to normal levels at 2-5 days. There may be false positives in cases of cholecystitis, macroamylasemia and gynecological processes, among other causes. On the other hand, serum lipase increases its values 4-8 hours after the beginning of acute pancreatitis and decreases its values to normal levels at 8-14 days. It has a greater sensitivity and specificity than amylase in the diagnosis of acute pancreatitis and is more useful than this in patients with hypertriglyceridemia [14].

After establishing the diagnosis and the possible etiology of acute pancreatitis, it is necessary to know the severity of it. Several scales have been developed, which have in common a high false predictive rate, but a low positive predictive rate. There is not a gold standard scale, but it is well recognized its importance to increase the accuracy of treatment. This issue is especially relevant in the non-delay o surgery of local complications as well as the management of acute pancreatitis in the Critical Care Unit if it is required [15-17].

In the Emergency Department, the scales most used are the Ranson criteria and the modified Glasgow score (Table 2). Modified Glasgow score is applicable within 48 hours of admission. Other scales less used in emergencies due to greater complexity would be Acute Physiology and Chronic Health Evaluation II (APACHE II), radiological criteria of Balthazar, and the Bedside Index for Severity in Acute Pancreatitis (BISAP) scale. The last one is very easy to use and is applicable from the beginning of the disease [15,16]. Atlanta classification (updated in 2012) represents a clinical and radiologic nomenclature for acute pancreatitis and associated complications. This classification divide acute pancreatitis into two distinct subtypes, necrotizing pancreatitis and interstitial edematous pancreatitis, based on the

presence or absence of necrosis, respectively. Instead, four distinct collection subtypes are identified on the basis of the presence of pancreatic necrosis and time elapsed since the onset of pancreatitis. Acute peripancreatic fluid collections and pseudocysts occur in interstitial edematous pancreatitis and contain fluid only. Acute necrotic collections and walled-off necrosis occur only in patients with necrotizing pancreatitis and contain variable amounts of fluid and necrotic debris. Attending to the presence of organ failure (failure of 3 main organs) and local complications (acute peripancreatic fluid collections, pseudocysts, acute necrotic collections and walled-off necrosis), acute pancreatitis may be classified in three types [17]:

- Mild acute pancreatitis: No organ failure. No local complications

- Moderate acute pancreatitis: Transient organ failure (<48h). Local complications.

- Severe acute pancreatitis: Organ failure >48h.

Treatment

Fluid resuscitation: Substantial third-space loss and intravascular volume depletion are the basis for many of the negative predictive features of acute pancreatitis [18,19]. Actually, is recommended early and vigorous fluid administration due to the decrease of mortality, systemic inflammatory response syndrome, organ failure at 72 hours, length of hospital stay, and a lower rate of intensive care unit admission [20,21]. Due to that, vigorous fluid therapy is most important during the first 24 hours. It is recommended the administration of a balanced crystalloid solution at a rate of 5 to 10 ml per kilogram of body weight per hour, which usually amounts to 2500 to 4000 ml within the first 24 hours [18]. The goal of fluid therapy is to decrease BUN levels as well as to produce a urine output of at least 0.5 ml/kg/hr [21].

The main risk of vigorous fluid therapy is volume overload. Excessive fluid administration results in increased risks of the abdominal compartment syndrome, sepsis, need for intubation, and death [22]. Several recommendations on fluid resuscitation are observed in the literature. Attending to the type of resuscitation fluid there are few studies in the literature. If it is possible, Lactated Ringer's should be used due to the decrease in systemic inflammatory response syndrome incomes as well as decreased c-reactive protein at 48 hours compared to normal saline [23]. Randomized trials are needed to address the type of fluid, the rate of administration, and the goals of therapy [24,25].

Pain control

Pain control is an important part of the supportive management of patients with acute pancreatitis. Therefore, in the absence of any patient-specific contraindications, a multimodal analgesic regimen is recommended, including narcotics, nonsteroidal anti-inflammatories and acetaminophen [25].

Feeding

Several studies observed that total parenteral nutrition is more expensive, riskier, and no more effective than enteral nutrition in patients with acute pancreatitis [18,26]. In patients affected by mild acute pancreatitis who do not have organ failure or necrosis, oral feeding may be started before the complete resolution of pain or normalization of pancreatic enzyme levels [27]. A low fat diet is safe and associated with shorter hospital stays than is a clear-liquid diet with slow advancement to solid foods [28]. Attending to these theories, patients with mild acute pancreatitis in absence of severe pain, nausea, vomiting, and ileus should start on a low-fat diet soon after admission.

