CONSENSUS STATEMENT

SEMICYUC 2012. Recommendations for intensive care management of acute pancreatitis

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Recommendations

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1 For the jury and member list, see Annex A of the additional material.
Abstract
Objective: Significant changes in the management of acute pancreatitis have taken place since the 2004 Pamplona Consensus Conference. The objective of this conference has been the revision and updating of the Conference recommendations, in order to unify the integral management of potentially severe acute pancreatitis in an ICU.

Participants: Spanish and international intensive medicine physicians, radiologists, surgeons, gastroenterologists, emergency care physicians and other physicians involved in the treatment of acute pancreatitis.

Levels of evidence and grades of recommendation: The GRADE method has been used for drawing them up.

Drawing up the recommendations: The selection of the committee members was performed by means of a public announcement. The bibliography has been revised from 2004 to the present day and 16 blocks of questions on acute pancreatitis in an ICU have been drawn up. Firstly, all the questions according to groups have been drawn up in order to prepare one document. This document has been debated and agreed upon by computer at the SEMICYUC Congress and lastly at the Consensus Conference which was held with the sole objective of drawing up these recommendations.

Conclusions: Eighty-two recommendations for acute pancreatitis management in an ICU have been presented. Of these 84 recommendations, we would emphasize the new determinants-based classification of acute pancreatitis severity, new surgical techniques and nutritional recommendations.

Note. This summary only lists the 84 recommendations of the 16 questions blocks except blocks greater relevance and impact of its novelty or because they modify the current management.

The full document, in Spanish and English, references, tables and list of authors is available on-line (additional material): http://dx.doi.org/10.1016/j.medin.2013.01.007.
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PALABRAS CLAVE
Pancreatitis; Cuidados intensivos; Guías de práctica clínica

SEMICYUC 2012. Recomendaciones para el manejo en cuidados intensivos de la pancreatitis aguda

Resumen
Objetivo: Se han producido grandes cambios en el manejo de la pancreatitis aguda desde la Conferencia de Consenso de Pamplona 2004. El objetivo ha sido revisar dichas recomendaciones y actualizarlas, para uniformizar el manejo integral de la pancreatitis aguda potencialmente grave en la UCI.

Participantes: Médicos intensivistas nacionales e internacionales, radiólogos, cirujanos, gastroenterólogos, médicos de los servicios de urgencias y otros médicos implicados en el tratamiento de la pancreatitis aguda.

Niveles de evidencia y grados de recomendación: Se ha seguido el método GRADE para su elaboración.

Elaboración de las recomendaciones: La elección de jurados y vocales se realizó mediante convocatoria pública. Se ha realizado la revisión bibliográfica desde 2004 hasta la actualidad, y se han elaborado 16 bloques de preguntas sobre el manejo de la pancreatitis aguda en la UCI. Primeramente se han trabajado las preguntas por grupos, para posteriormente elaborar un documento único. Dicho documento se ha discutido y consensuado por vía informática, en el Congreso de la SEMICYUC, y finalmente en la Conferencia de Consenso realizada expresamente para su elaboración.

Conclusiones: Se han descrito 82 recomendaciones para el manejo de la pancreatitis aguda en la UCI. De ellas destacaríamos la nueva clasificación de la pancreatitis aguda basada en determinantes evolutivos, las nuevas técnicas quirúrgicas y las recomendaciones nutricionales.

Nota. En este resumen solamente se enumeran las 84 recomendaciones de los 16 bloques de preguntas, excepto los bloques de mayor relevancia e impacto por su novedad o porque modifican el manejo habitual.

El documento completo, en versión española e inglesa, referencias bibliográficas, tablas y relación de autores se puede consultar on-line (material adicional): http://dx.doi.org/10.1016/j.medin.2013.01.007.
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Justification of the consensus conference

Acute pancreatitis (AP) management has changed in recent years, thanks to a better understanding of physiopathology, the improvement of therapeutic armamentarium in Intensive Care Units, advances in nutritional support in acute pancreatitis, dynamic approaches of continuous extra renal replacement techniques (TCRR –TCDE), acknowledgement of the central role of pancreatic infection, and improvements in surgical techniques.

While the pathways for AP in an Intensive Care Unit (ICU) were published, the Committee realized that many aspects of ICU management were suboptimal and out-of-date. In particular, the lack of uniformity in applying the AP severity criteria is evident and that could be one of the reasons for different mortality rates between the studies. We also agree with Dr. Petrov and colleagues that the classification of AP should be based on actual severity factors rather than predicted factors. The new international classification of AP stresses the importance of defining the severity only on the basis of factors that determining the natural course: (peri) pancreatic necrosis and organ failure (OF).

Further, some of the recommendations of the Severe Acute Pancreatitis (SAP) Consensus Conference of the Spanish Society of Intensive Medicine and Coronary Units–SEMICYUC 2004 had changed, and other emerging recommendations provided basis for the current revision and update of the guidelines. Taking these arguments into account, the AP Pathways Study Group of the SEMICYUC initiated the update of recommendations for AP patients hospitalized in an ICU.

The objective of this new project is to revise recommendations for management of AP in Intensive Medicine.

Methodology and design

General description of the process

The organizing committee for the new edition of the AP recommendations designed the project, organization, the subcommittee (in multidisciplinary working groups composed of specialists in Emergencies, Digestive Medicine, Radiology, General Surgery and Intensive Medicine), the reference terms and the development of an adaptation plan and the writing up of the recommendations. In addition, the Consensus Conference was presented with the collaboration of SEMICYUC at the XLVI National SEMICYUC Congress held in Santander (Spain) in 2012. Lastly, an international meeting was held, in line with the regulations of the Society, in order to officially present these recommendations in Madrid on 30th October 2012.

The group has decided to use the existing recommendations on the treatment of severe AP and adapt them to the needs of the target population, using the GRADE method in adapting the ACCP (American College of Chest Physicians) articles, due to their applicability and simplicity, although similar versions exist.

The GRADE method (Table 1) classifies the recommendations according to:

<table>
<thead>
<tr>
<th>Grades of recommendation</th>
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<tr>
<td>According to the balance between benefits, risks, costs and potential workloads:</td>
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<td>• Grade 1: Strong recommendation, or</td>
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<td>• Grade 2: Weak recommendation.</td>
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<tr>
<td>• No grade: There is no recommendation in this regard.</td>
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Quality of evidence

The system classifies the quality of the evidence in accordance with the factors that include study design, the consistency of the results, and the availability of evidence, as follows:

<table>
<thead>
<tr>
<th>Evidence</th>
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<td>A: Higher,</td>
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<td>B: moderate, or</td>
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<td>C: low.</td>
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Revision and analysis of the literature

Electronic search in MEDLINE, SCOPUS and EMBASE from 2004 to September 2012 of the literature regarding "severe acute pancreatitis" and everything related to the questions that had been posed.

