

## Therapeutic intervention and surgery of acute pancreatitis

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**Abstract** The clinical course of acute pancreatitis varies from mild to severe. Assessment of severity and etiology of acute pancreatitis is important to determine the strategy of management for acute pancreatitis. Acute pancreatitis is classified according to its morphology into edematous pancreatitis and necrotizing pancreatitis. Edematous pancreatitis accounts for 80–90% of acute pancreatitis and remission can be achieved in most of the patients without receiving any special treatment. Necrotizing pancreatitis

occupies 10–20% of acute pancreatitis and the mortality rate is reported to be 14–25%. The mortality rate is particularly high (34–40%) for infected pancreatic necrosis that is accompanied by bacterial infection in the necrotic tissue of the pancreas (Widdison and Karanjia in *Br J Surg* 80:148–154, 1993; Ogawa et al. in *Research of the actual situations of acute pancreatitis. Research Group for Specific Retractable Diseases, Specific Disease Measure Research Work Sponsored by Ministry of Health, Labour, and Welfare. Heisei 12 Research Report*, pp 17–33, 2001). On the other hand, the mortality rate is reported to be 0–11% for sterile pancreatic necrosis which is not accompanied by bacterial infection (Ogawa et al. 2001; Bradely and

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Allen in *Am J Surg* 161:19–24, 1991; Rattner et al. in *Am J Surg* 163:105–109, 1992). The Japanese (JPN) Guidelines were designed to provide recommendations regarding the management of acute pancreatitis in patients having a variety of clinical characteristics. This article describes the guidelines for the surgical management and interventional therapy of acute pancreatitis by incorporating the latest evidence for the management of acute pancreatitis in the Japanese-language version of JPN guidelines 2010. Eleven clinical questions (CQ) are proposed: (1) worsening clinical manifestations and hematological data, positive blood bacteria culture test, positive blood endotoxin test, and the presence of gas bubbles in and around the pancreas on CT scan are indirect findings of infected pancreatic necrosis; (2) bacteriological examination by fine needle aspiration is useful for making a definitive diagnosis of infected pancreatic necrosis; (3) conservative treatment should be performed in sterile pancreatic necrosis; (4) infected pancreatic necrosis is an indication for interventional therapy. However, conservative treatment by antibiotic administration is also available in patients who are in stable general condition; (5) early surgery for necrotizing pancreatitis is not recommended, and it should be delayed as long as possible; (6) necrosectomy is recommended as a surgical procedure for infected necrosis; (7) after necrosectomy, a long-term follow-up paying attention to pancreatic function and complications including the stricture of the bile duct and the pancreatic duct is necessary; (8) drainage including percutaneous, endoscopic and surgical procedure should be performed for pancreatic abscess; (9) if the clinical findings of pancreatic abscess are not improved by percutaneous or endoscopic drainage, surgical drainage should be performed; (10) interventional treatment should be performed for pancreatic pseudocysts that give rise to symptoms, accompany complications or increase the

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diameter of cysts and (11) percutaneous drainage, endoscopic drainage or surgical procedures are selected in accordance with the conditions of individual cases.

**Keywords** Necrotizing pancreatitis · Infected pancreatic necrosis · Sterile pancreatic necrosis · Pancreatic abscess · Pancreatic pseudocyst

## Necrotizing pancreatitis

**CQ1** In which cases is infected pancreatic necrosis suspected?

*Worsening clinical manifestations and hematological data, blood bacteria culture test positive, blood endotoxin test positive, and the presence of gas bubbles in and around the pancreas on CT scan are indirect findings that lead to suspicions of infected pancreatic necrosis.*

Findings of suspected infected pancreatic necrosis include worsening of clinical manifestations and hematological data, positive blood bacteria culture test, positive blood endotoxin test, and the identification of gas bubbles in and around the pancreas on CT scan, but they are findings merely suggesting the presence of infection.

**CQ2** What is the most useful procedure for making a definitive diagnosis of infected pancreatic necrosis?

*Bacteriological examination by means of fine needle aspiration is useful for making a definitive diagnosis of infected pancreatic necrosis. (Recommendation A)*

The method that has been established to detect infected pancreatic necrosis is bacteriological examination performed by means of CT- or US-guided local fine needle aspiration (FNA). The rate of making a correct diagnosis with this procedure is high (89–100%) (Level 2b) [5, 6]. By selecting an appropriate puncture route, the procedure can be performed safely without giving rise to complications such as intestinal injury.