If artificial enteral feeding is required, nasojejunal tube feeding is best for minimizing pancreatic secretion. Nasogastric or nasoduodenal feeding is clinically equivalent [29]. Total parenteral nutrition should be reserved, only being initiated when enteral nutrition is not tolerated or nutritional goals are not met.

Early initiation of nasoenteric feeding (within 24 hours after admission) is not superior to a strategy of attempting an oral diet at 72 hours [30]. Patients predicted to have severe or necrotizing pancreatitis do not benefit from very early initiation of enteral nutrition through a tube. Oral feeding may usually be initiated when symptoms improve, with an interval of 3 to 5 days before tube feeding is considered. In patients who cannot tolerate oral feeding after this time, tube feeding should be initiated with the use of a standard nasoduodenal feeding (Dobhoff) tube and a standard polymeric formula [6].

Antibiotic therapy

Antibiotic therapy is not recommended for prophylaxis of infected pancreatic necrosis attending to the results of several trials [31,32] and meta-analyses [33,34]. Antibiotics are only indicated if another source of infection is clinically suspected.

Endoscopic therapy

Endoscopic retrograde cholangio pancreatography is used primarily in patients with pancreatitis caused by gallstone and is indicated in those who have evidence of cholangitis superimposed on gallstone pancreatitis. This procedure is also performed in patients affected by choledocholithiasis [18,35].

Plasmapheresis

Severe hypertriglyceridemia is a well known etiology of acute pancreatitis and is currently the third leading cause of this disease after alcohol and gallstones in the United States. The exact pathophysiological mechanism remains unclear, but it is suggested that the increase of free fatty acids concentrations due to the hydrolization of Triglycerides (TGs) by high level of pancreatic lipase causes acinar-cell and pancreatic-capillary injury [36]. Plasmapheresis may be used for rapid removal of plasma lipoproteins. Reduction of TGs is the primary goal in patients who have hypertriglyceridemia-associated pancreatitis, especially in patients who are at high risk of pancreatic necrosis and requiring intensive care. There are few studies in the literature about this treatment. However, it is proposed that plasmapheresis should be performed as early as possible, at 24-to-48 h intervals, until TGs levels have been lowered to (ideally) <500 mg/dl (5.6 mmol/l) [37].

Treatment of Fluid Collections and Necrosis

Acute peripancreatic fluid collections do not require therapy. Pseudocysts should be managed primarily through endoscopic techniques if are symptomatic [38]. Necrotizing pancreatitis involves pancreatic gland necrosis as well as peripancreatic fat necrosis [18]. Primarily, the necrotic collection is formed by semisolid and solid tissue. After that (4 weeks or longer), the collection becomes encapsulated by a visible wall with a liquid content. Not infected necrosis does not require therapy except in the case of the obstruction of a nearby viscus, including duodenal, bile duct, or gastric obstruction. If the necrotic collection

is infected, therapy must be realized.

Necrotic collections are usually monomicrobial and may be produced by gram-negative rods, enterobacter species, or gram-positive organisms. Fever, leukocytosis, and increasing abdominal pain suggest infection of the necrotic tissue. Diagnosis is confirmed by CT scan, which may reveals air bubbles in the necrotic cavity. Treatment is based in broadspectrum antibiotics without aspiration or culture of the collection. The aim of the treatment is to delay any invasive intervention for at least 4 weeks to allow for walling off of the necrotic collection. This delay provides an easier drainage and debridement and reduces the risk of complications or death [6,39]. In not stable patients, percutaneous drain in the collection should be considered to reduce sepsis and allow the delay of the intervention. Studies revealed that 60% of patients would be treated with noninvasively treatment with a low risk of death [40]. This approach is preferred to traditional open necrosectomy due to the decreased risk of major complications or death. In addition, one third of patients treated with broadspectrum antibiotics combined with percutaneous drainage will not require debridement [39]. If debridement is required, it may be realized via minimally invasive techniques, including percutaneous, endoscopic, laparoscopic, and retroperitoneal approaches. Standard treatment following major pancreatic surgery includes the administration of pancreatic enzyme preparations and inhibition of acid secretion by proton pump inhibitors to decrease gastric pH as well as prevent ulcus [41,42].

