Austin Pancreatic Disorders

Open Access

Austin Publishing Group

Short Communication

Management of Acute Pancreatitis

Cianci P*, Giaracuni G, Vovola F, Tartaglia N, Fersini A, Ambrosi A and Neri V

Department of Medical and Surgical Sciences, University of Foggia, Italy

***Corresponding author:** Cianci P, Department of Medical and Surgical Sciences, University of Foggia, Italy

Received: March 08, 2017; **Accepted:** March 16, 2017; **Published:** March 21, 2017

Short Communication

Acute pancreatitis is a disease characterized by inflammation of the pancreas associated with a systemic response due to auto-digestion of the gland and peripancreatic tissues. The disease can occur in mild form with simple tissue edema or severe form with local necrotizing inflammation and systemic complications as systemic inflammatory response syndrome (SIRS) and organ failure. The initial process which is the basis of acute pancreatitis is the activation of pancreatic enzymes that from their inactive form become activated enzymes, this process takes place in the parenchyma of the gland where typically does not occur. The most frequent causes are biliary obstruction and alcohol consumption that occurring in almost 80% of patients. In 20% of cases the etiology can be genetic (hereditary pancreatitis), obstructive (tumours, pancreas divisum, biliary pancreatitis), metabolic (hypercalcemia, hyperlipidemia), pharmacological. The etiologic assessment can be a guide to therapeutic program. A detailed history and a careful clinical examination may reveal the characteristic signs and symptoms of this disease: nausea, vomiting, tachycardia, tachypnea, hyperthermia, and upper abdominal pain radiated to the back with abdominal wall tenderness, and muscular rigidity of varying degrees. A left pleural effusion can be present. During auscultation, bowel sounds can be reduced or absent. The diagnostic criteria also include specific laboratory data such as increased values of pancreatic amylase and lipase. Serum amylase increases at the onset of the disease and decreases in a few days (3-5 days); on the contrary the lipase tends to remain elevated for longer. The increase level of serum amylase has not correlation with severity of pancreatitis. Liver function tests, fasting serum calcium and lipid profile contribute to define biliary etiology of pancreatitis. In the evaluation of acute pancreatitis and its clinical course, radiological examinations play a central role. Abdominal ultrasound (US) may demonstrate gallbladder lithiasis and/or gallstones, sludge, microlithiasis in the common bile duct (CBD) with its dilatation (>8mm) or a real impacted stone of the CBD. Contrast enhanced computed tomography (CT) and magnetic resonance imaging (MRI) are considered second-level exams, with the aim to evaluate the damage of pancreatic parenchyma, the involvement of pancreatic tissue, presence of fluid-necrotic collections and on the other hand the detection of bile stones, CBD dilatation. The last two give us the suspicion of biliary origin of pancreatitis.

