Multidisciplinary approach for severe acute pancreatitis in a low-volume hospital.

Introduction:

Acute pancreatitis is one of the most frequent reasons for hospital admittance due to bilio-pancreatic diseases (1-2). The main etiologies of acute pancreatitis are biliary and alcohol consumption although in other cases the origin of the disease is unknown (3). Most of the patients have an uneventful course but up to 25 % of all patients with acute pancreatitis develop severe complications and are classified as severe pancreatitis with an associated death rate up to 30-50% (2-4).

Treatment of acute pancreatitis and in particular severe acute pancreatitis (SAP) has progressively evolved and improved. Probably one of the reasons for this improvement is the fact that step by step algorithms have been incorporated to the decision-making process (5-6). Similarly, a step-up approach has been proposed for pancreatic necrosis (7). In order to offer treatment in accordance to the severity of the disease, we need to obtain an accurate view of the expected evolution and prognosis. For that purpose, patients have to be stratified on the bases of standard classifications. One of the first classifications is the Ranson criteria that includes several laboratory and clinical data to obtain an estimated mortality (8-9). Radiological features observed on CT-scan that consider pancreatic necrosis and the appearance of the pancreas point out an estimated mortality rate (10). Simplified acute physiology score version 3 (SAPS 3) is a mathematical model that provides predicted mortality and is widely used in ICUs. It is a useful index for severely ill patients (11). The revised Atlanta classification of acute pancreatitis provides a graduation of two phases of the disease: early and late phases and severity is classified as mild, moderate or severe by using clinical and radiologic features (5-12).

As mortality of severe pancreatitis is usually high, patients are expected to undergo long intensive care unit (ICU) and hospital stay. Beside medical treatment for single or multiple organ failure, various complications may require percutaneous, endoscopic or surgical procedures. In some circumstances, major complications have to be addressed in order to improve outcomes in terms of morbid-mortality. Although surgical procedures are unlikely, surgery is required for abdominal sepsis due to hollow viscera necrosis/perforation or persistent abdominal sepsis spite medical treatment and percutaneous procedures (13). Compartment abdominal syndrome is associated to high complication and mortality rates. Failure of aggressive medical and non-operative treatment is expected to lead to surgery after multidisciplinary evaluation (6, 14, 15). Necrotizing pancreatitis with infected pancreatic necrosis is associated to high mortality rates. If a “Step-up” approach does not solve the pancreatic focus of sepsis by the means of percutaneous drainage among others, this approach may require to be completed by retroperitoneal access to pancreatic necrosis (6, 7). However early open access to the pancreatic necrosis has also been advocated (16). Considering that severe acute pancreatitis represents a challenging disease and may be associated to high mortality and morbidity rates as well as to high costs related to its treatment, it has been suggested to transfer patients to referral centres. The International Association of Pancreatology and the American pancreatic association IAP/APA guidelines recommend transferring patients with severe acute pancreatitis and those who may need interventional radiologic, endoscopic or surgical intervention to a specialist centre. This statement is based on a strong agreement with low quality of evidence. A specialist centre in the management of acute pancreatitis is defined as a high-volume centre with up-to-date intensive care facilities including options for organ replacement therapy, and with daily (i.e. 7 days per week) access to interventional radiology, interventional endoscopy with endoscopic ultrasound and endoscopic retrograde cholangiopancreatography assistance as well as surgical expertise in managing necrotizing pancreatitis. This recommendation is stated on weak agreement with low quality of evidence as there are no studies comparing requirements for specialist centres (6).

High-volume hospitals to treat acute pancreatitis have been defined based on a nation-wide American study that supports the idea of more than 118 patients per year (35). Similarly, a more recently nation-wide Japanese study finds better outcomes and length of stay for medium and severe pancreatitis in high-volume hospitals but there is still a lack of accuracy in terms of volume admittance (18).

We suggest that implementation of best practice guidelines and multidisciplinary protocols may also be important factors. The aim of this study is to expose the results of treatment of patients with severe acute pancreatitis in a low volume hospital with a multidisciplinary approach and a step-by-step comprehensive chart-flow design.

Materials and Methods:

This study is the result of a retrospective analysis from a prospectively sustained database. The main objective is to evaluate the results in single low-volume hospital in which a multidisciplinary approach, the use of best

practice guidelines and updated protocols that have been introduced for SAP from 2008 to 2018. Over this time frame, 1075 patients with the diagnosis of acute pancreatitis have been attended at our secondary level low-volume Hospital (19). Out of this group, 44 patients have been admitted to the ICU due to severe acute pancreatitis according to the revised Atlanta classification as well as the critical care society criteria for ICU admission based on general and/or local conditions (5-20). Total number of admissions to the ICU was 52 as some of the patients presented during the period of study more than one episode of SAP. All patients were classified as severe acute pancreatitis in accordance to the modified Atlanta classification (5). We used the SAPS 3 severity index to predict mortality and to assess patient's severity as well as the Ranson criteria for pancreatitis and the Balthazar computed tomography severity index (9-10). Criteria for ICU admission were determined by the modified Atlanta Classification, considering Ranson and Balthazar grades and the guidelines of the Society of Critical Care Medicine (20). Descriptive data of our group of study are shown in table 1. A multidisciplinary chart flow that includes ICU resources, gastroenterologists, radiologists and general surgeons was initiated and a daily decision-making process was activated (diagram 1).