Emerging treatments

Autodigestion from proteases has been observed to play an important role in acute pancreatitis features. Due to that, protease inhibitors would theoretically provide benefit. However, studies on gabexate mesliate and aprotinin have not demonstrated an improvement in patient outcomes [43,44]. Platelet activating factor antagonist as lexipafant, antioxidants, corticosteroids, nitroglycerin, IL-10 or TNF-α antibodies, have shown no benefit in the treatment of acute pancreatitis [45]. Nevertheless, melatonin (an indoleamine produced from the amino acid l-tryptophan,) and its analogues has been observed to prevent acute pancreatitis as well as reduces pancreatic damage. This effect is related to its direct and indirect antioxidant action, to the strengthening of immune defense, and to the modulation of apoptosis [46]. More studies are required to increase the knowledge in this area.

Prevention of recurrence

Cholecystectomy prevents recurrent gallstone pancreatitis. If surgery is delayed for more than a few weeks, the risk of relapse rises up to 30% [47]. In addition, in mild pancreatitis, if surgery is performed during the initial hospitalization, the rate of subsequent gallstone-related complications is reduced by 75% compared to cholecystectomy performed 25 to 30 days after discharge [48]. In severe or necrotizing pancreatitis, cholecystectomy should be delayed to diminish the infection. Patients who are not considered to be candidates for surgery, endoscopic biliary sphincterotomy will reduce the risk of recurrent biliary pancreatitis but may not reduce the risk of subsequent acute cholecystitis and biliary colic [49]. Alcohol abstinence should be considered in patients with alcohol-associated acute pancreatitis because of the high risk of recurrence [50]. Control of hyperlipidemia may prevent a relapse of pancreatitis caused by hypertriglyceridemia [51]. Primary prevention of pancreatitis is possible only in the case of pancreatitis caused by ERCP. This treatment is based in two different therapies: temporary placement of pancreatic duct stents [52] and pharmacologic prophylaxis with nonsteroidal antiinflammatory drugs [53].

Tables

Table 1: Etiology of acute pancreatitis.

CAUSE	FREQUENCY	DIAGNOSTIC CLUES	COMMENTS
Gallstones	40%	Gallbladder stones or sludge, abnormal liver-enzyme levels.	Endoscopic ultrasonography may reveal it.
Alcohol	30%	Acute flares superimposed on underlying chronic pancreatitis.	Diagnosis is based on anamnesis.
Hypertriglyceridemia	2–5%	Fasting triglycerides >1000 mg/dl (11.3 mmol per liter).	
Genetic causes	Not known	Recurrent acute pancreatitis and chronic pancreatitis without other causes.	
Drugs	<5%		The condition is idiosyncratic and usually mild.
Autoimmune cause	<1%	Type 1: obstructive jaundice, elevated serum IgG4 levels, response to glucocorticoids Type 2: possible presentation as acute pancreatitis; occurrence in younger patients; no IgG4 elevation; response to glucocorticoids.	Type 1 is a systemic disease affecting the pancreas, salivary glands, and kidneys. Type 2 only affects pancreas.
ERCP	5–10% (among patients under-going ERCP)		The symptoms may be reduced with rectal NSAIDs or temporary placement of a stent in the pancreatic duct.
Trauma	<1%	Blunt or penetrating trauma.	
Infection	<1%	Viruses: CMV, mumps, and EBV most common. Parasites: ascaris and clonorchis.	

Surgical complication	5–10% (among patients under-going cardiopulmonary bypass)		The condition is probably due to pancreatic ischemia. Pancreatitis may be severe.
Obstruction	Rare	Celiac disease and Crohn's disease, pancreas divisum (controversial), and sphincter of Oddi dysfunction (very controversial).	On rare occasions, malignant pancreatic duct or ampullary obstruction is seen.

CMV: Cytomegalovirus; EBV: Epstein–barr virus; ERCP: Endoscopic retrograde cholangiopancreatography; NSAIDs: Nonsteroidal anti inflammatory drugs.

Table 2: Ransom criteria and Modified Glasgow score as predictors of severe index. AST: Aspartate transaminase; BUN: Blood urea nitrogen.