On the other hand, there is a report demonstrating that the false negative rate with FNA is 20–25% [7], so it can be said that the consensus concerning the indications, timing and frequency for this procedure is not sufficient [8].

**CQ3** What is the treatment policy for sterile pancreatic necrosis?

*Conservative treatment should be performed as a rule in sterile pancreatic necrosis. (Recommendation B)*

It is generally agreed that sterile pancreatic necrosis should be managed conservatively as a rule (Level 5) [9–11]. Many

of the patients with sterile necrosis achieve remission in response to conservative management (Level 2c–3b) [3, 8, 12, 13], although there are reports showing that surgical intervention is indicated in patients who have failed to respond to intensive conservative management (Level 2c–3b) [14–17].

**CQ4 What is the treatment policy for infected pancreatic necrosis?**

*Infected pancreatic necrosis is an indication for interventional therapy including surgery, interventional radiology (IVR) and endoscopic treatment. (Recommendation B). However, follow-up while giving conservative treatment by means of antibiotic administration is also available in patients who are in stable general condition. (Recommendation C)*

Currently, there are many reports on the treatment policy for infected pancreatic necrosis [7, 18–22]. According to Runzi et al. [19], despite prophylactic administration of antibiotics in 88 cases with necrotizing pancreatitis, 28 cases were diagnosed as having infected pancreatic necrosis, so the type of antibiotics was changed on the basis of bacteriological examination and conservative management was continued. Of these 28 cases, 12 cases underwent surgical intervention after waiting for an average of 36 days because of local infection after a diagnosis of infected pancreatic necrosis had been made and death occurred in 2 cases (16.6%). The remaining 16 cases completed conservative management by antibiotic administration (8 weeks at the longest) and death occurred in 2 cases. Also, there is a report [23] demonstrating that, of 24 cases with infected pancreatic necrosis, necrosectomy was performed in 18 cases in aggravated general condition and death occurred in 5 cases (28%), but that 6 cases in stable general condition required no surgical intervention and they all recovered with management at ICU including long-term administration of antibiotics. There is another report [24] showing that, of 31 cases with infected pancreatic necrosis, antibiotics were administered in 8 cases as the initial treatment and drainage was performed in 23 cases (percutaneous drainage in 18 cases and endoscopic drainage in 5 cases) and that 4 of these 23 cases which underwent drainage required necrosectomy due to worsening of physical condition while 8 cases which received antibiotic administration required no further treatment, of which death occurred in one of the percutaneous drainage cases and the remaining cases recovered.

Therefore, even in patients with infected pancreatic necrosis, conservative management can be the first choice of treatment on condition that their general condition is stable.

**CQ5 What is the optimal timing for surgical intervention for necrotizing pancreatitis ?**

*Early surgery for necrotizing pancreatitis is not recommended. (Recommendation D) If surgery (necrosectomy) is performed, it should be delayed as long as possible. (Recommendation C1)*

Severe acute pancreatitis often causes major organ failure in the early stage after onset, so early surgical intervention was recommended in the past when it was accompanied by signs of organ failure. However, the high mortality rate of 65% arising from early surgical intervention [1] has cast doubts on its benefits [7, 21, 22, 25–28].

A retrospective study conducted to investigate the optimal timing of surgical intervention for severe acute pancreatitis (necrotizing pancreatitis) [25] has found that the mortality rate (12%) in patients who underwent delayed surgery decreased significantly compared with that (39%) in patients who underwent early surgery. This result emphasizes the importance of delaying surgical intervention for severe acute pancreatitis as long as possible. According to the data (pancreatic resection or necrosectomy) of the only randomized controlled trial (RCT) [26] comparing early surgery (within 72 h after onset) and delayed surgery (12 days after onset), the mortality rate was 56% for early surgery and 27% for delayed surgery, respectively, and the difference was not statistically significant. However, this trial was terminated because of the very high mortality rate in patients who underwent early surgery.

A study [27] was conducted using multivariate analysis to investigate retrospectively the prognostic factors involved in surgical intervention for pancreatitis. The study compared potential factors contributing to the prognoses in 56 patients who underwent surgery (necrosectomy combined with local lavage) for necrotizing pancreatitis. Of these 56 patients, 22 patients underwent early surgery (within 12 days after onset, median: 5 days) and 34 patients underwent late surgery (after 12 days following onset, median: 20 days). According to the data of that study, the mortality rate was 54.5% for early surgery and 29.4% ( $p = 0.06$ ) for late surgery, respectively.

