

Using a multidisciplinary team for the staged management and optimally minimally invasive treatment of severe acute pancreatitis

Junxiang Yin^{1,§}, Zhi Chen^{2,§}, Wei Niu^{1,§}, Lili Feng^{3,§}, Bing Fan³, Longfei Zhou¹, Bingliang Zeng³, Jun Zhang¹, Hui Chen⁴, Bo Tong⁵, Lingfei Tong⁶, Xiaoliang Chen^{1,*}

¹Hepatobiliary Surgery, Jiangxi Provincial People's Hospital Affiliated to Nanchang University, Nanchang, China;

²Critical Care Medicine, Jiangxi Provincial People's Hospital Affiliated to Nanchang University, Nanchang, China;

³Medical Imaging Department, Jiangxi Provincial People's Hospital Affiliated to Nanchang University, Nanchang, China;

⁴Microbiology Department, Jiangxi Provincial People's Hospital Affiliated to Nanchang University, Nanchang, China;

⁵Pulmonary and Critical Care Medicine, Jiangxi Provincial People's Hospital Affiliated to Nanchang University, Nanchang, China;

⁶Clinical Pharmacy Department, Jiangxi Provincial People's Hospital Affiliated to Nanchang University, Nanchang, China.

SUMMARY Severe acute pancreatitis (SAP) is a common critical disease with a high mortality rate that involves a complex, rapid change in condition and multiple organ systems. Therefore, a multidisciplinary team (MDT), including staff from the emergency department, intensive care unit, pancreatic surgery, gastroenterology, and imaging, is necessary for the early diagnosis, evaluation, and treatment of patients with SAP. This involves managing the systemic inflammatory response and maintaining organ function in the early stage and managing systemic infection and treatment of peripancreatic complications in the middle-to-late stages. The MDT should be led by departments corresponding to the clinical characteristics of each stage, and those departments should be responsible for the coordination and implementation of treatment by other relevant departments. In the late stage, pancreatic surgery and gastroenterology are the main departments that should manage peripancreatic complications. In line with the principle of minimally invasive treatment, the timely and reasonable selection of endoscopic or minimally invasive surgical debridement can achieve good therapeutic outcomes. Open surgery is also an effective method for treating an intractable massive hemorrhage in the abdominal cavity or necrotic cavity, intractable abdominal compartment syndrome, visceral perforation, and fistulae.

Keywords multidisciplinary team; staged management, severe acute pancreatitis, optimally, minimally invasive

1. Introduction

Severe acute pancreatitis (SAP) is a critical disease involving multiple organ dysfunction or even failure and is characterized by peripancreatic lesions and a systemic inflammatory response (1). SAP is a major concern because of its prevalence, unpredictable onset, rapid progression, and high mortality rate. Due to the complexity of SAP, the close relationship between peripancreatic local lesions and systemic inflammation, and the interaction between various organs, the diagnosis and treatment of SAP must involve timely and accurate assessment of the disease. In addition, the function of multiple important organs must be maintained, nutritional support and fluid treatment must be provided, infection must be controlled, drainage must be performed, and peripancreatic complications

must be treated endoscopically or surgically. These efforts must involve the emergency department, intensive care unit (ICU), and emergency treatment unit. This multidisciplinary team (MDT) must, therefore, include departments such as hepatobiliary and pancreatic surgery, gastroenterology, medical imaging (ultrasound, computed tomography [CT], and interventional radiology), microbiology, nutrition, and traditional Chinese medicine (2) (Figure 1). Depending on the clinical characteristics in different stages of the development of SAP, different departments will be involved; however, the most important aspect is to provide timely and accurate assessment of the disease at all stages and to formulate the best treatment plan accordingly (3).

2. Management during the first visit

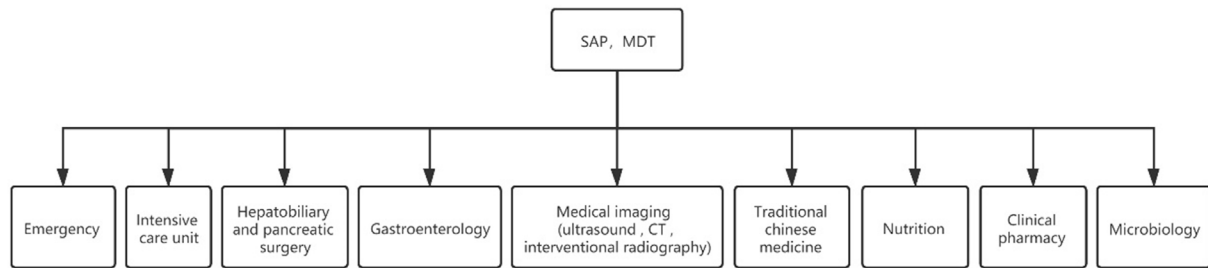


Figure 1. Multidisciplinary team for severe acute pancreatitis.