In the majority of the patients (70-80%), the acute pancreatitis occurs as a mild – moderate disease; in the 20-30% shows a severe course. The critical forms shows a very severe disease with early hypoxaemia, progressive mulptiple organ dysfunction, compromised computed tomography severity index (CTSI), increased incidences of necrosis, infection, and sometime abdominal compartment syndrome (ACS). Therefore, these severe forms of pancreatitis have a short course and a high percentage of mortality up to 40%. The first phase (first two week) of severe acute pancreatitis typically manifests with an early toxic-enzymatic injury, SIRS, and a late phase (third and fourth week) characterized by septic complications of necrotic tissue and the appearance of peripancreatic fluid necrotic collections [1]. The first phase of pancreatitis can develop in most cases with disease quickly responsive to intensive care based on aggressive rehydration. The revision of the Atlanta criteria has Indicated that the pancreatic necrosis can be a risk factor for worsening of severe acute pancreatitis and some data from the literature suggest that it may occurs also with minimal pancreatic necrosis [2-48]. Mild pancreatitis has generally favorable evolution without mortality risk; in the moderate forms there is minimal risk of mortality. Predictive factors of severity, except clinical evaluation, may be divided into direct and indirect. The direct factors are based on morphological and anatomical compromission of the pancreas and assessed by imaging exams (US, CT, MRI). The indirect methods can be divided into mono factorial and multi factorial. The first can make the prognostic assessment by means of single laboratory marker (Table 1). These consist of several hepatic, urinary biochemical data that can be early detector of systemic inflammatory response and multi organ failure. Into these markers are reliable and very early CRP (C-reactive protein), TAP (urinary trypsinogen activation peptide), procalcitonin. The multi factorial prognostic scoring systems consist of Ranson and Glasgow scores, specific for the pancreatitis and APACHE II score which is not specific (Table 2). The new scoring systems meet the need to assess severity of disease within the first 24h. The Harmless Acute pancreatitis score [49], aims to identify the mild/moderate pancreatitis. On the other hand there is the Bedside index of Severity in Acute pancreatitis (BISAP) [50] based on the evaluation of 5 criteria: blood urea nitrogen (BUN) > 25mg/dL, age >60 years, impaired mental status, SIRS and pleural effusion. For BISAP a score of > 2 is associated with a 10 fold increase in mortality risk. CT images obtained within 72 h of onset allow the use of CTSI and modified CT severity index (MCTSI) with Balthazar scoring for grading of acute pancreatitis and points for necrosis. The classification is based on morphological and functional feature: local or diffuse enlargement of the pancreas, pancreatic gland abnormalities, peripancreatic inflammation with pancreatic and peripancreatic fluid collections and areas of non-enhanced parenchyma (that is necrotic). The imaging evaluation should be integrated and completed always within 24-72 hrs by CT assessment of pancreatic size index (PSI), extra pancreatic inflammation on CT index score (EPIC) and extra-pancreatic score (EP) [51]. In summary the evaluation of severity of AP should employ several detector following the onset and development of acute attack. At the admission can be useful BUN, hematocrit, procalcitonin, chest x ray; at 24–48 h, BISAP, Ranson, Glasgow score, APACHE II; after

Citation: Cianci P, Giaracuni G, Vovola F, Tartaglia N, Fersini A, Ambrosi A, et al. Management of Acute Pancreatitis. Austin Pancreat Disord. 2017; 1(1): 1003.

Table 1: Mono factorial markers of severity most recurrent in the literature.

	Sensibility	Specificity	Accuracy	References
CRP* (> 150mg/L at 24 and 48h)	57-94.1%	60-90%	76-80%	***[3-14]**
TAP* (increased at admission and after 12h)	58-100%	73-89.7%	-	***[3,12-18]**
Procalcitonin* (> 160 f mol/mL at admission) infected pancreatic necrosis marker altered permeability of gut barrier marker	67-100%	20-89%	85%	***[6,19-26]**
Hct* (at admission and after 24h) cut off: 43%M – 39%F	61-74%	38-45%	-	***[27-30]**
Hyperglycemia* (>125mg/dL) pancreatic necrosis index complication index	83-100%	49%	-	***[29,31-33]**

Table 2: Multi factorial bio-clinic scores.

	Sensibility	Specificity	Accuracy	References
Ranson	33-83%	79-98%	78-89%	**[34-48]**
Glasgow	33-83%	79-98%	78-89%	
APACHE II > 7	52-62%	77-86%	-	
APACHE II > 9	50-75%	69-72.4%	-	

the 48h MCTSI and CTSI. MRI provides images and pathological data overlappable to CT.

The therapeutic approach of AP usually develops in two phases following the evolution of the disease. In mild-moderate forms at the onset of the disease (first phase) the treatment includes simple fluid rehydration and control of abdominal pain. In the severe forms, at first phase, the therapeutic approach consists of intensive care, initial fluid, aggressive resuscitation, low dose steroids, anticoagulatory agents for anti inflammatory properties, correction of hypoxaemia, enteral nutrition to preserve the intestinal integrity and antibiotic prophylaxis. In conclusion in this first phase of severe forms the central purpose is to control and treat, by intensive care support, the damage of the general conditions and possible organ failure [52]. The later phase of the disease (third and fourth week) is characterized by septic complications of pancreatic or peripancreatic fluid – necrotic collections. In the severe forms the therapeutic approach is more complex with early fluid resuscitation for the correction of hypovolemia [53]. Hypovolemia is due, over the all, to third space extravasation, secondly to vomiting, respiratory losses, and diaphoresis. The specific purpose of the correction of hypovolemia is to avoid the decrease of macro/microcirculation and sequently the cascade of events leading to pancreatic necrosis [54].