Development of the consensus based on the evidence

The working group decides to use the 2004 Pamplona Recommendations on the treatment of severe acute pancreatitis and update them to 2012 by using the GRADE method.

Guideline and conflicts of interest

No limitations on conflicts of interest were identified.

Definitions and abbreviations used

(See on-line full version). The definitions and complications of the illness are summarized in each chapter and in the subsequent tables that are shown in this document and in the 2011 AP Pathways (7).

1st Question: Diagnosis of Acute Pancreatitis in Emergency Services. (Summary version only. Complete version on-line)

Recommendation 1. Diagnosis of acute pancreatitis: At least two of the following criteria should be present. Strong grade of recommendation (1), high quality of evidence (A).
- Abdominal pain suggesting pancreatitis, which is a symptom considered at the onset of acute pancreatitis.
- Levels of lipase and/or amylase in serum which are three or more times greater than the normal value.
- Characteristic findings in CT or ultrasound studies.
2nd Question: Classification of Acute Pancreatitis. (Complete version)

Early identification of severity signs in a patient with AP during the first three days following hospital admission has been shown to improve the prognosis and reduce mortality (7). For this reason, prompt classification of severity is necessary. For this purpose, a new AP classification was drawn up in 2012 (8), which is based on two fundamental principles:

First, it is based on real severity factors instead of predictive factors. The use of systems with multifactorial scoring (APACHE II, Ranson criteria, Imrie-Glasgow criteria, etc.) which had been utilized in the original Atlanta classification complicates the situation and has little clinical applicability because of misclassification error in 30–40% of patients. Consequently, the identification of early persistent OF markers and pancreatic alarm signs defined later on (7) is important.

Second, the new classification defines the severity only on the basis of the determining factors of the patient’s progress: pancreatic (peri) necrosis and organ failure (OF). The three most frequent and determining OFs in the patient’s progress are cardiovascular, renal and respiratory(16). The appearance of any one of them is sufficient for determining the severity.

The definitions used for the severity categories in the new classification are based on the characteristics of the "local determinants" (lack of, or sterile or infected peri/pancreatic necrosis) and "systemic determinant" (insufficiency of a lacking, transitory or persistent organ), as well as the possibility of interaction among the determining factors during the same AP episode. Clinical or analytical parameters other than these determinants should not be used to classify severity of AP.

Definitions

- **Mild Acute Pancreatitis (MiAP)** is characterized by the absence of both pancreatic (peri) necrosis and organ failure.
- **Moderate Acute Pancreatitis (MAP)** is characterized as the presence of any type of sterile pancreatic (peri) necrosis and/or transient organ failure.
- **Severe Acute Pancreatitis (SAP)** is characterized as the presence of any degree of infected pancreatic (peri) necrosis or persistent organ failure.
- **Critical Acute Pancreatitis (CAP)** is characterized as the presence of infected pancreatic (peri) necrosis and persistent organ failure.
- **Transitory organ failure**. Data on an OF that are resolved in a short period of time after having applied adequate support measure.
- **Transitory organ failure**. Data on an OF that are not resolved in a short period of time after having applied adequate support measures.

The authors of the new international multidisciplinary classification define transitory or persistent as an OF that is not resolved in less or more than 48 h, although we believe that this deadline is too long for certain OFs and we adopted the definition of Sepsis Surviving Campaign.17

Definition of organ failure

- **Hypotension.** Systolic arterial pressure (SAPS) less than 90 mmHg or a reduction of 40 mmHg in basal SAP, with tissular hypoperfusion signs (lactate >3 mMol/L); Saturation of central venous oxygen ScVO2 < 70%.
- **Respiratory failure.** PaO2 < basal 60 mmHg (with supplementary O2); or PaO2/FiO2 < 300 mmHg.
- **Acute renal failure.** an increase of basal creatinine by 2 (AKI-2, o RIFLE-I) and/or reduction of urinary flow (oliguria) <0.5 ml/kg/h x 12 h.

Another classification has also been proposed that suggests dividing AP into three categories18-22:

- **Mild AP.** AP without complications or organ failure.
- **Moderate AP.** AP with local complications and without organ failure;
- **Severe AP.** AP with organ failure, with or without local complications.

Although both classifications have similarities,23 the Committee advocates the classification with four categories of severity as it emphasizes the worst-case prognosis of the relationship of organ failure and pancreatic infection, as compared to organ failure without pancreatic infection,24,25

**Recommendation 2.** We recommend to discontinue the use of the Atlanta classification. Strong grade of recommendation (1), high quality of evidence (A).

**Recommendation 3.** We recommend the use of the 2012 "determinant-based" international multidisciplinary classification of AP that classifies AP on the basis of four different levels and is based on the appearance or non-appearance of organ failure and local complications: MiAP=lack of pancreatic (peri) necrosis and without OF; MAP=presence of any type of sterile pancreatic (peri) necrosis or transitory OF; SAP=presence of any grade of infected pancreatic (peri) necrosis or persistent OF; y CAP=presence of infected pancreatic (peri) necrosis or persistent OF and persistent OF. Strong grade of recommendation (1), moderate quality of evidence (B).

3rd Question: Organization for integral acute pancreatitis management. Protocolized management. (Complete version)

Different AP treatment guides have been published in the last several years. A variety of medical specialists have contributed to these guides which have been drawn up in a multidisciplinary way. Many of these guides recommend that patients in severe stages of this illness be treated in hospitals with prior experience in treating this illness and that they should have a multidisciplinary team of physicians to handle AP26-29. The so-called "solitary AP" syndrome, which is defined as an AP patient who is left unattended in a waiting room without subsequent monitoring. Hospitals in Spain have AP Pathways with a multidisciplinary approach ensuring that an AP patient who is admitted to a hospital receives adequate treatment (7).
Nonetheless, we do not know of any study that compares protocolized and multidisciplinary treatment of AP to treatment according to clinical criteria followed by the acting physician.

A recently published study indicates that of the 49 hospitals surveyed in Sweden, only 25 (51%) had a standardized protocol treatment, although most of them are interested in participating in an AP register. According to another study performed in Great Britain, Ireland and Canada, only 33.5% of the hospitals covered by the study had a multidisciplinary team for AP treatment. Another two studies showed a very low level of compliance with the principal measures of the treatment guides, although another study indicated a notable improvement.

To summarize, medical societies prepare treatment guides for multidisciplinary treatment, recommend the creation of specialized teams and the drawing up of AP management protocols, although the clinical impact has yet to be measured. In addition, the level of compliance on an International scale has been poor.

Since AP is an illness where a range of medical specialists are involved in its treatment, with a complex, prolonged and unpredictable patient recovery, we recommend that the patients in complicated stages of AP be referred to hospitals with multidisciplinary teams for AP management, and these hospitals should draw up their own protocol based on the recommendations made by the local medical societies.

