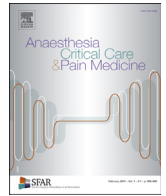




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Editorial

Improving the management of severe acute pancreatitis: The new guidelines from the French Society of Anaesthesia and Intensive Care Medicine



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Acute pancreatitis incidence has increased over the last decade and is affecting 48/100,000 inhabitants in UK and 275,000 patients per year in USA [1,2]. Necrotising pancreatitis develops in 20 to 30% of patients with acute pancreatitis and is associated with a hospital mortality above 20% [3]. Early recognition of the patients at risk of developing organ dysfunction is therefore mandatory in order to offer early adequate supportive care [4].

In the current issue of *Anaesthesia Critical Care and Pain Medicine*, the French Society of Anaesthesia and Intensive Care Medicine (SFAR), in collaboration with French societies of Gastroenterology, Surgery, Radiology, Nutrition and Digestive endoscopy, is providing an important update in the guidelines for the management of severe acute pancreatitis (SAP) [5]. The recommendations have been established by a group of 22 experts. Using the rules of the Grading of Recommendation Assessment, Development and Evaluation (GRADE) system each question was formulated in a Patients Intervention Comparison Outcome (PICO) format. Fourteen questions were studied and classified in three fields according to the natural history of the disease: evaluation and admission to ICU, treatment during the initial toxic phase, treatment and management of the later complications. Finally, the experts' work resulted in 24 recommendations with a vast majority of high and moderate levels of evidence.

The management of the severe forms of necrotising pancreatitis is typically a team process involving various specialists that will have to intervene at various steps, as this disease process is associated with multiple complications. It is therefore needed to have a general consensus and guidelines to help this team process for offering the best care to the patients and reduce the associated morbidity and mortality.

The new guidelines proposed by SFAR are clarifying multiple unresolved questions and are providing to critical care physicians the most recent update in the management of SAP.

1. At admission

One of the first steps after admission for SAP is to triage patients and detect those at risk of developing organ dysfunction and extensive necrosis. The first recommendation provides the clinical signs as radiological and biological criteria to orient patients to ICU or to the general ward. Multiple scoring systems are available but none of them is sufficiently predictive for severity with the possible exception of the haematocrit at admission [6]. The timing of imaging, in particular contrast enhanced CT-scan, has for long been a matter of debate and if performed too early believed to underestimate the necrosis extension. Here, early abdominal CT-scan is recommended mainly in the context of diagnostic uncertainty.

2. First days

Two important aspects of the early care of SAP have been emphasised. Firstly, intra-abdominal pressure (IAP) needs to be monitored in ventilated patients. The incidence of intra-abdominal hypertension (IAH) is elevated in SAP and associated with a significant increase in mortality [7]. The hyperpermeability observed in the more severe forms together with the administration of large amounts of fluids are the main risk factors of IAH. Secondly, the former observation is guiding the recommendation on the initial fluid resuscitation. Large amounts of crystalloids have often been proposed to improve pancreas perfusion, reduce the extension of the necrosis and the incidence of organ dysfunction. The quality of studies on the optimal amount of fluid to be given during the first days is limited. A recent meta-analysis was unable to demonstrate the benefit of aggressive fluid resuscitation [8]. The appropriate recommendation made by SFAR is to not systematically indicate volume from 3 to 5 mL (kg/h) during the first 24 hours. Volume loading should be individualised and closely monitored to prevent volume overload and IAH.

The nutritional approach in SAP has been adapted in the new recommendations. While it is clearly accepted that enteral nutrition is reducing the infectious complications and mortality compared with total parenteral nutrition [9], the timing, route of administration and the choice of enteral formula have been more often debated. Early nutrition within the first 2–3 days after admission, the use of semi-elemental mixtures and enteral

immuno-nutrition have not demonstrated a benefit on outcome, infectious complications and ICU stay [10]. A new recommendation is the intravenous administration of L-glutamine as a complement to total parenteral nutrition, if enteral nutrition is not tolerated or contraindicated, to reduce morbidity and mortality. This strong recommendation is supported by a series of meta-analysis [11,12].

In the context of acute biliary pancreatitis, endoscopic retrograde cholangiopancreatography performed within the first 72 h has for long been indicated to improve outcome. This early intervention, in the absence of ascending cholangitis, is no longer mandated since not associated with a benefit on morbidity and mortality [13].

Hypertriglyceridaemia-induced SAP management has never been definitely defined. The combinations of insulin and heparin are often able to lower triglycerides plasma levels, yet, when sustained elevated levels of triglycerides are maintained the strong agreement from experts is to initiate therapeutic plasma exchange despite the absence of randomised controlled trials showing a mortality reduction. It is indeed difficult to compare standard of care with plasma exchange when the former intervention has often been indicated for the most severe forms [14].

3. Pancreas necrosis monitoring

Infection of the pancreatic necrosis is the most common complication after the initial toxic phase of SAP and associated with increased mortality. Prophylactic antibiotics administration to prevent this complication is no longer debated since not demonstrated to reduce pancreas infection, the need for necrosis drainage or surgery or to improve outcome [15].

The experts here had a strong agreement on the use of clinical signs and abdominal CT-scan to suspect or suggest the diagnosis of infected pancreatic necrosis rather than the use of fine-needle aspiration as associated with too many false negative diagnoses. In the context of infected necrosis, the use of systemic antimicrobials alone is not sufficient to reduce mortality and a step-up to reduce control the source of infection is confirmed in these recommendations.