Another study was conducted for 53 patients who underwent surgery for necrotizing pancreatitis to investigate retrospectively the relationship between the timing of surgery and the mortality rate. The study compared retrospectively the mortality rates in 14 patients who underwent early surgery (within 14 days following hospitalization), 11 patients who underwent intermediate surgery (15–29 days after onset), and 26 patients who underwent late surgery (waiting for 30 days after onset) and found that the mortality rate was 75% for early surgery, 45% for

intermediate surgery and 8% ( $p = 0.001$ ) for late surgery, respectively [21]. A systematic review of 1136 cases reported in 11 references show that the earlier an operation is, the higher the mortality rate is [21].

The above findings suggest that necrosectomy for necrotizing pancreatitis should be delayed as long as possible [9, 28]. The rationale for this is that the border between normal and necrotic pancreatic tissue becomes more distinct with the passage of time, which may make it possible to minimize intraoperative hemorrhage and avoid unnecessary removal of the normal pancreas involved in necrosectomy.

**CQ6 What is the optimal intervention for infected pancreatic necrosis ?**

***Necrosectomy is recommended as a surgical procedure for infected necrosis. (Recommendation A)***

Necrosectomy with debridement of the necrotic pancreatic and peripancreatic tissue and drainage is generally agreed as a valid surgical procedure for infected pancreatic necrosis. Sufficient open necrosectomy and single-stage debridement with closed packing conducted from 1990 through 2005 yielded favorable results and the mortality rate in 167 cases of necrotizing pancreatitis (including 113 cases of infected necrosis) was 15.0% for infected pancreatitis and 4.4% for sterile pancreatitis, respectively. So, these results have become a milestone for assessing the current treatment modalities [7].

Less-invasive procedures by various approaches are currently being employed and better outcomes are reported than those achieved by conventional open surgery [29–40]. As the pancreas is a retroperitoneal organ, a combination treatment of necrosectomy by the retroperitoneal approach along with local lavage can be employed [29–31]. Also employed as a procedure using IVR is percutaneous necrosectomy, which is conducted by inserting a CT-guided drainage tube through the left abdomen to the retroperitoneum, followed by extension of fistulas and endoscopic removal of necrotic mass [32–34, 37]. There is also a report on the laparoscopic approach to the necrotic mass around the pancreas [38]. Less-invasive new treatment procedures including endoscopic transgastric necrosectomy [35, 36, 41–43] are under trial, although selection of appropriate treatment should be made considering the condition in individual cases.

**CQ7 Is a long-term follow-up necessary after necrosectomy ?**

***Following necrosectomy, a long-term follow-up paying attention to endocrine and exocrine pancreatic function and complications including the stricture of the bile duct***

***and the stenosis of the pancreatic duct is necessary. (Recommendation A)***

Concerning the long-term prognosis of necrosectomy, there are reports indicating that necroscopy is not infrequently accompanied by decreased endocrine and exocrine pancreatic function, stricture of the bile duct and stenosis of the pancreatic duct [44–47].

According to the results of a report [47] studying the long-term prognosis of necrosectomy in 63 patients (median duration of follow-up: 28.9 months), complications occurred in 39 patients (62%) excluding pancreatic dysfunction, of which 10 patients (16%) required surgical or endoscopic treatment. Complications included 8 cases of pancreatic fistula, 4 cases of biliary tract stricture and 5 cases of pseudocysts. Also, exocrine pancreatic dysfunction occurred in 25% of cases and diabetes mellitus in 33% of cases, respectively. Furthermore, a study of 98 patients after necrosectomy [51] found that 14 patients (14.3%) developed recurrent pancreatitis caused by the stenosis of the pancreatic head and body, so they required pancreatectomy, pancreaticojejunostomy or pseudocystojejunostomy. A study [45] was conducted to investigate the endocrine and exocrine pancreatic function during the 12 months following necrosectomy in patients who survived severe gallstone-induced necrotizing pancreatitis. The patients were separated into groups: necrosectomy group (12 cases) and non-necrosectomy group (15 cases). The results show that the frequency of occurrence of steatorrhea was 25% for the former group and 0% for the latter group and the frequency of insulin replacement therapy was 33.3% for the former group and 0% for the latter group, showing that the decrease in pancreatic function was significant in the former group.

In patients who underwent necrosectomy, long-term follow-up paying attention to pancreatic duct stenosis and bile duct stricture along with other complications is required.