**Recommendation 4.** We recommend that patients with MAP, SAP, and CAP be treated in hospitals with known expertise in AP treatment and that they have multidisciplinary teams for treating AP patients: Emergency Treatment, Digestive Medicine (with experienced endoscopy technicians), Radiology (with computerized tomography and invasive radiology), Biliary-pancreatic Surgery, Internal Medicine and Intensive Medicine. Otherwise, patients with MAP, SAP and CAP should be referred to a specialized hospital. Strong grade of recommendation (1), low quality of evidence (C).

**Recommendation 5.** We recommend that hospitals treating patients with MAP, SAP and CAP prepare pathways in a multidisciplinary way for AP treatment based on the recommendations made by the local medical societies and suitable to their resources. Strong grade of recommendation (1), low quality of evidence (C).

**4th Question: Criteria for early admission to an Intensive Care Unit - New concepts.** (Complete version)

- "Pancreatic alarm signs", versus previous early severe criteria. In Emergency Services, Digestive Medicine, ICU and others.
- Potentially severe acute pancreatitis - PSAP
- Assessment criteria and admission of PSAP patients in an ICU.

A new dynamic and evolutionary classification and assigning a category of severity (especially SAP and CAP) is therefore "a posteriori". This is a potential disadvantage of the new classification, since it is impossible to diagnose MAP, SAP, and CAP upon patient admission to the hospital (7). Consequently, from a practical standpoint, we introduced the concept of "Potentially severe acute pancreatitis" (PSAP). To summarize, we define PSAP as a form of acute pancreatitis that presents one or more organ failures (arterial hypotension, respiratory problems, renal) or alarm signs (7) and it is useful for initial patient management.

At the same time, some of the previously published severity criteria (9) indicate that patients may fail to recover satisfactorily and we call these criteria "alarm signs". The alarm signs are those forms of data or symptoms/signs in an AP patient that indicate a possible failure to recover satisfactorily and these signs can be of a clinical, radiological or analytical nature or prognostic scales that were enumerated in the Atlanta classification.

The pancreatic alarm signs are the following (7):

- **Clinical:** obesity, age, abdominal defenses, pleural effusion, alteration of consciousness.
- **Analytical:** C-reactive protein (CRP) > 150 mg/L, or a progressive increase in 48 h; Hematocrit > 44%, Procalcitonin greater than 0.5 mg/ml during the first 24 hours.
- **Radiological:** pleural effusion, free peritoneal fluid.
- **Prognosis scales:** APACHE II > 8; APACHE-0 > 6; Ranson-Glasgow > 3 points.

There is increasing evidence that any delay in reviving the patient, especially in the supply of volume, has a negative impact on AP patient recovery. For this reason, we recommend the early detection of AP patients that are developing OF in order to revive the patient with the best material and human resources, according to the structure of each hospital. Reviving the AP and OF patients should be performed early, managed according to objectives and continuously monitored. Since postponing the treatment has a negative impact on the patient’s recovery, and current clinical, radiological, and analytical markers show low sensibility and specificity (21), we suggest that AP patients receive a clinical, protocolized analytical, and regular follow-up during the first 72 h for early detection of OF and commencing energetic treatment a quickly as possible (7). In other words, "solitary AP" syndrome should be avoided. This term is defined as an AP patient who is left unattended in a waiting room for the first several hours, without being subjected to a well-defined protocol or pathways or subsequent monitoring.

The major factor in AP patient recovery is the existence or non-existence of OF, especially if it persists for a long period of time. For this reason, all the patients with OF who do not respond to the initial support measures should be admitted to Intensive Care Service.

The development of pancreatic infectious complications is the second major factor in AP patient recovery, especially infected necrosis (18, 19, 43, 45). The appearance of a pancreatic infection without OF indicates a morbi-mortality which is much less than if it had been associated with an OF. We recommend close monitoring of patient recovery and quick admission of patients with pancreatic infection associate with OF to the Intensive Medicine Service.
**Recommendation 6.** We suggest using the category of PSAP for patients with either OF or an alarm sign at the onset of patient recovery, presuming that transitory or persistent organ failure or pancreatic infection will appear. Strong grade of recommendation (1), low quality of evidence (C).

**Recommendation 7.** We recommend the detection and early treatment of AP patients who are developing OF in order to initiate invasive measures to revive the patient as soon as possible. Strong grade of recommendation (1), high quality of evidence (A).

**Recommendation 8.** We recommend admitting patients who are developing OF and who do not respond to initial measures to revive them to an ICU. Strong grade of recommendation (1), high quality of evidence (A).

**Recommendation 9.** We recommend admitting patients with pancreatic infectious complications associated with OF to an ICU. Strong grade of recommendation (1), high quality of evidence (A).

### 5th Question: Biomarkers. Inflammatory and Infection Markers. (Summary version only. Complete version on-line)

**Recommendation 10.** The decision to use CRP within 48 hours from the onset of symptoms with a cutoff value of 150 mg/L could help to identify promptly those patients that develop AP in its complicated stages. Strong grade of recommendation (1), moderate quality of evidence (B).

**Recommendation 11.** IL6 is a reliable and early predictor of severity in the first 24 hours following patient admission. Strong grade of recommendation (1), moderate quality of evidence (B).

**Recommendation 12.** PCT is an early severity marker in the first 24 hours following patient admission with a cutoff value of 0.5 ng/mL. Strong grade of recommendation (1), low quality of evidence (C).

**Recommendation 13.** The increase of PCT with values greater than 1.8 ng/mL in the developing phase of pancreatitis may prove useful for distinguishing between sterile pancreatic necrosis and infected pancreatic necrosis. Strong grade of recommendation (1), moderate quality of evidence (B).

### 6th Question: Role of Radiology in acute pancreatitis. Diagnosis of infected necrosis. Percutaneous Drainage. (Summary version only. Complete version on-line)

#### Role of radiology in acute pancreatitis

**Recommendation 14.** Abdominal CT with IV contrast is not indicated for all AP patients, but only for PSAP patients. Strong grade of recommendation (1), moderate quality of evidence (B).

**Recommendation 15.** The following are considered severe alarm criteria of AP: the existence of pancreatic necrosis (defined as the lack of glandular enhancement with iodinated IV contrast) and/or the presence of peripancreatic collections (Grades D and E by CT of the Balthazar Index).

Strong grade of recommendation (1), moderate quality of evidence (B).

**Recommendation 16.** Abdominal CT with IV contrast is to be performed in the first 24 h in those cases with an uncertain diagnosis. For an accurate assessment of pancreatic necrosis, the best option is to perform the CT between 48 and 72 h from the onset of the outbreak. Strong grade of recommendation (1), moderate quality of evidence (B).

**Recommendation 17.** MRI is a good alternative to CT in patients who are allergic to iodinated contrast or who suffer from renal insufficiency. Weak grade of recommendation (2), moderate quality of evidence (B).

### Diagnosis of infected necrosis. Fine-needle aspiration

**Recommendation 18.** If there is a suspicion of pancreatic necrosis, infection and/or of pancreatic collections abdominal fine needle puncture should be performed for diagnostic purposes, directed by either ultrasound or CT. Strong grade of recommendation (1), moderate quality of evidence (B).