The onset of SAP is unpredictable, sudden, and often occurs first in the emergency department; therefore, proper anticipation and timely diagnosis of SAP and its complications in the emergency department are particularly important. SAP occurs in 15-25% of cases of acute pancreatitis (4). In the early stage of acute pancreatitis, inflammatory mediators and cytokines are transmitted and amplified in a "cascade." Systemic inflammatory response syndrome (SIRS) occurs rapidly, and then multiple organ dysfunction syndrome (MODS), which includes the heart, lungs, and kidneys, can occur (5). Prolonged MODS affects the respiratory, circulatory, digestive, renal, and coagulation systems (5-7). Therefore, within the MDT framework, a practical and feasible protocol must be formulated that involves the training of emergency doctors to closely monitor the blood oxygen, blood pressure, and renal function of patients recently diagnosed with acute pancreatitis and to evaluate cardiopulmonary and renal function with the improved Marshall scoring system to detect and diagnose SAP early. The emergency department should call for an MDT conference, manage SAP in a timely and appropriate manner according to standards, reduce the inflammatory response, maintain tissue and organ perfusion, and protect the organ function environment (8).

2.1. Scoring systems

At the authors' facility, SAP was diagnosed when patients had a bedside index for severity in acute pancreatitis (BISAP) score > 3. The BISAP score was evaluated repeatedly during the course of the disease, allowing for any changes to be monitored dynamically. Patients with organ failure for more than 48 h (defined according to the revised Atlanta classification standard) were transferred to the ICU for treatment (9,10).

The initial diagnosis and management of SAP was mostly done in the emergency department. Therefore, the development of an MDT process is conducive to timely and accurate evaluation and appropriate treatment. Doctors from relevant departments with extensive experience in treating SAP can be contacted for treatment advice and protocols. When patients need to be transferred to the ICU, they can be transferred

smoothly *via* the MDT path.

3. Early management

The initial phase of SAP may last 1-2 wks, and early SIRS and persistent (≥ 48 h) dysfunction of more than two organs are the main clinical manifestations. The first peak in mortality occurs at this time (10). The management of this stage should be led by the ICU or internal and external departments that are capable of providing intensive care, and treatment should focus on fluid resuscitation, respiratory and circulatory support, improvement in ventilation and tissue perfusion, and maintenance of organ function (11).

3.1. Fluid resuscitation

Fluid resuscitation is essential for maintaining circulation stability and ensuring organ perfusion and should be implemented as soon as possible after diagnosis (12). The decrease in mortality associated with acute pancreatitis in recent years has been attributed to an improvement in microcirculation during fluid resuscitation, which has helped prevent pancreatic necrosis (5). Early fluid resuscitation can be performed to optimize tissue perfusion before hemodynamic deterioration. The first 12-24 h of active intravenous rehydration is the most beneficial, and isotonic crystalloid solution is the preferred fluid. The goal-directed fluid therapy recommended in the American Gastroenterological Association treatment guidelines for acute pancreatitis in 2018 includes quickly supplementing isotonic crystalloid solution (0.9% sodium chloride or lactate Ringer's solution) in order to restore end organ perfusion (13). Initially, a bolus of 20 mL/kg of fluid is administered within 30 minutes at a rate of 5-10 mL/kg/h, and then continuous intravenous fluid is added at a rate of 3 mL/kg/h for 8-12 h. Indications that fluid therapy has been effective include a central venous pressure of 8-12 cmH₂O, a mean arterial pressure ≥ 65 mmHg, urine volume ≥ 0.5 mL/kg/h, oxygen saturation ≥ 0.70 , central or mixed venous hematocrit > 0.3, and decreased blood urea nitrogen (14). However, excessive fluid therapy can increase the burden on the heart, affect the lungs,

and increase intra-abdominal pressure. Therefore, blood volume responsiveness and blood volume status should be evaluated, and the infusion volume and infusion rate should be dynamically adjusted as necessary. In addition, invasive hemodynamic monitoring may be indicated (11).