### **Pancreatic abscess**

**CQ8 How should pancreatic abscess be managed ?**

***Drainage including percutaneous, endoscopic and surgical procedure should be performed for pancreatic abscess. (Recommendation B)***

Liquid puss collection is the main lesion in most patients with pancreatic abscess, so it has been reported recently that 78–86% of the patients can be cured by percutaneous drainage alone (Level 3b) [48, 49]. If a safe puncture route is assured by an imaging guidance, percutaneous drainage

may be the first choice of procedure as a radical treatment for pancreatic abscess.

**CQ9** What is the indication for surgical drainage in pancreatic abscess?

*If the clinical findings of pancreatic abscess are not improved by percutaneous or endoscopic drainage, surgical drainage should be performed immediately. (Recommendation B)*

However, it should be noted that the favorable results reported for this treatment have all been based on retrospective studies, so some of the cases were not necessarily those of pancreatic abscess. For example, in severe cases with Ranson score of 5 or more (Level 2b) [50] and cases with multiple abscess (Level 4) [51], one-stage cure rate by percutaneous drainage is low to 30–47%.

Therefore, when signs of infection persist after drainage of the abscess, open drainage should be performed [52]. In addition to percutaneous drainage, other drainage procedures including percutaneous transgastric puncture drainage [53], endoscopic transgastric drainage [36] and endoscopic transpapillary drainage [54, 55] are also being tried, but further accumulations of cases treated by these procedures are needed.

### Pancreatic pseudocysts

**CQ10** What are the indications for intervention in pancreatic pseudocysts ?

*Interventional treatment should be performed for pancreatic pseudocysts that give rise to symptoms, accompany complications or increase the diameter of cysts. (Recommendation A)*

Indications for drainage procedures in pancreatic pseudocysts include (1) cysts accompanying symptoms such as abdominal pain, (2) those giving rise to complications such as infection and/or bleeding, (3) those increasing in size during follow-up, (4) those with a diameter of 6 cm or more, and (5) those without any tendency to decrease in size during more than 6 weeks of follow-up. Although (4) and (5) are known as “6 cm–6 week criteria”, they are not absolute indications for drainage (Level 3b–4) [56, 57].

**CQ11** How is interventional treatment selected for pancreatic pseudocysts?

*Percutaneous drainage, endoscopic drainage or surgical procedures are selected in accordance with the conditions of individual cases including the communication with the*

*pancreatic duct and the positional relationship between the digestive tract walls. (Recommendation A)*

Treatment procedures for pancreatic pseudocysts include percutaneous drainage, endoscopic drainage, surgical drainage. There are opinions that percutaneous drainage can be an alternative procedure to surgical drainage in view of the cure rate of 80–100% that percutaneous drainage yields (Level 2c–3b) [58, 59]. However, there are also opinions that recurrence occurs in not just a few cases of pseudocysts that have temporarily resolved following percutaneous drainage (Level 3b) [60], so that surgical drainage is superior in the complete cure rate (Level 3b) [61, 62].

The only prospective controlled study (Level 2b) [50] conducted to date has found that the one-stage healing rate was 77% (20/26) for percutaneous drainage and 73% (18/26) for surgical drainage and that no differences were observed in cure and recurrence rates between the two types of drainage.

Because it has been reported that the average duration of catheterization for percutaneous drainage is 16–42 days in cases that exhibit response (Level 2c–3b) [58, 59] surgical drainage should be considered instead if no tendency to improve is observed after that duration has passed. Furthermore, percutaneous drainage has been found to be effective in cases where the morphology of the pancreatic duct is normal but does not communicate with the cysts despite the presence of pancreatic duct stenosis [63].

Endoscopic treatment including transgastric puncture, transduodenal puncture and transpapillary drainage (Level 4) is available [64–66]. Safe performance of transgastric puncture drainage was made possible using endoscopic ultrasound-guidance (Level 4) [67]. Transpapillary drainage is indicated for cases with communication between cysts and the pancreatic duct.

Surgical treatment is indicated in patients who do not respond to conservative management, percutaneous drainage or endoscopic drainage and those who are accompanied by infection and/or bleeding.

Surgical treatment is classified into fistulating operation by anastomosis between cysts and the digestive tract (cystogastrostomy and cystojejunostomy) and resection. Cases of laparoscopic surgery are reported currently [68]. External fistulating operation is selected for cases in which anastomosis is not indicated because of the immature cystic wall, and resection involving the pancreatic tail and the spleen is selected for cases in which drainage is difficult [69].

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