In the most frequent forms with biliary etiology, must be ensured the control of papillary patency and, if necessary, its treatment with endoscopic retrograde cholangiopancreatography/endoscopic sphyncterotomy (ERCP/ES), can be considered the cornerstone of therapeutic program based on the confirmation by instrumental exams (US, MRCP) of papillary obstacle (stones, sludge, papillary sclerosis, etc.) or, if it is present, cholestasis or cholangitis. ERCP/ES can assure papillary flow and CBD cleaning if lithiasis obstacle, sludge, microlithiasis are present. Following this general considerations on the pathophysiology of acute biliary pancreatitis, the therapeutic use of ERCP/ES is based on several data to be evaluated:

a. Confirmation of papillary obstacle, persistent or transient, generally due to biliary lithiasis.

b. Indication of procedure: which patients (with acute biliary pancreatitis) should be submitted to ES.

c. Timing of the procedure.

d. Complications.

Biliary etiology of pancreatitis can be established at the onset with first level etiological assessment by the research, on abdominal US, of gallbladder lithiasis, and/or gallstones, sludge, microlithiasis in the CBD or also a dilatation of CBD (>8 mm) besides with liver function tests/cholestasis indexes, fasting serum calcium and lipid profile. The second level diagnostic study, that is MRCP and/or endoscopic US usually should confirm the biliary origin of pancreatitis in majority of patients. In very few patients the etiology of pancreatitis remain unexplained [55]. More complex is the answer to the following question: which patients should be submitted to ERCP/ES? The choice of the patients for ERCP/ES and its timing in ABP are now a day's still controversial despite many years since its introduction in the therapeutic program. There are many studies in the literature about this topic. Some of these are now "historic": Neoptolemos [56], Fan [57], Nowak [58], Folsch [59].

Recent systematic review has been published [60-62]. The conclusion of these studies agrees on some points:

- Early ERCP/ES has not advantage for patients with mild pancreatitis and is not indicated;
- Early ERCP/ES may be indicated in patients with severe disease, biliary obstruction or cholangitis.

Also in one review [62] early ERCP/ES may reduce complications in patients with predicted severe pancreatitis. Tse F et al. published a cochrane database Systematic Review. Their conclusions are that early ERCP/ES does not significantly notify mortality, local and systematic complications [63]. However early ERCP/ES should be recommended for patients with severe or moderate pancreatitis with co-existing papillary obstruction (laboratory – instrumental demonstration) or cholangitis.

In conclusion this therapeutic procedure can be proposed in all patients with severe, early severe acute biliary pancreatitis and recurrent pancreatitis and also in several patients with moderate or moderate – severe disease. Obviously all these patients should achieve laboratoristic, strumental (US or MRCP), confirmation of a papillary or CBD lithiasis obstacle, some time complicated by angiocholithis. The timing of ERCP/ES after identification of patients should be choiced within the first 48 – 72 hours from the onset of pancreatic attack. Finally ERCP/ES in patients with severe acute pancreatitis, severe impairment of general conditions and requirement of intensive care and assisted ventilation can be high risk procedure. This therapeutic choice is very difficult and without worldwide consent. Complications of ERCP/ES are not unusual. They include post-procedural pancreatitis, perforations, bleeding and infections.

The interventional procedures in the treatment of severe acute pancreatitis require a radical revision. In septic necrotic collections

the role of the surgery should be limited to percutaneous drainage that in most cases could reduce the need for surgery. If major surgical interventions are required, these should be more conservative as possible and preferred minimally invasive approaches. Recent data from the literature showed the high number of patients treated with percutaneous drainage (22 – 55%) and the technical success rate of 99% [64]. In conclusion it is not clear the best procedure for the treatment of septic necrotic pancreatic collections. No single approach can be right and suitable for all patients. The procedures for drainage of collections and/or debridement of septic – necrotic tissue among the several therapeutic choices proposed should be tailored based on patient presentation and anatomy [65]. Open necrosectomy remains the last option after the failure of less invasive procedures.