3.2. Analgesia

Patients with SAP may have abdominal pain and pain associated with other diseases (various invasive surgeries or bed rest). Therefore, appropriate analgesics and sedatives should be administered within 24 h of admission to improve comfort and reduce clinical symptoms associated with increased oxygen consumption and stress (15).

3.3. Lung protection

The lungs are the main target of inflammatory mediators and toxins. The increase in pulmonary capillary permeability, the decrease in alveolar surface-active substances, and the decrease in pulmonary perfusion lead to ventilation dysfunction. The sharp increase in intra-abdominal pressure associated with SAP also raises the diaphragm, thus affecting ventilation. Therefore, symptoms of acute respiratory distress syndrome, such as chest tightness, respiratory distress, and progressive hypoxemia, may appear in the early stage of SAP (16). A persistent hypoxic state can lead to hypoxia in tissues and organs throughout the body, potentially worsening MODS if it is not corrected quickly. When oxygen therapy is ineffective, noninvasive or invasive ventilation is often indicated. When, however, the removal of bronchial secretions is ineffective or the patient is exhausted, tracheal intubation should be performed and positive pressure ventilation should be used to improve oxygenation and ventilation. The strategy of using ventilation to protect the lungs should be adopted during invasive ventilation. The tidal volume should be 6 mL/kg, plateau pressure should be 30 cm H₂O, and positive end expiratory pressure should be titrated accordingly. Pleural effusion should also be drained promptly (17).

3.4. Renal protection

Acute kidney injury (AKI) is a common complication of SAP. Approximately 70% of patients with SAP develop AKI (18). The main causes of AKI are hypoperfusion and inflammatory mediator toxin attack. The first manifestation is oliguria or even anuria (19). The diagnostic criteria for AKI include an increase ≥ 0.3 mg/dL in serum creatinine (SCR) within 48 h, a 1.5-fold or greater increase in SCR from baseline, or a continuous urine volume < 0.5 mL/kg/h over 6 h (20). Sodium retention and the accumulation of water and toxic substances can lead to a disturbance in the acid-

base balance. In addition, dysfunction of organs such as the lungs and the respiratory center in the brain can also occur. Therefore, continuous renal replacement therapy should be performed in patients with SAP who develop AKI when adequate fluid resuscitation is ineffective or abdominal compartment syndrome occurs (21).

3.5. Antibiotics

The prophylactic use of antibiotics has not been found to reduce mortality in patients with acute pancreatitis. Therefore, the routine use of antibiotics is not recommended for all patients with acute pancreatitis. However, antibiotics should be promptly administered to patients with acute cholangitis or extrapancreatic infections (2).

3.6. Enteral nutrition

Early enteral nutrition is helpful at maintaining the intestinal barrier and reducing bacterial translocation and the incidence of multiple infections. Patients should be encouraged to eat early; however, enteral nutrition (oral, nasogastric, and jejunal) and nutritional support should be tailored individually depending on the patient's intra-abdominal pressure and gastrointestinal function (13).

4. Interim management

4.1. Infection control

Once the systemic inflammatory response has subsided in patients with SAP, the functioning of the lungs, kidneys, heart, liver, and other organs will recover; effective circulating blood volume increases; tissue perfusion improves, tissue hypoxia diminishes, and respiratory function improve; and urine output volume increases. Ten to fourteen d after the onset of the disease, however, some patients have obvious symptoms of infection and enter a period of systemic infection (10). The causes of SAP infection are as follows: 1) translocation of intestinal flora; 2) a retrograde infection caused by percutaneous catheter drainage; 3) biliary calculi and obstruction complicated by infection; 4) respiratory insufficiency and hypoxemia; and 5) reduced immunity (22). Most of the pathogens responsible are Gram-negative bacteria, and *Escherichia coli* is the most common (23). Currently, MDT management requires close cooperation between the ICU, pancreatic surgery, and gastroenterology. Systemic infections may cause the disease to recur; therefore, a broad-spectrum antibiotic that can treat a wide range of bacteria and pass through the blood-pancreatic barrier must be selected while keeping respiratory, circulatory, and renal function stable, the etiological cause must be quickly diagnosed, and more sensitive drugs must then be administered either

immediately or after symptom control (24,25). SAP has a long course, so clinicians should be alert for multi-drug resistant bacteria or fungal infections (26,27). The optimal use of antibiotics can be determined under the guidance of microbiologists and clinical pharmacists on the MDT (Figure 2).