RANSOM CRITERIA (severe ≥ 3)	
At admission	**During initial 48 hours**
Age> 55 years Leukocytes > 16,000 U/mm^3 Glucose > 200 mg/dL LDH > 350 IU/L AST > 250 IU/L	Hematocrit fall > 10% BUN rise > 5 mg/dL Calcium < 8 mg/dL PaO_2 < 60 mmHg Base deficit > 4 mEq/L Fluid sequestration > 6L
MODIFIED GLASGOW SCORE (severe ≥ 3)	
PaO_2 < 60 mmHg **A**ge> 55 years **N**eutrophils > 15,000 U/mm^3 **C**alcium < 2 mmol/L **R**enal function (Urea > 16 mmol/L) **E**nzymes (LDH > 600 IU/L, AST > 200 IU/L) **A**lbumin < 32 g/dL **S**ugar (Glucose > 10 mmol/L)	

Conclusion

The incidence of acute pancreatitis has been increased recently with an important mortality rate. The most common causes of acute pancreatitis are gallstones and binge alcohol consumption. Diagnosis is based in clinical as well as complementary test results, including serum lipase or amylase levels and cross-sectional imaging (CT or MRI). After diagnosis process, prediction of severity should be realized using one of the several scales developed. Fluid resuscitation and adequate feeding without delay of enteral feeding are the basis of the treatment. Antibiotics should be provided only if another source of infection is clinically suspected and for treatment of fluid collections and necrosis before percutaneous drainage. Emerging treatments including antioxidants requires future studies to know the role in acute pancreatitis. In addition, plasmapheresis should be realized as soon as possible in patients affected by acute pancreatitis secondary to hypertriglyceridemia. Attending to the prevention of recurrence, cholecystectomy prevents recurrent gallstone pancreatitis. Control of risk factors (hyperlipidemia, alcohol intake) is also indicated, as well as ERCP.

Finally, the knowledge about acute pancreatitis management should continue to improve, recommending the development of more clinical research and guidelines.

References

1. Neoptolemos JP, Raraty M, Finch M, Sutton R. Acute pancreatitis: the substantial human and financial costs. Gut. 1998; 42: 886-891.
2. Peery AF, Dellon ES, Lund J, Crockett SD, McGowan CE, Bulsiewicz WJ, et al. Burden of gastrointestinal disease in the United States: 2012 update. Gastroenterology. 2012; 143: 1179-87.
3. Banks PA. Epidemiology, natural history, and predictors of disease outcome in acute and chronic pancreatitis. Gastrointest Endosc. 2002; 56: 226-230.
4. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013; 62: 102-111.
5. Yadav D, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. Gastroenterology. 2013; 144: 1252-1261.
6. Forsmark CE, Vege SS, Wilcox CM. Acute Pancreatitis. N Engl J Med. 2016; 375: 1972-1981.
7. Roberts SE, Morrison-Rees S, John A, Williams JG, Brown TH, Samuel DG. The incidence and aetiology of acute pancreatitis across Europe. Pancreatology. 2017; 17: 155-165.
8. Coté GA, Yadav D, Slivka A, Hawes RH, Anderson MA, Burton FR, et al. North American Pancreatitis Study Group. Alcohol and smoking as risk factors in an epidemiology study of patients with chronicpancreatitis. Clin Gastroenterol Hepatol. 2011; 9: 266-273.

9. Whitcomb DC, LaRusch J, Krasinskas AM, Klei L, Smith JP, Brand RE, et al. Alzheimer's Disease Genetics Consortium. Common genetic variants in the CLDN2 and PRSS1-PRSS2 loci alter risk for alcohol-related and sporadic pancreatitis. Nat Genet. 2012; 44: 1349-1354.

10. Nitsche C, Maertin S, Scheiber J, Ritter CA, Lerch MM, Mayerle J. Drug-induced pancreatitis. Curr Gastroenterol Rep. 2012; 14: 131-138.

11. Goud M, Nayal B, Deepa K, Devi OS, Devaki RN, Anitha M. A case of acute pancreatitis with occupational exposure to organophosphorus compound. Toxicol Int. 2012; 19: 223-224.

12. Rawla P, Bandaru SS, Vellipuram AR. Review of Infectious Etiology of Acute Pancreatitis. Gastroenterology Res. 2017; 10: 153-158.

13. Ashkar M, Gardner TB. Role of endoscopic ultrasound in pancreatic diseases: a systematic review. Minerva Gastroenterol Dietol. 2014; 60: 227-245.

14. Ismail OZ, Bhayana V. Lipase or amylase for the diagnosis of acute pancreatitis? Clin Biochem. 2017; 50: 1275-1280.

15. Kuo DC, Rider AC, Estrada P, Kim D, Pillow MT. Acute Pancreatitis: What's the Score? J Emerg Med. 2015; 48: 762-770.

16. Balcı Z, Kılıç MÖ, Şenol K, Erdoğan A, Tez M. Prognostic scores in acute pancreatitis: A review. Acta Gastroenterol Belg. 2016; 79: 337-347.