Statistically analysis:
Quantitative variables are expressed as median and interquartile ranges due to the small sample size. Qualitative variables are described in absolute numbers and percentages.

Results:
All patients with required criteria were admitted to the ICU. General, hemodynamic and respiratory supports were supplied whenever needed. Patients were conservatively treated unless instability due to a septic abdomen (6 patients), pancreatic necrosis unsolved by other means (8 patients) or compartment abdominal syndrome (6 patients) was identified. In those cases, an urgent laparotomy was performed. 4 patients underwent right colectomy due to right colon necrosis and 1 patient was operated for duodenal perforation after ERCP. 1 patient was operated on due to biliary peritonitis caused by gallbladder perforated cholecystitis. In 6 patients a bilateral subcostal laparotomy with a mesh-mediated temporary abdominal closure was performed for compartment abdominal syndrome. 22 patients presented pancreatic necrosis; in those cases, a "step-up" approach was initiated. Among patients with pancreatic necrosis, 8 patients underwent retroperitoneoscopy and pancreatic necrosis debridement.
4 patients underwent a combination of retroperitoneoscopy for pancreatic necrosis and open abdomen for compartment abdominal syndrome. 25 patients underwent percutaneous drainage of abdominal or retro-peritoneal collections. 2 patients required percutaneous cholecystostomy for acute cholecystitis. In 17 patients a single drainage was sufficient and 8 patients required 2 or more drains or needed drain tube replacement. 8 patients underwent endoscopic retrograde cholangiopancreatography (ERCP) and 1 patient received trans-gastric retroperitoneal drainage with endoscopic prosthesis. 3 patients underwent urgent ERCP due to common bile duct obstruction and cholangitis less than 7 days after the onset of SAP. 2 patients received ERCP
for pancreatic fistula associated to peri-pancreatic collections and massive pleural effusion one month after the onset of SAP and one patient for pancreatic duct disruption. 2 patients underwent ERCP for peri-pancreatic collections not accessible percutaneously and 1 patient for sustained pancreatic leak after retro-peritoneoscopy and pancreatic necrosectomy (Diagram 2).
Oral intake was re-initiated as soon as possible according to patient´s condition and used instead of parenteral feeding. Naso-jejunal feeding tube was placed in 9 patients (21).
Abdominal hypertension was routinely monitored with the bladder method and the world society for the abdominal compartment syndrome (WSACS) recommendations were implemented in accordance to intra-abdominal pressure (22-23). Intra-abdominal hypertension (IAP) was defined into four grades by a sustained or repeated pathologic elevation of IAP $\geq$ 12 mmHg. Abdominal compartment syndrome (ACS) was defined as a sustained IAP > 20 mmHg with or without an abdominal perfusion pressure < 60 mmHg if associated with new organ dysfunction/failure. Whenever the patient was diagnosed of ACS, aggressive non-surgical strategy was started. In the circumstance of failure of non-surgical treatment, decompressive laparotomy and temporary abdominal wall closure was performed until improvement of the patient. Upon improvement of general and local conditions, definitive abdominal wall closure was carried out. Otherwise abdominal wall repair was postponed and performed on a latter surgical schedule.
4 patients died during the period of study (9,1 %). The cause of death was intra-operative massive non-contained bleeding associated to open retro-pancreatic drainage while performing a decompressive laparotomy due to ACS 48 hours after ICU admittance in one patient. One patient died on day 5 after the onset

of SAP due to failure of respiratory management in the context of ACS. The cause of death at the 11th of one patient was severe abdominal sepsis due to right colon ischemia. One patient died on day 6 as a consequence of ACS. All patients that died presented multi-organ failure and systemic inflammatory response syndrome. Median ICU stay was 8 days (4,5; 19,5) and median hospital stay was 15 days (10; 23).

Discussion:

Severe acute pancreatitis is associated to important morbidity and mortality and is a costly disease. There is a trend towards "step by step" approach for SAP to reduce those variables (6, 12, 24). Mortality has decreased in patients that have been offered less-invasive approaches compared to previous strategies (25). Similarly, Treatment of pancreatic necrosis has evolved from open necrosectomy to less aggressive surgical strategy defined as "step-up" approach (7, 26, 27).