**Recommendation 19.** Given that there is a 10% risk of false negatives with the use of FNA, it should be repeated if the clinical suspicion of infection persists. Weak grade of recommendation (2), low quality of evidence (C).

#### Percutaneous drainage. Acute fluid collections/pseudocysts

**Recommendation 20.** We advise drainage (internal-external endoscopic drainage or percutaneous drainage) in the following cases: a) Acute fluid collections or infected pseudocysts, b) if there is clinical pain or biliary obstruction. The choice of one or another technique is based on the anatomical characteristics of the collections, the availability of personnel to perform the technique and experience in performing it. Strong grade of recommendation (1), low quality of evidence (C).

**Recommendation 21.** We recommend the drainage of infected collections only. Strong grade of recommendation (1), moderate quality of evidence (B).

### Infected necrosis

**Recommendation 22.** In patients with high surgical risks, a percutaneous drainage of infected necrosis is recommended prior to surgery. The main objective of percutaneous drainage is control of the sepsis. It is considered a technical "bridge" until a more permanent treatment can be administered, because it can be beneficial for patients whose severe condition prevents them from having any type of necrosectomy. It is also worth mentioning that up to 50% of patients with infected necrosis who have been treated with percutaneous drainage survive without the need for subsequent surgery. Weak grade of recommendation (2), moderate quality of evidence (B).
7th Question: antiproteases and continuous arterial regional infusion. (Summary version only. Complete version on-line)

Is the continuous intravenous administration of protease inhibitors useful in the treatment of SAP?

Is regional intra-arterial infusion of protease inhibitors and antibiotics to reduce mortality and frequency of infectious SAP complications useful?

Are protease inhibitors/NSAIDS useful for the prevention of post-ERCP pancreatitis (PPC)?

Are continuous regional arterial infusion and decompression by laparotomy in the SAP with ACS useful?

**Recommendation 23.** Intravenous administration of protease inhibitors in PSAP may reduce mortality and complication rates, though we do not recommend its widespread use. Weak grade of recommendation (2), moderate quality of evidence (B).

**Recommendation 24.** Local intra-arterial administration of protease inhibitors and antibiotics in the early phase of PSAP may lead to a decrease in mortality and infectious complications. Nowadays more studies are needed to confirm its efficacy. Weak grade of recommendation (2), moderate quality of evidence (B).

**Recommendation 25.** Intravenous administration of protease inhibitors does not prevent post-ERCP pancreatitis (PPC). Strong grade of recommendation (1), high quality of evidence (A).

**Recommendation 26.** We recommend the administration of indomethacin rectally after ERCP in high risk patients. Strong grade of recommendation (1), moderate quality of evidence (B).

8th Question: control of intra-abdominal pressure and approaches to abdominal compartmental syndrome. (Summary version only. Complete version on-line)

**Concept**

Intra-abdominal pressure (IAP) is the pressure within the abdominal cavity. Its normal value in noncritical patients is subatmospheric (<0 mmHg) and it is <12 mmHg critical patients. An increase in IAP or in intra-abdominal hypertension (IAH) (PIA ≥ 12 mmHg) was detected more than a century, and it has been known to cause alterations in the functioning of the organism.48-52

The ACS is defined as IAP ≥20 mmHg, which was maintained and associated with new organ dysfunctions, regardless of the etiology.53-56 AIP values of which predict OF and mortality, and recommendations for optimizing both the medical and surgical treatment of ACS51-64 have even been established.

Both the AIP values and the abdominal perfusion pressure (APP) should be considered, by taking into account that APP = MAP – IAP, when MAP is the average arterial pressure. The objective is to achieve an AIP of 50–60 mmHg, and ACS is diagnosed below this figure if it is associated with organ dysfunction.

**Treatment**

Inasmuch as our goal is to achieve a correct APP (50–60 mmHg) we can act by improving the mean arterial pressure (MAP) and/or reducing the IAP. The improvement in MAP is achieved initially by volume replacement, while bearing in mind that an excessive volume can worsen ACS55,66 and, after replacement has been completed and, if necessary, we will initiate vasoactive amines.

The reduction of the AIP will be achieved by non-surgical techniques and/or surgical techniques.

If attempts to reduce and optimize AIP are unsuccessful and optimize APP, surgical management should be considered. Among the surgical techniques, percutaneous drainage should be considered (only in those cases where there is a lot of free intraabdominal fluid)57,68 and/or decompressive laparotomy.69,70 If decompressive surgery is performed and there is no suspicion of infected necrosis it is important that no necrosectomy be performed to prevent infected necrosis from occurring.

**Recommendation 27.** IAP should be measured in all the patients with PSAP. PSAP is to be measured when the patient is in a supine position at the end of expiration every 6-8 h and through the urinary bladder by instilling a maximum of 25 ml of isotonic saline and this will be measured in mmHg. IAH is considered when the IAP ≥ 12 mmHg is sustained or repeated and ACS will be considered when IAP ≥ 20 mmHg is sustained and associated with SDMO de novo. In the case of IAH episodes and SCA development, our objective will be to achieve an APP of 50–60 mmHg. Strong grade of recommendation (1), moderate quality of evidence (B).

**Recommendation 28.** ACS treatment of in PSAP should consist of increasing MAP or reducing IAP in order to improve APP. Strong grade of recommendation (1), low quality of evidence (C).

**Recommendation 29.** Among the non-surgical therapies used to reduce AIP aspiration of intestinal contents by means of a gastric and/or rectal probe, the administration of prokinetics (metoclopramide, erythromycin, neostigmine), sedation and relaxation and a reduction of the third space with diuretics and/or renal replacement techniques should be considered. Strong grade of recommendation (1), low quality of evidence (C).

**Recommendation 30.** Among the surgical therapies used to reduce AIP percutaneous drainage and/or decompression laparotomy should be considered. The pancreatic area should only be treated when it is infected. Strong grade of recommendation (1), low quality of evidence (C).

9th Question: pain control and sedation. (Summary version only. Complete version on-line)

**Recommendation 31.** Analgesia is essential in the treatment of AP. Strong grade of recommendation (1), low quality of evidence (C).

**Recommendation 32.** A comprehensive assessment must be performed to identify potential for surgery that may reduce the progression of pancreatic damage or
complications. Strong grade of recommendation (1), low quality of evidence (C).

Recommendation 33. There is no analgesic guideline to choose from that is based on evidence. Drugs ranging from non-opioid analgesics to opiates should be chosen, depending on the intensity of the pain. Strong grade of recommendation (1), moderate quality of evidence (B).

Recommendation 34. Patient-controlled analgesia (PCA) by means of a pump is a good option when pain is particularly intense in the postoperative stage. Strong grade of recommendation (1), low quality of evidence (C).