There is a worldwide agreement that in severe acute pancreatitis surgical procedures should be performed as late as possible. After four weeks, in average, from the onset of the acute disease, can develop and present the optimal operative conditions characterized by well demarcated tissue necrosis that allows single surgical debridement. These self-limiting operative procedures are accompanied by minor risk of bleeding, and surgery related loss of vital pancreatic tissue. The surgical management of acute pancreatitis showed in the past two decades critical changes. The different severity of the disease should determine the choice of surgical procedure. In mild or moderate pancreatitis can be enough remove the etiological factors such as in biliary lithiasis the cholecystectomy and if necessary to restore the papillary flow with ERCP/ES. These therapeutic procedures are also useful for prevention of recurrent pancreatitis. In the severe acute pancreatitis with pancreatic necrosis damage and peripancreatic tissue involvement and peripancreatic fluid necrotic collections, the surgical procedures are related to eventual pancreatic infection. In this case, if possible, the intervention should be delayed (three/four weeks from onset). Infected necrosis (clinical or instrumental confirmation) is the crucial conditions for surgical choice. The improved surgical management is based on minimally invasive procedures such as percutaneous drainage, endoscopic therapy; if the patients need surgical debridement, can be useful primary closed continuous postoperative lavage. Mini-invasive treatment should be performed in the complications as pancreatic abscess. The first treatment of choice is the percutaneous drainage in the pancreatic abscess. Also in case of acute post-necrotic pseudo cysts the first approach can be mini-invasive as endoscopic trans mural drainage that is increasingly becoming the preferred method. The surgical treatment becomes necessary if failure of conservative or minimally invasive management or in case of complications as bleeding.