It seems also important to follow one of the expert opinion and recommendation. The management of infected necrosis requires a multi-disciplinary team. In the absence of sufficient resources, patients requiring an infection source control should be referred to large centres with expertise in this field.

The antimicrobial selection cannot easily be recommended as the patient may develop early or late infection and may have received previous antimicrobial therapy with an impact on its bacterial flora and resistance. However, the experts recommend here to target resistant enterobacteriaceae, *Enterococcus faecium*, *Pseudomonas aeruginosa* and yeast according to the most recent data on microbiology in SAP [16]. What remains unresolved at this stage is the duration of antibiotic treatment according to the presence or absence of infected necrosis drainage.

4. Vascular complications

The second most feared complications in the later stages of SAP are bleeding and thrombotic events. While bleeding phenomena are often caused by the development of pseudoaneurysms and are to be treated first by endovascular interventional radiology, the prevention and treatment of thrombotic events is more difficult to define. Splenic vein thrombosis is quite common in SAP and in general with little clinical consequences, while portal vein thrombosis in the context of infected necrosis is associated more

often with a poor outcome. At this stage, there is no clear demonstrated recommendation in the use of therapeutic anticoagulation to prevent thrombotic events in SAP in order to improve survival.

5. Conclusion

The recommendations in the management of SAP made by SFAR should definitely help clinicians in their daily practice and are expected to improve the quality of care and the outcome in this difficult-to-treat population.

Disclosure of interest

P.-F.L. is consultant at Inotrem and Adrenomed. C.C. declares that she has no competing interest.

References

- [1] Spagnolo D, Greer P, Ohlsen C, Mance S, Ellison M, Breze C, et al. Acute and chronic pancreatitis disease prevalence, classification, and comorbidities: a cohort study of the UK BioBank. *Clin Transl Gastroenterol* 2022;13(1):e00455.
- [2] Peery A, Crockett S, Barritt A, Dellon E, Eluri S, Gangarosa L, et al. Burden of gastrointestinal, liver, and pancreatic diseases in the United States. *Gastroenterology* 2015;149(7) [1731–1741.e3].
- [3] Mederos M, Reber H, Girgis M. Acute pancreatitis: a review. *JAMA* 2021;325(4):382–90.
- [4] Thapa R, Iqbal Z, Garikipati A, Siefkas A, Hoffman J, Mao Q, et al. Early prediction of severe acute pancreatitis using machine learning. *Pancreatology* 2022;22(1):43–50.
- [5] Jaber S, Garnier M, Asehounne K, Bounes F, Buscaill L, Chevaux JB, et al. Guidelines for the management of patients with severe acute pancreatitis. *Anaesth Crit Care Pain* 2022;41(3):101059.
- [6] Koutroumpakis E, Wu B, Bakker O, Dudekula A, Singh V, Besselink M, et al. Admission hematocrit and rise in blood urea nitrogen at 24 h outperform other laboratory markers in predicting persistent organ failure and pancreatic necrosis in acute pancreatitis: a post hoc analysis of three large prospective databases. *Am J Gastroenterol* 2015;110(12):1707–16.
- [7] van Brunschot S, Schut AJ, Bouwense SA, Besselink MG, Bakker OJ, van Goor H, et al. Abdominal compartment syndrome in acute pancreatitis: a systematic review. *Pancreas* 2014;43(5):665–74.
- [8] Gad MM, Simons-Linares CR. Is aggressive intravenous fluid resuscitation beneficial in acute pancreatitis? A meta-analysis of randomized control trials and cohort studies. *World J Gastroenterol* 2020;26(10):1098–106.
- [9] Yao H, He C, Deng L, Liao G. Enteral versus parenteral nutrition in critically ill patients with severe pancreatitis: a meta-analysis. *Eur J Clin Nutr* 2018;72(1):66–8.
- [10] Bakker OJ, van Brunschot S, van Santvoort HC, Besselink MG, Bollen TL, Boermeester MA, et al. Early versus on-demand nasoenteric tube feeding in acute pancreatitis. *N Engl J Med* 2014;371(21):1983–93.
- [11] Asrani V, Chang WK, Dong Z, Hardy G, Windsor JA, Petrov MS. Glutamine supplementation in acute pancreatitis: a meta-analysis of randomized controlled trials. *Pancreatol* 2013;13(5):468–74.
- [12] Jafari T, Feizi A, Askari G, Fallah AA. Parenteral immunonutrition in patients with acute pancreatitis: a systematic review and meta-analysis. *Clin Nutr* 2015;34(1):35–43.
- [13] Schepers NJ, Hallensleben ND, Besselink MG, Anten MGF, Bollen TL, da Costa DW, et al. Urgent endoscopic retrograde cholangiopancreatography with sphincterotomy versus conservative treatment in predicted severe acute gallstone pancreatitis (APEC): a multicentre randomised controlled trial. *Lancet* 2020;396(10245):167–76.
- [14] Samarasinghe S, Avari P, Meeran K, Cegla J. Management of hypertriglyceridaemic pancreatitis in the acute setting and review of literature. *BMJ Case Rep* 2018;11(1).
- [15] 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(5):674–83.
- [16] Lu JD, Cao F, Ding YX, Wu YD, Guo YL, Li F. Timing, distribution, and microbiology of infectious complications after necrotizing pancreatitis. *World J Gastroenterol* 2019;25(34):5162–73.

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