Recommendation 35. In the case of uncontrollable pain with opioids administered intravenously, loco-regional epidural analgesia can be a good alternative. Strong grade of recommendation (1), low quality of evidence (C).

Recommendation 36. Sedation can be used as an adjunct to analgesia, mechanical ventilation or treatment of the alcohol withdrawal syndrome. There is no scientific evidence in this regard. Strong grade of recommendation (1), low quality of evidence (C).

Recommendation 37. There may be other methods of analgesia and sedation control. More studies on analgesia and sedation in patients with PA are needed. Strong grade of recommendation (1), low quality of evidence (C).

10th Question: Volemia replacement and hemodynamic monitoring. In critically ill patients with or without mechanical ventilation. In general wards and intensive care units. (Summary version only. Complete version on-line)

In patients with PSAP early administration of fluids is recommended, mainly during the first 72 h, during which the first 24 h are the most important.\textsuperscript{79,72} Progressive, controlled and monitored administration of fluids is probably more beneficial than the aggressive administration of fluids, which is widely recommended in most clinical guidelines, primarily in patients with PSAP whose condition is unstable and who show signs of hypoperfusion (ScvO\textsubscript{2} < 70\% or SvmO\textsubscript{2} < 65\%, lactate > 4 mmol/l, oliguria) (17), as well as associated morbidities (patients with heart, kidney and/or liver disease).\textsuperscript{73} The administration of more than 3–4 liters of fluids in the first 24 h seems to be related to a poor prognosis due to an increased rate of acute respiratory failure and a greater need for admission to intensive care units, either because of the deleterious direct effects of fluid infusion, or because it involves a patient with complicated AP.\textsuperscript{36,73,74}

Regarding the type of fluid to be administered, crystalloid versus colloid, there is no general recommendation for AP, although balanced crystalloid solutions (Ringer Lactate) have been observed to control SRIS in PSAP, as well as CRP levels when compared to physiological saline serum.\textsuperscript{39,75–78}

The classic standard static parameters for assessing and functional hemodynamic parameters are discussed in full online version.

Interpreting these parameters in patients with intra-abdominal hypertension, which must be performed fairly frequently with SAP or CAP patients, merits special mention. Pulse pressure variation (PPV), stroke volume variation (SVV), systolic pulse variation (SVP) and the overall volume at the end of diastole can be considered useful parameters for assessing IAH patient response to fluids, when taking into account that the response thresholds that distinguish responders from nonresponders can be increased.\textsuperscript{79,80} It is also important to bear in mind the difficulty of interpreting the response to fluids after the maneuver for the passive elevation of the legs of mechanically ventilated patients with intra-abdominal pressures above 16 mmHg has been performed.\textsuperscript{81}

Recommendation 38. We recommend early administration of fluids in patients with PSAP, who are in unstable condition and show signs of hypoperfusion (central venous O\textsubscript{2} saturation < 70\% or mixed venous saturation O\textsubscript{2} < 65\%, lactate > 4 mmol/l, diuresis < 0.5 ml/kg/h). Strong grade of recommendation (1), low quality of evidence (C).

Recommendation 39. Balanced crystalloids in the amount not exceeding 4.3 liters in the first 24 hours are preferable. Special care must be taken with reviving patients with more severe pancreatitis and/or more comorbidities. Strong grade of recommendation (1), low quality of evidence (C).

Recommendation 40. We recommend not using hydroxyethyl starch with a molecular weight > 200 kDa and/or degree of replacement 0.4 in cases of shock and/or renal dysfunction. Strong grade of recommendation (1), low quality of evidence (C).

Recommendation 41. Monitoring the administration of fluids in patients with PSAP, mainly in the first 72 h, is important. Accurate prediction of the response to fluids before volume expansion is crucial. Classic static parameters for monitoring and assessing response to fluids, such as central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP) and average arterial pressure (MAP) should therefore be interpreted with caution in patients on either mechanical ventilation or spontaneous breathing. Strong grade of recommendation (1), low quality of evidence (C).

Recommendation 42. Monitoring dynamic parameter measures the cardiac response to changes in preload. Systolic volume variation (SVV) and the pulse pressure variation (PPV) have proven useful as predictors of response to volume in mechanically ventilated and sinus rhythm patients. Strong grade of recommendation (1), low quality of evidence (C).

Recommendation 43. Numerous studies have demonstrated the usefulness of the maneuver of leg elevation as a predictor of response to volume (increase ≥ 10\% in cardiac output during the first 60–90 seconds of its initiation) in spontaneously breathing patients in critical condition. Strong grade of recommendation (1), low quality of evidence (C).

Recommendation 44. The presence of intra-abdominal hypertension, which is common in this type of patients, requires carefully interpreted static and dynamic parameters in patients on mechanical ventilation or those who are spontaneously breathing. Strong grade of recommendation (1), low quality of evidence (C).
11th Question: Nutritional and specialized metabolic support of critically ill patients with potentially severe acute pancreatitis. (Summary version only. Complete version on-line)

Since this topic was last reviewed a few, but highly valuable, contributions have been made. PSAP and its evolutionary forms, SAP and CAP, produce a SIRS which leads to a highly catabolic, hyper-metabolic and hyper-dynamic stress situation.1,3,8 The previous nutritional status of the patient will be a determining factor in patient recovery, so chronic alcohol intake and obesity are factors that do not depend on severity.

Currently, the classic concept of treating PSAP, consisting of bowel rest and implementing total parenteral nutrition which was limited to reversing the catabolic situation, has changed. Several studies show increased morbidity and mortality risk with this traditional approach.85,86

A recent study of several intestinal functionalism markers concluded that intestinal barrier dysfunction appears early in the course of PSAP and that it is associated with pancreatic necrosis infection, the onset of MOF, and the severity of the pancreatitis with an increase in mortality.87

Therefore, emerging data suggest that the route, time, quantity and composition of artificial nutrition aim to reduce pancreatic secretion, treat and/or prevent malnutrition associated with a situation of severe metabolic-catabolic stress, modulate inflammatory response and prevent the development of local and systemic infections.88-91 Nutritional support has become one of the most important elements in the management of PSAP patients.

Recommendations

Recommendation 45. Specialized nutritional support in potentially severe acute pancreatitis, in its SAP and CAP forms, should be started early, within the first 48 hours after initial resuscitation. Strong grade of recommendation (1), moderate quality of evidence (B).

Recommendation 46. Enteral jejunal nutrition is preferable to parenteral nutrition. Strong grade of recommendation (1), high quality of evidence (A).

Recommendation 47. Parenteral nutrition is indicated if enteral nutrition cannot be administered, if there is intolerance to this nutrition or if it results in an exacerbation of pancreatitis. Strong grade of recommendation (1), moderate quality of evidence (B).