References

1. Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. Am J Gastroenterol. 2006; 101: 2379 – 2400.
2. Fu CY, Yeh CN, Hsu JT, Jan YY, Hwang TL. Timing of mortality in severe acute pancreatitis: experience from 643 patients. World J Gastroenterol. 2007; 13: 1966 – 1969.
3. Yadav D, Agarwal N, Pitchumoni CS. A critical evaluation of laboratory tests in acute pancreatitis. Am J Gastroenterol. 2002; 97: 1309 –1318.
4. Wilson C, Heads A, Shenkin A, Imrie CW. C-reactive protein, antiproteases and complement factors as objective markers of severity in acute pancreatitis. Br J Surg. 1989; 76: 177 – 181.
5. Gürleyik G, Emir S, Kiliçoglu G, Arman A, Saglam A. Computed tomography severity index, APACHE II score, and serum CRP concentration for predicting the severity of acute pancreatitis. JOP. 2005; 6: 562 – 567.
6. Pindak D, Parrak V, Pechan J, Vavrecka A, Kuzela L, Fuchs D, et al. The clinical value of procalcitonin in prediction of severity and outcome in acute pancreatitis. Hepatogastroenterology. 2003; 50: 208-209.
7. Jiang CF, Shiau YC, Ng KW, Tan SW. Serum interleukin-6, tumor necrosis factor alpha and C-reactive protein in early prediction of severity of acute pancreatitis. J Chin Med Assoc. 2004; 67: 442-446.
8. Barauskas G, Svagzdys S, Maeckas A. C-reactive protein in early prediction of pancreatic necrosis. Medicina (Kaunas). 2004; 40: 135–140.
9. Del Prete M, Castiglia D, Meli M, Perri S, Nicita A, Dalla Torre A, et al. Prognostic value of C-reactive protein in acute pancreatitis. Chir Ital. 2001; 53: 33-38.
10. Ignjatović S, Majkić-Singh N, Mitrović M, Gvozdenović M. Biochemical evaluation of patients with acute pancreatitis. ClinChem Lab Med. 2000; 38: 1141-1144.
11. Mayer JM, Raraty M, Slavin J, Kemppainen E, Fitzpatrick J, Hietaranta A, et al. Serum amyloid A is a better early predictor of severity than C-reactive protein in aute pancreatitis. Br J Surg. 2002; 89: 163-171.
12. Triester SL, Kowdley KV. Prognostic factors in acute pancreatitis. J ClinGastroenterol. 2002; 34: 167–176.
13. Sandberg AA, Borgstorm A. Early prediction of severity in acute pancreatitis. Is this possible? JOP. 2002; 3: 116-125.
14. Neoptolemos JP, Kemppainen EA, Mayer JM, Fitzpatrick JM, Raraty MG, Slavin J, et al. Early prediction of severity in acute pancreatitis by urinary trypsinogen activation peptide: a multicentre study. Lancet. 2000; 355: 1955-1960.
15. Johnson CD, Lempinen M, Imrie CW, Puolakkainen P, Kemppainen E, Carter R, et al. Urinary trypsinogen activation peptide as a marker of severe acute pancreatitis. Br J Surg. 2004; 91: 1027-1033.
16. Liu ZS, Jiang CQ, Qian Q, Sun Q, Fan LF, Ai ZL. Early prediction of severe acute pancreatitis by urinary trypsinogen activation peptide. Hepatobiliary Pancreat Dis Int. 2002; 1: 285-289.
17. Khan Z, Vlodov J, Horovitz J, Jose RM, Iswara K, Smotkin J, et al. Urinary trypsinogen activation peptide is more accurate than hematocrit in determing severity in patients with acute pancreatitis: a perspective study. Am J Gastroenterol. 2002; 97: 1973-1977.
18. Lempinen M, Kylänpää-Bäck ML, Stenman UH, Puolakkainen P, Haapiainen R, Finne P, et al. Predicting the severity of acute pancreatitis by rapid measurement of trypsinogen-2 in urine. ClinChem. 2001; 47: 2103-2107.
19. Bülbüller N, Doğru O, Ayten R, Akbulut H, Ilhan YS, Cetinkaya Z. Procalcitonin is a predictive marker for severe acute pancreatitis. Ulus TramvaAcilCerrahiDerg. 2006; 12: 115-120.
20. Modrau IS, Floyd AK, Thorlacius – Ussing O. The clinical value of procalcitonin in early assessment of acute pancreatitis. Am J Gastroenterol. 2005; 100: 1593-1597.
21. Rau B, Schilling MK, Beger HG. Laboratory markers of severe acute pancreatitis. Dig Dis. 2004; 22: 247-257.
22. Yonetci N, Sungurtekin U, Oruc N, Yilmaz M, Sungurtekin H, Kaleli I, et al. Is procalcitonin a reliable marker for the diagnosis of infected pancreatic necrosis? Am J Surg. 2004; 74: 591-595.
23. Ammori BJ, Becker KL, Kite P, Snider RH, Nylén ES, et al. Calcitonin precursors: early markers of gut barrier dysfunction in patients with acute pancreatitis. Pancreas. 2003; 27: 239-243.
24. Ammori BJ, Becker KL, Kite P, Snider RH, Nylén ES, et al. Calcitonin precursors in the prediction of severity of acute pancreatitis on the day of admission. Br J Surg. 2003; 90: 197-204.
25. Mándi Y, FarkasG, Takács T, Boda K, Lonovics J. Diagnostic relevance of procalcitonin, IL-6, and sICAM-1 in the prediction of infected necrosis in acute pancreatitis. Int J Pancreatol. 2000; 28: 41-49.

26. Kylänpää-Bäck ML, Takala A, Kemppainen EA, Puolakkainen PA, Leppäniemi AK, Karonen SL, et al. Procalcitonin, soluble interleukin-2 receptor and E-selectine in predicting the severity of acute pancreatitis. Crit Care med. 2001; 29: 63-69.

27. Remes-Troche JM, Duarte-Rojo A, Morales G, Robles-Díaz G. Hemoconcentration is a poor predictor of severity in acute pancreatitis. World J Gastroenterol. 2005; 11: 7018-7023.

28. Lankisch PG, Mahlke R, Blum T, Bruns A, Bruns D, Maisonneuve P, et al. Hemoconcentration: an early marker of severe and/or necrotizing pancreatitis? A critical apparisal. Am J Gastroenterol. 2001; 96: 2081-2085.

29. Lankisch PG, Blum T, Maisonneuve P, Lowenfels AB. Severe acute pancreatitis: when to be concerned? Pancreatology. 2003; 3: 102-110.