4.2. Invasive surgery

A local infection should be treated with minimally invasive, safe, and effective drainage. Percutaneous catheter drainage should be performed immediately in case of definite local infection or high pressure. Surgical treatment needs to be carefully considered during the early stage and is preferably performed 4 wks after onset (28). Biliary SAP with a biliary obstruction should be treated with CT or B-ultrasound-guided percutaneous transhepatic cholangial drainage and percutaneous transhepatic gallbladder drainage. Alternatively, endoscopic retrograde cholangiopancreatography, endoscopic sphincterotomy, or nasobiliary drainage can also be selected (29,30).

4.3. Reducing abdominal pressure

Gastrointestinal emptying disorders and abdominal hypertension are common in the early stage of SAP. Abdominal hypertension, digestive and absorption

disorders, intestinal barrier damage, and bacterial translocation lead to acid-base disorders and abdominal compartment syndrome and can aggravate respiratory and circulatory dysfunction, infection, and the systemic inflammatory response, all of which play an important role in the progression of the disease and its prognosis (31). However, relieving pressuring of the small intestine using a conventional gastric tube is difficult and open surgery is rarely used because of the associated trauma and complications (32,33). In traditional Chinese medicine, acute pancreatitis is categorized as abdominal pain and epigastric pain. Its etiology and pathogenesis are mainly related to the accumulation of heat and toxins, obstruction of the viscera, blood stasis, or stagnation of qi in the liver (34). Because of its "cold and bitter" properties, rhubarb is believed to treat diarrhea by relieving "heat and fire;" combined with rhubarb, mirabilite is believed to "moisten dryness" and increase the "heat-relieving" effect of rhubarb (alleviating diarrhea) (35). A mixture of rhubarb and mirabilite can promote intestinal peristalsis, accelerate the recovery of intestinal function, regulate inflammatory mediators, promote the elimination of oxygen free radicals, and reduce systemic inflammation (36). Guided by B-ultrasound, X-ray, or gastroscopy and in consultation with traditional Chinese medicine, an indwelling nasogastric intestinal catheter can be placed by manually at the bedside. This catheter