Recommendation 48. Enteral or parenteral nutritional intake shall be achieved on the basis of recommendations for specialized metabolic and nutritional support of critically ill patients. SEMICYUC-SENPE (2011) Consensus: caloric intake of 25–30 Kcal/kg/d, without exceeding an intake of ≥4 g/kg/d of glucose, lipid intake of 0.7–1.5 g/kg/d and protein intake of 1–1.8 g/kg/d. Strong grade of recommendation (1), moderate quality of evidence (B).

Recommendation 49. Polymeric and elemental diets are equally recommendable. Weak grade of recommendation (2), moderate quality of evidence (B).

Recommendation 50. Assessing the possibility of maintaining a minimum supply of jejunal nutrients, even in patients with impaired jejunal nutrition who are being treated with parenteral nutrition, is suggested. Weak grade of recommendation (2), low quality of evidence (C).

Recommendation 51. The use of glutamine in patients with severe acute pancreatitis who receive parenteral nutrition is recommended. Strong grade of recommendation (1), moderate quality of evidence (B).

Recommendation 52. The use of prebiotics or probiotics in patients with potentially serious acute pancreatitis is not recommended. Strong grade of recommendation (1), moderate quality of evidence (B).

12th Question: Role of endoscopy/digestive endoscopy in critical, severe, and acute pancreatitis. (Summary version only. Complete version on-line)

Role of endoscopic retrograde pancreatic cholangiography and endoscopic sphincterotomy (ERCP-EE) in biliar acute pancreatitis

Role of endoscopy in the management of pancreatic pseudocysts

Interventionist endoscopy. Role of endoscopy in the management of infected pancreatic necrosis. Recent studies show the effectiveness of endoscopic necrosectomy, which is an effective technique, but it should be performed only in specialized centers because it presents complications,92 which are equal to or greater than surgical complications; the level of safety is acceptable.93

Both the guided drainage of pancreatic collections by conventional endoscopy such as endoscopic ultrasound-guided methods can be considered first-line drainage collections which lead to extrinsic compression. However, endoscopic ultrasound-guided drainage must be the first choice in those cases in which there is no extrinsic compression.

Direct endoscopic necrosectomy of organized pancreatic necrosis may be a technique that, in experienced hands, is effective and has an acceptable level of safety compared to surgery. Endoscopic transmural drainage is a perfectly valid option for patients who cannot undergo surgery or any other drainage technique using large collections or who suffer from necrosis and/or suspected infection. In an unorganized infected necrosis, however, surgery is still the preferred option.

Recommendation 53. ERCP-EE. When confronted with biliary AP having cholangitis data, ERCP should be performed urgently (within 24 hours) with biliary drainage. Strong grade of recommendation (1), moderate quality of evidence (B).

Recommendation 54. When confronted with biliary AP having an obstruction of the biliary duct, performing ERCP (ERCP-EE) with early (first 72 hours) cleaning of the bile
duct may prove beneficial. Strong grade of recommendation (1), moderate quality of evidence (B).

**Recommendation 55.** In patients with biliary AP and predictors of severity, performing urgent ERCP is controversial if no cholangitis or biliary obstruction data are available. Weak grade of recommendation (2), moderate quality of evidence (B).

**Recommendation 56.** In patients with mild or moderate biliary AP without cholangitis or persistent biliary obstruction, performing ERCP does not significantly reduce the risk of complications or death. Strong grade of recommendation (1), high quality of evidence (A).

**Recommendation 57.** In centers where ERCP is not available in the first 48–72 hours and the patient shows signs of cholangitis or obstructive jaundice, the patient should undergo percutaneous transhepatic drainage of the gallbladder or biliary surgery within this timeframe. Strong grade of recommendation (1), high quality of evidence (A).

**Recommendation 58.** Performing ERCP with endoscopic sphincterotomy is an alternative to cholecystectomy as a prophylaxis for new episodes of biliary AP in patients with high surgical risk or who have refused to undergo surgery. Strong grade of recommendation (1), moderate quality of evidence (B).

**Recommendation 59.** Only symptomatic pseudocyst drainage is considered suitable. Strong grade of recommendation (1), low quality of evidence (C).

**Recommendation 60.** The endoscopic drainage route is usually the first choice. Strong grade of recommendation (1), low quality of evidence (C).

**Recommendation 61.** The use of ultrasound endoscopy limits the development of complications resulting from this technique and it is useful for differential diagnosis with other pancreatic cystic lesions. Strong grade of recommendation (1), moderate quality of evidence (B).

**Recommendation 62.** Infected or symptomatic pancreatic necrosis indicates the need for treatment. The approach should be performed in stages with medical treatment, radiological drainage or endoscopic or surgical endoscopic debridement. Strong grade of recommendation (1), high quality of evidence (A).

**Recommendation 63.** The ideal time to perform this treatment for an infected or symptomatic pancreatic necrosis is at least 3 or 4 weeks from the onset of pancreatitis. Strong grade of recommendation (1), low quality of evidence (C).

**Recommendation 64.** Direct endoscopic necrosectomy is an alternative to surgical debridement when performed in specialized centers. It offers acceptable levels of efficacy, although it is not free of morbidity and mortality. Therapeutic/interventional ultrasound endoscopy (USE) shall be considered an option for the management of pseudocysts and/or asymptomatic or complicated abscesses, as well as for performing necrosectomies in patients with infected necrosis whose baseline counter indicate the surgical option. We wish to point out that if this therapeutic option is chosen, it should be performed in centers that are especially "devoted" to this pathology and which have a multidisciplinary team composed of expert endoscopists, surgeons and interventional radiologists. Strong grade of recommendation (1), moderate quality of evidence (B).

**13th Question: Antibiotic prophylaxis in potentially severe acute pancreatitis. (Summary version only. Complete version on-line)**

**Prophylactic antibiotics in acute pancreatitis**

- Does antibiotic treatment play an important role in the treatment of AP?
- Does AP with intraabdominal fungal infection (IFI) offer a worse prognosis than intraabdominal bacterial infection (IIB)?

**The role of "early antifungal treatment"** (incorrectly called "antifungal prophylaxis")

- What is the role of DDS in SAP?
- What is the next step?

**Recommendation 65.** The use of prophylactic antibiotics in PSAP patients with or without pancreatic necrosis is not recommended. Strong grade of recommendation (1), moderate quality of evidence (B).

**Recommendation 66.** The analysis of individual patients may be important for identifying potential candidates who might benefit from antibiotic prophylaxis. Weak grade of recommendation (2), low quality of evidence (C).

**Recommendation 67.** The role of "early antifungal treatment" (misnamed antifungal prophylaxis) with fluconazole is unclear and requires further study. But once the fungal infection appears an antifungal with a greater spectrum than fluconazole should be used as soon as possible and by extension the same criteria used in SAP and CAP with bacterial infection are applied. Weak grade of recommendation (2), moderate quality of evidence (B).

**Recommendation 68.** Empiric antifungal treatment based on clinical findings without microbiological confirmation does not appear to be effective. Weak grade of recommendation (2), moderate quality of evidence (B).