17. Foster BR, Jensen KK, Bakis G, Shaaban AM, Coakley FV. Revised Atlanta Classification for Acute Pancreatitis: A Pictorial Essay. Radiographics. 2016; 36: 675-687.

18. Tenner S, Baillie J, DeWitt J, Vege SS. American College of Gastroenterology guideline: management of acute pancreatitis. Am J Gastroenterol. 2013; 108: 1400-1415.

19. Yang CJ, Chen J, Phillips AR, Windsor JA, Petrov MS. Predictors of severe and critical acute pancreatitis: a systematic review. Dig Liver Dis. 2014; 46: 446-451.

20. Gardner TB, Vege SS, Chari ST, Petersen BT, Topazian MD, Clain JE, et al. Faster rate of initial fluid resuscitation in severe acute pancreatitis diminishes in-hospitalmortality. Pancreatology. 2009; 9: 770-776.

21. Warndorf MG, Kurtzman JT, Bartel MJ, Cox M, Mackenzie T, Robinson S, et al. Early fluid resuscitation reduces morbidity among patients with acute pancreatitis. Clin Gastroenterol Hepatol. 2011; 9: 705-709.

22. Mole DJ, Hall A, McKeown D, Garden OJ, Parks RW. Detailed fluid resuscitation profiles in patients with severe acute pancreatitis. HPB (Oxford). 2011; 13: 51-58.

23. Wu BU, Hwang JQ, Gardner TH, Repas K, Delee R, Yu S, et al. Lactated Ringer's solution reduces systemic inflammation compared with saline in patients with acute pancreatitis. Clin Gastroenterol Hepatol. 2011; 9: 710-717.

24. Haydock MD, Mittal A, Wilms HR, Phillips A, Petrov MS, Windsor JA. Fluid therapy in acute pancreatitis: anybody's guess. Ann Surg. 2013; 257: 182-188.

25. Janisch NH, Gardner TB. Advances in Management of Acute Pancreatitis. Gastroenterol Clin North Am. 2016; 45: 1-8.

26. Yi F, Ge L, Zhao J, Lei Y, Zhou F, Chen Z, et al. Meta-analysis: total parenteral nutrition versus total enteral nutrition in predicted severe acute pancreatitis. Intern Med. 2012; 51: 523-530.

27. Eckerwall GE, Tingstedt BB, Bergenzaun PE, Andersson RG. Immediate oral feeding in patients with mild acute pancreatitis is safe and may accelerate recovery — a randomized clinical study. Clin Nutr. 2007; 26: 758-763.

28. Teich N, Aghdassi A, Fischer J, Walz B, Caca K, Wallochny T, et al. Optimal timing of oral refeeding in mild acute pancreatitis: results of an open randomized multicenter trial. Pancreas. 2010; 39: 1088-1092.

29. Chang YS, Fu HQ, Xiao YM, Liu JC. Nasogastric or nasojejunal feeding in predicted severe acute pancreatitis: a metaanalysis. Crit Care. 2013; 17: 118.

30. Bakker OJ, van Brunschot S, van Santvoort HC, Besselink MG, Bollen TL, Boermeester MA, et al. Dutch Pancreatitis Study Group. Early versus on-demand nasoenteric tube feeding in acute pancreatitis. N Engl J Med. 2014; 371: 1983-1993.

31. Isenmann R, Rünzi M, Kron M, Kahl S, Kraus D, Jung N, et al. German Antibiotics in Severe Acute Pancreatitis Study Group. Prophylactic antibiotic treatment in patients with predicted severe acute pancreatitis: a placebo-controlled, double-blind trial. Gastroenterology. 2004; 126: 997-1004.

32. Dellinger EP, Tellado JM, Soto NE, Ashley SW, Barie PS, Dugernier T, et al. Early antibiotic treatment for severe acute necrotizing pancreatitis: a randomized, double-blind, placebo-controlled study. Ann Surg. 2007; 245: 674-683.

33. Villatoro E, Mulla M, Larvin M. Antibiotic therapy for prophylaxis against infection of pancreatic necrosis in acute pancreatitis. Cochrane Database Syst Rev. 2010; 5: CD002941.

34. Lim CL, Lee W, Liew YX, Tang SS, Chlebicki MP, Kwa AL. Role of antibiotic prophylaxis in necrotizing pancreatitis: a meta-analysis. J Gastrointest Surg. 2015; 19: 480-491.