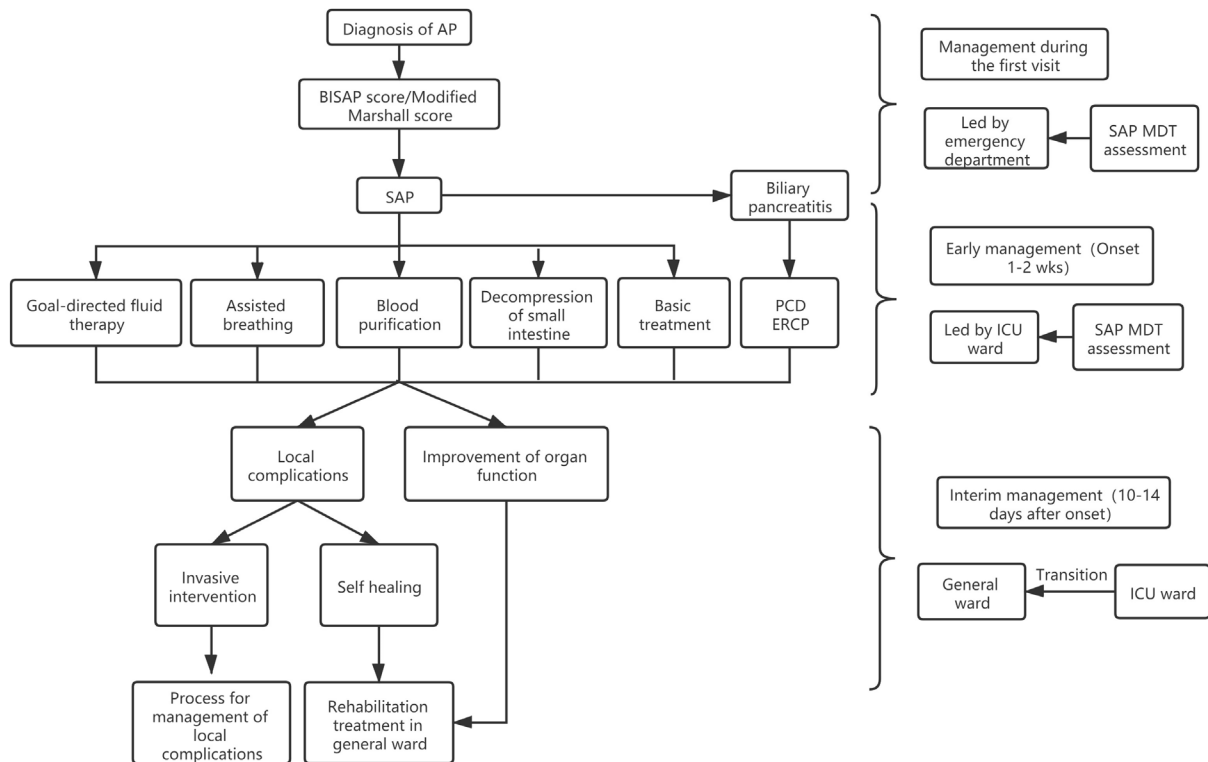


Figure 2. SAP phased management

can reach the distal part of the small intestine and effectively drain intestinal effusion and gas at the same time and, when combined with rhubarb, the external application of mirabilite, and an enema, can quickly reduce the pressure on the gastrointestinal tract and abdominal cavity (37,38). It is safe, noninvasive, simple, and effective. After the recovery of intestinal function, the catheter can also be used for enteral nutrition.

4.4. Nutritional support

Gastrointestinal dysfunction, high energy consumption, and anabolic disorders often lead to malnutrition in patients with SAP. The goal of nutritional support is to provide energy and metabolic substrates, maintain the function of cells, tissues and organs, correct a negative nitrogen balance, reduce the inflammatory response, and avoid energy depletion. Nutrition should be administered through the whole process of SAP treatment (13). Due to a dysfunction in gastrointestinal absorption and emptying and a high abdominal pressure, total parenteral nutrition must be administered in the early stage of SAP. To avoid high fat input, glucose is generally the main form of energy administered. Albumin as a colloidal supplement is helpful in correcting hypoproteinemia (39). Glutathione, polyunsaturated fatty acids, nucleotides, and other therapeutic nutrients are also used (40). Once intestinal function has recovered, enteral nutrition should be promptly started. This helps to protect the intestinal mucosal barrier, maintain the balance of intestinal microorganisms, and reduce the translocation of intestinal flora (41).

5. Late management and optimally minimally invasive treatment of peripancreatic complications

Four wks after the onset of SAP, the inflammatory response in some patients is effectively reduced, and the function of the heart, lungs, kidneys, and other important organs gradually recover and stabilize. The main problem at this stage is infectious necrosis of the pancreas and retroperitoneum, which leads to the second peak in mortality. In this stage, the MDT should be led by gastroenterology or pancreatic surgery (10,42). The pancreas is a retroperitoneal organ. Activated pancreatic juices are placed under increased pressure and erode the adjacent portal vein, causing necrotic pancreatic tissue to spread along the left and right retroperitoneum. Necrosis can span from the diaphragm to the sacroiliac joint. Therefore, acute peripancreatic fluid collection, acute necrotic collection, pancreatic pseudocyst, walled-off necrosis, and infectious pancreatic necrosis are the main causes of mortality (2).

5.1. Minimally invasive approach

For the treatment of peripancreatic lesions (Figure 3), the MDT needs to be led by pancreatic surgery and gastroenterology. The "3D" principle (delay, drainage, and debridement) should be followed with the help of imaging and interventional radiology. Debridement is a minimally invasive treatment with ascending steps (43,44). In the early stage (within the first 4 wks), acute peripancreatic fluid collection and acute necrotic collection mainly occur. If the disease requires treatment, CT or B-ultrasound-guided percutaneous catheter drainage can be performed. Abscesses are liquefied. This can both reduce the inflammatory response and the abdominal and retroperitoneal pressure and promote the recovery of gastrointestinal function (45). In the middle and late stages of the