30. Gan SI, Romagnuolo J. Admission hematocrit: a simle, useful and early predictor of severe pancreatitis. Dig Dis Sci. 2004; 49: 1946-1952.

31. Meek K, Toosie K, Stabile BE, Elbassir M, Murrell Z, Lewis RJ, et al. Simplified admission criterion for predicting severe complications of gallstone pancreatitis. Arch Surg. 2000; 135: 1048-1052.

32. Lankisch PG, Blum T, Bruns A, Dröge M, Brinkmann G, Struckmann K, et al. Has blood glucose level measured on admission to hospital in a patient with acute pancreatitis any prognostic value? Pancreatology. 2001; 1: 224-229.

33. Meek K, de Virgilio C, Murrell Z, Stabile BE, Elbassir M, Renslo R, et al. Correlation between admission laboratory values, early abdominal computed tomography and severe complications of gallstones pancreatitis. Am J Surg. 2000; 180: 556-560.

34. Gürleyik G, Emir S,Kiliçoglu G, Arman A, Saglam A. Computed tomography severity index, APACHE II score, and serum CRP concentration for predicting the severity of acute pancreatitis. JOP. 2005; 6: 562 -567.

35. Liu ZS1, Jiang CQ, Qian Q, Sun Q, Fan LF, Ai ZL. Early prediction of severe acute pancreatitis by urinary trypsinogen activation peptide. Hepatobiliary Pancreat Dis Int. 2002; 1: 285-289.

36. Gan SI, Romagnuolo J. Admission hematocrit: a simple, useful and early predictor of severe pancreatitis. Dig Dis Sci. 2004; 49: 1946-1952.

37. Roseano M, Lovadina S, Calligaris L, Ursic I, Cuviello A, Liguori G. The multidisciplinary management of acute pancreatitis: a review of 244 cases. Ann Ital Chir. 2004; 75: 443-453.

38. Mentula P, Kylänpää ML, Kemppainen E, Jansson SE, Sarna S, Puolakkainen P, et al. Early prediction of organ failure by combined markers in patients with acute pancreatitis. Br J Surg. 2005; 92: 68-75.

39. Kong L, Santiago N, Han TQ, Zhang SD. Clinical characteristic and prognostic factors of severe acute pancreatitis. World J Gastroenterol. 2004; 10: 3336-3338.

40. Taylor SL, Morgan DL, Denson KD, Lane MM, Pennington LR. A comparison of Ranson, Glasgow, APACHE II scoring systems to a multiple organ system score in predicting patient outcome in pancreatitis. Am J surg. 2005; 189: 219-222.

41. Poves Prim I, FabregatPous J, GarcíaBorobia FJ, JorbaMartí R, FiguerasFelip J, JaurrietaMas E. Early onset of organ failure is the best predictor of mortality in acute pancreatitis. Rev EspEnferm Dig. 2004; 96: 705-709, 709-713.

42. Halonen KI, Leppäniemi AK, Lundin JE, Puolakkainen PA, Kemppainen EA, et al. Predicting fatal outcome in the early phase of severe acute pancreatitis by using novel prognostic models. Pancreatology. 2003; 3: 309-315.

43. Compañy L, Sáez J, Martínez J, Aparicio JR, Laveda R, Griñó P, et al. Factors predicting mortality in severe acute pancreatitis. Pancreatology. 2003; 3: 144-148.

44. Liu TH, Kwong KL, Tamm EP, Gill BS, Brown SD, Mercer DW. Acute pancreatitis in intensive care unit patients: value of clinical and radiologic prognostic factors as predicting clinical course and outcome. Crit Care Med. 2003; 31: 1026-1030.

45. Khan AA, Parekh D, Cho Y, Ruiz R, Selby RR, Jabbour N, et al. Improved prediction of outcome in patients with severe acute pancreatitis by the APACHE II score at 48hours after admission compared with the APACHE II score at admission. Acute physiology and chronic health evaluation. Arch Surg. 2002; 137: 1136-1140.

46. Eachempati SR, Hydo LJ, Barie PS. Severity scoring for prognostication in patients with severe acute pancreatitis: comparative analysis of the Ranson score and APACHE III score. Arch Surg. 2002; 137: 730-736.