We have defined a "step by step" diagram flow (diagram 1) starting with the less aggressive procedure available. Upon patient's evolution, supplementary procedures where considered. If clinical and radiological conditions didn't evolve satisfactorily a percutaneous drain was inserted both for intra-abdominal and retro-peritoneal infected collections with ultrasound or CT-scan control (28, 29). Drains were replaced if necessary. In the case of abdominal infected collections or retroperitoneal infected necrosis on the onset of sepsis an aggressive approach was initiated. In patients with walled of necrosis or retro-peritoneal abscess without improvement after percutaneous drain, retro-peritoneoscopy and necrosectomy was performed (30). In those cases, the access to the retroperitoneal space was guided by a percutaneous drain placed under CT-scan control in the area identified as more accessible (11). Drains for continuous lavage were inserted as well along this procedure. Even though endoscopic management for pancreatic necrosis has been recently used depending on the location of the pancreatic necrosis it is still not standard of care (31, 32). We have performed such procedure in one patient. Intra-abdominal hypertension, which is relatively common in severe acute pancreatitis, may lead to abdominal ACS (33). ACS is a life-threatening event that has to be addressed to prevent deleterious effects (34). In our group of patients, abdominal hypertension was routinely monitored and specific management initiated (23, 35). Once ACS was diagnosed, medical treatment with initiated with hollow viscera decompression by the means of naso-gastric or rectal catheter or colonoscopy. Percutaneous drainage was used to decrease intra-abdominal volume whenever intra-abdominal collections were identified. If ACS presented no response non-surgical approach, decompressive laparotomy with temporary abdominal closure was indicated (22, 36). Some patients may present abdominal sepsis related to colon ischemia and/or hollow viscera perforation. In those circumstances urgent surgical treatment was performed. We limited access to the retroperitoneal space to minimise the risk of massive retro-peritoneal bleeding if walled of necrosis was not assured. Early oral nutrition has been shown to have beneficial effects in terms of morbidity and mortality among patients with severe acute pancreatitis (6). Oral intake was promoted as soon as possible and a naso-jejunal feeding tube whenever oral intake was not sufficient.

As far as we know, two studies have shown impact of hospital volume on the outcomes of acute pancreatitis (37, 38). High-volume hospital has been defined based on a nation-wide American study that supports the idea of more than 118 patients per year (37). This study based on a very large number of patients concluded that high-volume hospitals admit most of the patients with acute pancreatitis and that those hospitals had a shorter length of stay, lower hospital charges and lower mortality rate but did not stratify patients regarding severity of pancreatitis. Similarly, a more recently nation-wide Japanese study demonstrated that hospital volume influenced mortality in both patients with mild and those with severe acute pancreatitis in high-volume hospitals (38). This study did not use standard severity scores for acute pancreatitis in all cases. Even if bias related to patient distribution was balanced, this study showed that elderly patients were more frequently treated in low-volume hospitals. Although both studies demonstrate a clear relationship between hospital volume and better outcomes for acute pancreatitis, they do not consider the treatment strategies provided, in particular step-up-approach for pancreatic necrosis.

The International Association of Pancreatology and the American pancreatic association IAP/APA guidelines recommend transferring patients with severe acute pancreatitis and those who may need interventional radiologic, endoscopic or surgical intervention to a specialist centre. This statement is based on a strong agreement with low quality of evidence. A specialist centre in the management of acute pancreatitis is defined as a high-volume centre with up-to-date intensive care facilities including options for organ replacement therapy, and with daily (i.e. 7 days per week) access to interventional radiology, interventional endoscopy with endoscopic ultrasound and ERCP assistance as well as surgical expertise in managing necrotizing

pancreatitis. This recommendation is stated on weak agreement with low quality of evidence as there are no studies comparing requirements for specialist centres (6).
Although our institution is considered to be a low-volume hospital, it is important to highlight that we provide treatment based on a multidisciplinary chart flow, best practice based on international guidelines and streamlined processes of care. Standard care for SAP has evolved over the years and it could be arguable that previous studies based on hospital volume have considered strategies that may not have included step-by-step strategies. Although low-volume hospitals are likely to have scarcity of resources in comparison with high-volume, implementation of comprehensive and updated protocols for SAP has not been evaluated so far.
This study has several limits: first of all, it is a small sample of patients. This is a cause and a consequence as our hospital is defined as a low-volume institution. Secondly, it is a retrospective analysis of a prospectively conducted database. As it is not a comparative study, we only can draw suggestions. However, this study takes into account all the cases of SAP over a large period of time. One way to solve this small number of patients would probably be to perform such study with on a multicentre base among small-volume hospitals and compare with high-volume hospitals in terms of mortality, morbidity, length of stay and costs. Despite those limitations we have evaluated the results of a prospectively sustained database in a single low-volume hospital. All decisions regarding treatment were obtained on the basis of a multidisciplinary decision-making process. In our study group, we have found a mortality rate (9,1%) which is comparable to other studies (2, 4, 39).

Conclusion:
Severe acute pancreatitis represents a complex pathology that usually requires multidisciplinary approach. Establishing best practice treatment and evidence-based guidelines for severe acute pancreatitis may improve outcomes in low-volume hospitals.

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