**Recommendation 69.** There is no conclusive evidence at present for recommending the routine use of SDD in PSAP. Weak grade of recommendation (2), moderate quality of evidence (B).

**14th Question: Hemofiltration in potentially severe acute pancreatitis. Dynamic approach to extra – renal replacement techniques: early hemofiltration; high-volume hemodiafiltration. (Summary version only. Complete version on-line)**

**Immunomodulation and therapeutic control attempts in severe acute pancreatitis treatment**

Back in the 1970s a group of pioneers suggested a change of strategy in the therapeutic approach of "reducing or mitigating the inflammatory process in the pancreas", by initially using peritoneal lavage.94-96
HF has several features that make it suitable for the removal of these proinflammatory substances, although there are conflicting data in the literature regarding the actual effectiveness of HF for removing inflammatory mediators (TNF-alpha, IL 1, PAF, IL-6 and complementary fractions), because it has not always been possible to demonstrate that this clearing has an impact at the systemic level.\textsuperscript{97–102} However, there are consistent data that support the beneficial effect of HF on the clinical situation and recovery of patients with SIRS or MOF, which contributes especially to the stabilization of the respiratory and hemodynamic systems.\textsuperscript{101–104}

Hemofiltration in the treatment of severe acute pancreatitis: Clinical experience

Hemofiltration in severe acute pancreatitis treatment: Current recommendations for its use

From what has been discussed above it follows that the use of CRRT as specific immunomodulating treatment in SAP is based on appealing arguments, such as the positive effect these techniques have on the function of certain organs, the impossibility of immunomodulating impaired inflammatory response, maintaining cellular defense capacity and hindering the development of infections and, finally, the possibility of having a positive impact on the prognosis of these patients. In these cases, the starting time of the treatment, the exchange dose used, and the filter replacement frequency may affect the efficacy of treatment. However, at present we must consider that the accumulated experience is still insufficient, because, although well-designed experimental work has yielded positive results, clinical experience is limited to a small group of cases that are difficult to assess, two case-control studies using a methodology that prevents them from being conclusive, and a randomized study with a small number of patients.\textsuperscript{105}

Finally, the indication is based on the concept of a CRRT dynamic approach for AP patients in critical condition; i.e., how and when to dosify (4), when and how to initiate and how to terminate TDE in these critically ill patients.\textsuperscript{105}

Management of patients with severe acute pancreatitis and acute renal failure

Recommendations

Recommendation 70. At present, with the experimental and clinical evidence accumulated the use of TCDE as immunomodulating therapy as in the Potentially Severe Acute Pancreatitis (PSAP) has a favorable recommendation but it is not conclusive. Weak grade of recommendation (2), moderate quality of evidence (B).

Recommendation 71. After considering the possible beneficial effect on patient’s immune response and the course of the illness, DTE should preferably be initiated early. Weak grade of recommendation (2), moderate quality of evidence (B).

Recommendation 72. A safety renal system for PSAP patients should be provided means of the creation of a prevention protocol, early detection and ARF handling both in ICUs and general hospital rooms. Strong grade of recommendation (1), high quality of evidence (A).

Recommendation 73. If an ARF patient has general and hemodynamic stability, any treatment that currently controls the internal environment (extended or continuous IHD) could be used for this purpose, based on the team and infrastructure experience. Strong grade of recommendation (1), high quality of evidence (A).

Recommendation 74. In the cases of acute renal failure in the course of SAP with hemodynamic instability, according to the experience accumulated in other related pathologies (there are no specific data on SAP), TCDE is recommended. Although there is no definitive study on this subject, the use of IHD in hemodynamically unstable patients is not recommended. Strong grade of recommendation (1), moderate quality of evidence (B).

Recommendation 75. TCDE should be started early in the course of acute renal failure. Strong grade of recommendation (1), moderate quality of evidence (B).

Recommendation 76. Based on the interest of using more cost-effective treatments and with the aim of reducing the complications of this type of therapies, a dynamic approach to these therapies would be very useful, based on the basis of the type of patient and the stage in his/her recovery. Strong grade of recommendation (1), low quality of evidence (C).

15th Question: Surgical approach to severe acute pancreatitis or critical acute pancreatitis with and without pancreatic necrosis and sepsis. (Complete version)

Surgical indications

Sterile necrosis

Currently, there is a consensus on the conservative management of patients with AP and sterile necrosis, which is based on the medical treatment. A recent national study on patients undergoing surgery,\textsuperscript{106} which had been published, shows that surgery for sterile necrosis is associated with increased mortality, and supports conservative treatment unless a pancreatic or peripancreatic infection is detected. Current management of AP patients with sterile necrosis is based on conservative treatment. However, after the acute stage, a small number of patients with non-infected necrosis may benefit from surgical treatment:

- Patients, who after several weeks of conservative treatment, still suffer from fever, lethargy, recurrent abdominal pain, nausea and/or vomiting and hyperamylasemia after attempts to return to an oral diet, typically have large amounts of necrotic tissue and often have concealed retroperitoneal infections in this devitalized tissue that are objectified after debridement.\textsuperscript{107}
- Patients with postnecrotic rupture of the main pancreatic duct, which is classified as “disconnected duct syndrome”, with a clinic similar to that discussed above, which are tributaries of surgical treatment\textsuperscript{108}
- Intestinal obstruction or biliary stenosis due to the organization of necrosis.
Infected necrosis
Contrary to the controversy that erupted regarding the treatment of sterile necrosis, there is virtual unanimity about the concept that patients with infected necrosis are tributaries of surgical treatment.

Some articles have appeared advocating conservative treatment, even in patients with infected pancreatic necrosis.109-112 Most of these studies have been conducted on patients who have refused surgery or have been considered to be at a very high surgical risk. Prolonged antibiotic treatment, occasionally supported by percutaneous drainage of intraabdominal collections, helps to get acceptable results.

Since mortality rates for patients undergoing conservative treatment who had infected pancreatic necrosis were very high, this treatment is not currently advisable unless patients refuse surgery or are considered inoperable due to a high comorbidity.113

However, recent data may question this assertion. Stern et al.114 note that FNA bacteriology does not determine either the surgical approach or the clinical status and the parenchymal impact. Invasive options should be increased, and the endoscopic and laparoscopic approaches versus the standard beginning laparotomy should be continued, if the clinical situation permits. Overall, neither does a positive bacteriology imply a surgical indication, nor does a negative bacteriology rule it out (there are no false negatives) and the same is true of the discovery of gas in CT.

In summary, patients with infected necrosis should be treated surgically based primarily on the clinical situation. A positive FNA or gas in the CT does not appear to be totally synonymous today with surgical treatment if the patient is able to undergo surgery from a clinical standpoint.

Surgical technique
The surgical technique for the treatment of AP with infected necrosis is based on a necrosectomy involving extensive debridement of the entire pancreatic and necrotic peripancreatic tissue, while preserving the viable tissue as much as possible in an attempt to prevent secondary necrotic fistulas and limiting where possible lesions to and/or removal of adjacent organs.