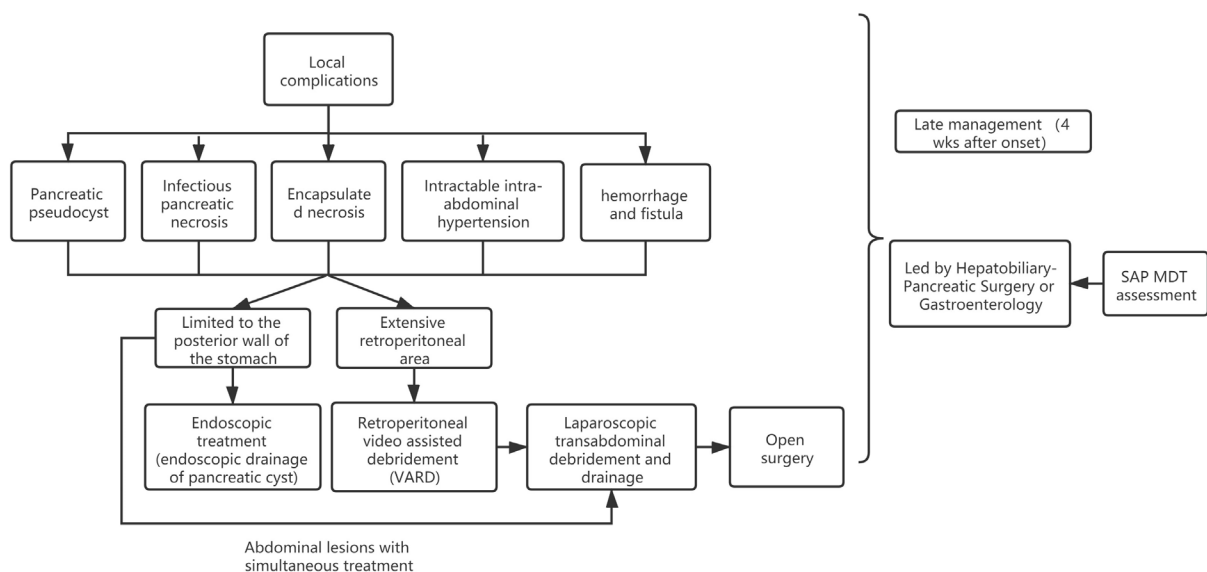


Figure 3. Process for management of local complications.

disease (4 wks after onset), necrotic tissues around the pancreas and retroperitoneum gradually liquefy and form a boundary, and the following manifestations may appear: 1) temperature $\geq 38.5^{\circ}\text{C}$ and elevated C-reactive protein and other inflammatory markers, 2) persistent organ failure or new onset of organ failure, 3) CT and other imaging findings indicating that the extent of necrosis has increased and a "bubble sign" evident in the necrotic focus, 4) fine-needle aspiration of necrotic tissue and positive Gram staining or culture (46). When pancreatic surgery is needed to treat tissue necrosis and an infection, minimally invasive debridement and drainage should be performed at the appropriate time. Common surgical techniques include video-assisted retroperitoneal debridement (VARD), endoscopic transmural drainage (ETD), laparoscopic debridement and drainage, and open surgery (47). VARD allows a direct view as the surgeon clears the necrotic tissue around the pancreas and pelvis under direct vision, so it is suitable for retroperitoneal necrosis that has not invaded the abdominal cavity. Gastroscopic debridement is suitable for peripancreatic cysts close to the posterior wall of the stomach and involves minimal surgical trauma. Stent placement can provide drainage to an extent, but it is not effective at debridement, plastic stents provide limited drainage, and metal stents need to be replaced regularly (48). Most cases of acute pancreatitis are treated with open surgery when there is a massive hemorrhage in the abdominal cavity or necrosis that cannot be readily controlled by conservative or interventional treatment, when compartment syndrome cannot be readily relieved, and when a visceral perforation or fistula is present (49). Each method of debridement and drainage has its advantages and disadvantages.

5.2. Timing and indications

The key to the treatment of peripancreatic lesions is to determine the timing and indications. Early inflammation, hyperemia, and exudation are the main causes. Patients with a severe systemic inflammatory response and multiple organ dysfunction should undergo percutaneous catheter drainage or some other minimally invasive method. Blindly expanding the surgery will only backfire, aggravate the trauma, and even lead to death. In the later stage, the patients with retroperitoneal infection and necrosis should be treated promptly, and appropriate debridement and drainage should be performed.

In short, SAP is a common surgical emergency with a high mortality rate. Its diagnosis and treatment involves multiple organ systems and portions of the pancreas. SAP should be treated by an MDT consisting of experts from relevant departments who are proficient in the latest techniques to diagnose and treat SAP. The MDT should effectively coordinate during the diagnosis and treatment process. Depending on the different

stages of the disease, the departments in charge should provide the patient with a standardized and optimal treatment plan. The treatment of peripancreatic complications should follow the principle of least invasiveness and provide the best form of treatment in a timely manner.

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§These authors contributed equally to this work.

*Address correspondence to:

Xiaoliang Chen, Department of the Hepatobiliary surgery, Jiangxi Provincial People's Hospital Affiliated to Nanchang University, Nanchang 330006, China.

E-mail: chenxiaoliang99@163.com

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