47. Osvaldt AB, Viero P, Borges da Costa MS, Wendt LR, Bersch VP, Rohde L. Evaluation of Ranson, Glasgow, APACHE II and APACHE-Q criteria to predict severity in actebiliar pancreatitis. Int Surg. 2001; 86: 158-161.

48. Gemelli F, Magon R. Simplified prognostic test in early detection of acute pancreatitis. Minerva Med. 2002; 93: 1-5.

49. Lankisch PG, Weber-Dany B, Hebel K, Maisonneuve P, Lowenfels AB. The hamless acute pancreatitis score: a clinical algorithm for rapid initial stratification of non-severe disease. Clin Gastroenterol Hepatol. 2009; 7: 702–705.

50. Wu BU1, Johannes RS, Sun X, Tabak Y, Conwell DL, Banks PA. The early prediction of mortality in acute pancreatitis: a large population based study. GUT. 2008; 57: 1698 –1703.

51. Delrue LJ, De Waele JJ, Durjck PO. Acute pancreatitis: radiologic scores in predicting severity and outcome. Abdom Imaging. 2010; 35: 349-361.

52. Beger HG, Rau BM. Severe acute pancreatitis: clinical course and management. 2007; 13: 5043 – 5051.

53. Aggarwal A, Maurai M, Kochhar R. Fluid resuscitation in acute pancreatitis. World J Gastroenterol. 2014; 20: 18092-18103.

54. Gardner TB, Vege SS, Pearson RK, Chari ST. Fluid resuscitation in acute pancreatitis. Clin Gastroenterol Hepatol. 2008; 6: 1070 – 1076.

55. Neri V, Lapolla F, Di Lascia A, Giambavicchio LL. Defining a therapeutic program for recurrent acute pancreatitis patients with unknown etiology. Clinical Med Insights: Gastroenterology. 2014; 7: 1-7.

56. Neoptolemos JP, Carr-Locke DL, London NJ, Bailey IA, James D, Fossard DP. Controlled trial of urgent endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy versus conservative treatment for acute pancreatitis due to gallstones. Lancet. 1988; 2: 979-983.

57. Fan ST, Lai EC, Mok FP, Lo CM, Zheng SS, Wong J. Early treatment of acute biliary pancreatitis by endoscopic papillotomy. N Eng J Med. 1993; 328: 228-232.

58. Nowak A, Nowakowska-Dulawa E, Marek T.A, Rybicka J. Final results of the prospective, randomized, controlled study on endoscopic sphincterotomy versus conventional management in acute biliary pancreatitis (abstract). Gastroenterology. 1995; 108: A380.

59. Fölsch UR, Nitsche R, Lüdtke R, Hilgers RA, Creutzfeldt W. Early ERCP and papillotomy compared with conservative treatment for acute biliary pancreatitis. The German Study Group on Acute Biliary Pancreatitis. N Engl J Med. 1997; 336: 237-242.

60. Behrns KE, Ashley SW, Hunter JG, Carr-Locke D. Early ERCP for gallstone pancreatitis: for whom and when? J Gastroenterol Surg. 2008; 12: 629-633.

61. Petrov MS, Uchugina AF, Kukosh MV. Does endoscopic retrograde cholangiopancreatography reduce risk of local pancreatic complications in acute pancreatitis? Gastrointest Surg. 2008; 12: 629-633.

62. Moretti A, Papi C, Aratari A, Festa V, Tanga M, Koch M, et al. Is early endoscopic retrograde cholangiopancreatography useful in the management of acute biliary pancreatitis? A meta – analysis of randomized controlled trials. Dig Liver Dis. 2008; 40: 379-385.

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

64. Raraty MG, Halloran CM, Dodd S, Ghaneh P, Connor S, Evans J, et al. Minimal access retroperitoneal pancreatic necrosectomy: improvement in morbidity and mortality with a less invasive approach. Ann Surg. 2010; 251: 787-793.

65. Dua MM, Worhunsky DJ, Tran TB, Friedland S, Park WG, Visser BC. Surgical strategies for the management of necrotizing pancreatitis. JOP J Pancreas (online). 2015; 16: 547 – 558.