35. Tse F, Yuan Y. Early routine endoscopic retrograde cholangiopancreatography strategy versus early conservative management strategy in acute gallstone pancreatitis. Cochrane Database Syst Rev. 2012; 5: CD009779.

36. Valdivielso P, Ramirez-Bueno A, Ewald N. Current knowledge of hypertriglyceridemic pancreatitis. Eur J Intern Med. 2014; 25: 689–694.

37. Joglekar K, Brannick B, Kadaria D, Sodhi A. Therapeutic plasmapheresis for hypertriglyceridemia-associated acute pancreatitis: case series and review of the literature. Ther Adv Endocrinol Metab. 2017; 8: 59-65.

38. Varadarajulu S, Bang JY, Sutton BS, Trevino JM, Christein JD, Wilcox CM. Equal efficacy of endoscopic and surgical cystogastrostomy for pancreatic pseudocyst drainage in a randomized trial. Gastroenterology. 2013; 145: 583-590.

39. Bakker OJ, van Santvoort H, Besselink MG, Boermeester MA, van Eijck C, Dejong K, et al. Dutch Pancreatitis Study Group. Extrapancreatic necrosis without pancreatic parenchymal necrosis: a separate entity in necrotizing pancreatitis? Gut. 2013; 62: 1475-1480.

40. van Santvoort HC, Bakker OJ, Bollen TL, Besselink MG, Ahmed Ali U, Schrijver AM, et al. Dutch Pancreatitis Study Group. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. Gastroenterology. 2011; 141: 1254-1263.

41. van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al. Dutch Pancreatitis Study Group. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med. 2010; 362: 1491-1502.

42. Bakker OJ, van Santvoort HC, van Brunschot S, Geskus RB, Besselink MG, Bollen TL, et al. Dutch Pancreatitis Study Group. Endoscopic transgastric vs surgical necrosectomy for infected

necrotizing pancreatitis: a randomized trial. JAMA. 2012; 307: 1053-1061.

43. Andriulli A, Leandro G, Clemente R, Festa V, Caruso N, Annese V, et al. Meta-analysis of somatostatin, octreotide and gabexate mesilate in the therapy of acute pancreatitis. Aliment Pharmacol Ther. 1998; 12: 237-245.

44. Heinrich S, Schäfer M, Rousson V, Clavien PA. Evidence-based treatment of acute pancreatitis: a look at established paradigms. Ann Surg. 2006; 243: 154-168.

45. Bang UC, Semb S, Nojgaard C, Bendtsen F. Pharmacological approach to acute pancreatitis. World J Gastroenterol. 2008; 14: 2968-2976.

46. Jaworek J, Leja-Szpak A, Nawrot-Porąbka K, Szklarczyk J, Kot M, Pierzchalski P, et al. Effects of Melatonin and Its Analogues on Pancreatic Inflammation, Enzyme Secretion, and Tumorigenesis. Int J Mol Sci. 2017; 18: 1014.

47. Sankaran SJ, Xiao AY, Wu LM, Windsor JA, Forsmark CE, Petrov MS. Frequency of progression from acute to chronic pancreatitis and risk factors: a meta-analysis. Gastroenterology. 2015; 149: 1490-1500.

48. da Costa DW, Bouwense SA, Schepers NJ, Besselink MG, van Santvoort HC, van Brunschot S, et al. Dutch Pancreatitis Study Group. Same-admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): a multicentre randomised controlled trial. Lancet. 2015; 386: 1261-1268.

49. McAlister VC, Davenport E, Renouf E. Cholecystectomy deferral in patients with endoscopic sphincterotomy. Cochrane Database Syst Rev. 2007; 4: CD006233.

50. Pelli H, Lappalainen-Lehto R, Piironen A, Sand J, Nordback I. Risk factors for recurrent acute alcohol-associated pancreatitis: a prospective analysis. Scand J Gastroenterol. 2008; 43: 614-621.

51. Valdivielso P, Ramirez-Bueno A, Ewald N. Current knowledge of hypertriglyceridemic pancreatitis. Eur J Intern Med. 2014; 25: 689-694.

52. Mazaki T, Mado K, Masuda H, Shiono M. Prophylactic pancreatic stent placement and post-ERCP pancreatitis: an updated meta-analysis. J Gastroenterol. 2014; 49: 343-355.

53. Elmunzer BJ, Scheiman JM, Lehman GA, Chak A, Mosler P, Higgins PD, et al. U.S. Cooperative for Outcomes Research in Endoscopy (USCORE). A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. N Engl J Med. 2012; 366: 1414-1422.