Rau’s study,115 where he compared the results on mortality published in the literature, between necrosectomy and declining drainage, necrosectomy and lavage by means of a closed and a necrosectomy plus programmed relaparotomy and an open or temporarily closed abdomen, indicated a mortality for different techniques of 42%, 20% and 21%, respectively.

These techniques have not been studied using well-controlled, randomized studies, so that there is no clear indication of one procedure over another.116 In this case, the experience of the surgical team, the proper management of these patients subjected to an open abdomen, temporary closure or continuous lavage by the nursing team that controls the treatment provide the principal criteria for selecting one technique or another.

Recently, Bradley113 reported that open abdomens should be reserved for those patients with acute pancreatitis and infected necrosis who present extensive collections that exceed the pancreatic cell and fill the entire retroperitoneal space behind the colon.

It is probably in these cases where the value of intraabdominal pressure (IAP) becomes more relevant. The patients that Bradley113 described are, without doubt, patients with elevated abdominal pressure, who frequently are sick with a universal necrosis that is not confined to the pancreas and who are certainly those who should be treated by means of a temporary closure of the abdomen; proceeding to the conventional closing of the laparotomy is a clear predisposing factor for the development of abdominal compartmental syndrome (ACS) with fatal consequences.

If the patient is stable during pancreatic surgery, cholecystectomy can also be performed. If the condition of the patient undergoing surgery is unstable, and there is a vesicular plastron, the gall bladder should not be operated on and only the necrosectomy should be performed.

Time for the surgical indication
Pancreatic necrosis is a dynamic process that has two distinct phases, the early and late phases. The conclusive evidence that advised against surgery of sterile necrosis115,117 indicates that the best time to indicate necrosectomy is during the late phase of the disease, i.e. the phase in which the necrosis infection is common (often after three or four weeks from its onset).118

In the early or initial phase (first two weeks after its onset) surgical indication should only be established in the following cases:

- Cases of MOF and diagnostic doubts between PSAP and mesenteric ischemia or perforation of an empty viscer.
- Cases of intestinal ischemia or a perforation which is secondary to the extension and/or compression pancreatic necrosis produced by pancreatic necrosis, either at the level of small intestine or colon.
- The appearance of ACS in the early days, by performing decompressive surgery without a necrosectomy.

In all patients with CAP or SAP AIP should be recorded regularly in search of the development of ACS that could make it necessary to perform decompressive surgery.

New surgical techniques
Minimally invasive pancreatic necrosectomy (MIN)119 has been developed according to two diametrically opposed philosophies. On the one hand, there is a group of surgeons who supports MIN as a complementary method of open necrosectomy, which is useful for the treatment of waste collection after conventional surgical treatment; this form of management has been referred to as “step-down” (5).

On the other hand, there is another group of surgeons who support “step-up” (5), which relegates open necrosectomy to a secondary option after the failure of a minimally invasive technique.

The transgastric route described by Baron120 is inspired by the classic surgical treatment of retrogastric pancreatic pseudocysts. By using this procedure, it has been possible to successfully debride pancreatic necrosis; however, it
requires a specific localization of the necrosis: encapsulation and liquefaction of the necrosis area located in the lesser sac and therefore delimited by the stomach, duodenum and colon transverse: ‘‘walled off pancreatic necrosis’’.

The retroperitoneal approach described by Carter’s group in Glasgow121 is an adaptation of the classic lumbotomy for debridement of infected pancreatic necrosis basically localized on the left side of the abdomen.

The randomized, controlled study conducted in the Netherlands (5) comparing an open necrosectomy to the ‘‘step-up’’ technique (percutaneous drainage and, if it is insufficient, minimally invasive retroperitoneal necrosectomy) shows that 35% of patients can only be treated with percutaneous drainage and the remainder require the combination of percutaneous drainage and minimally invasive retroperitoneal necrosectomy. There are fewer complications, 69% for open necrosectomy versus 40% for the ‘‘step-up’’; however, it was not possible to demonstrate a significantly lower mortality, 19% vs 16%.

The use of radiologically guided percutaneous catheters is considered a ‘‘bridge’’ technique until a more definitive treatment can be applied; it can be extremely useful for stabilizing patients whose condition is too serious to tolerate any type of necrosectomy.118 This technique has not been compared to surgical debridement, but in a systematic review of the literature on the usefulness of percutaneous drainage as the sole technique in the treatment of pancreatic necrosis, the use of drainage was found to be sufficient for 55.7% of patients who did not require surgical necrosectomy.

A new message has emerged from all these new techniques: necrosectomy in itself may be less important than achieving proper drainage.120

Currently endoscopic techniques, with some exceptions, have failed to demonstrate its superiority over conventional techniques; however, the future of minimally invasive techniques in the treatment of patients with infected pancreatic necrosis is promising, as long as the experience in handling it increases and the new technology needed for obtaining the best results appears.115,122

Conclusions

Recommendation 77. Surgery. Indications: Infected necrosis plus clinical deterioration; Intestinal ischemia or perforation secondary to pancreatic necrosis; Intestinal obstruction or biliary stricture due to the organization of necrosis. Strong grade of recommendation (1), high quality of evidence (A).


Recommendation 80. Surgery. New surgical techniques: Minimally invasive or not combined with percutaneous drainage; Retroperitoneal and transgastric. Weak grade of recommendation (2), low quality of evidence (C).

Recommendation 81. In a patient with infected necrosis and organ failure, current indication is surgical necrosectomy. Treatment by means of other options which are less invasive, such as radiological or endoscopic techniques, has yet to be determined. Radiological or endoscopic techniques can be used in a patient with infected necrosis and without organ failure. When the patient’s condition does not improve, surgical necrosectomy can be performed. Strong grade of recommendation (1), high quality of evidence (A).

16th Question: Costs of managing a potentially severe acute pancreatitis patient in an Intensive Care Unit. (Summary version only. Complete version on-line)

There are only a few economic assessment studies of patients with AP. Due to a limited number of studies on this topic we do not to make any recommendations on this aspect.

Conflict of interest

The authors declare no conflict of interest.

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Appendix A.

Endorsement of the SEMICYUC Scientific Committee

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♦ The Meeting of the Spanish Group Intensive Care Pancreas of SEMICYUC was held on October 10, 2012, Madrid.
♦ The abridged version of these Guidelines are attached PDF in Intensive Care Online: http://www.semicuyuc.org/.
Annex A. Supplementary data

Additional material can be found in this article in the online version available at http://dx.doi.org/10.1016/j.medine.2013.05.001.

References


47. Lankisch P. Natural course of acute pancreatitis: what we know today and what we ought to know for tomorrow. Pancreas. 2009;38:494–8.


68. Radenkov D, Bajec D. Decompressive laparotomy with temporary abdominal closure versus percutaneous puncture with placement of abdominal catheter in patients with abdominal


