



## SPECIAL ARTICLE

# Clinical pathways for acute pancreatitis: Recommendations for early multidisciplinary management

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**Abstract** There is a growing body of evidence that early management of patients with acute pancreatitis may alter the natural course of disease and improve outcomes of patients.

The aim of this paper is to optimize the management of patients with acute pancreatitis during the first 72 h after hospital admission by proposing several clinical care pathways. The proposed pathways are based on the SEMICYUC 2005 recommendations with incorporation of the latest developments in the field, particularly the determinants-based classification of acute pancreatitis severity. The pathways also include the "alarm signs", the use of therapeutic modalities known as PANCREAS, and the "call to ICU" criteria.

Further studies will need to assess whether adoption of these pathways reduces mortality and morbidity in patients with acute pancreatitis.

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Pancreatic warming signs

## PALABRAS CLAVE

Hoja de ruta;  
Pancreatitis;  
Clasificación de pancreatitis aguda;  
Pancreatitis aguda potencialmente grave;  
Algoritmos pancreatitis;  
Signos de alarma pancreática

The previous SEMICYUC guidelines for management of patients with acute pancreatitis in an Intensive Care Unit will need to be revised to reflect the recent developments in the field.  
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## Hoja de ruta de los cuidados clínicos para la pancreatitis aguda: recomendaciones para el manejo anticipado multidisciplinar (*clinical pathways*)

**Resumen** Existe una creciente evidencia de que el manejo precoz de los pacientes con pancreatitis aguda puede cambiar el curso natural de la enfermedad y mejorar los resultados de la evolución posterior de los pacientes.

El objetivo de este trabajo es optimizar el manejo de los pacientes con pancreatitis aguda durante las primeras 72 h después de su ingreso al proponer varias vías de atención clínica. Las vías propuestas se basan en las recomendaciones de la SEMICYUC 2005, la incorporación de los últimos avances en el campo, en particular la clasificación basada en los factores determinantes de la gravedad de la pancreatitis aguda. Las hojas de ruta también incorporan las «señales de alarma pancreática», el uso de modalidades terapéuticas resumidas con el acrónimo PANCREAS y los criterios de «llamada a la UCI».

Futuros estudios deberán evaluar si la adopción de estas vías disminuye la mortalidad y morbilidad en pacientes con pancreatitis aguda.

Las recomendaciones anteriores de la SEMICYUC 2005 sobre el manejo de los pacientes con pancreatitis aguda grave en Medicina Intensiva deberán ser revisadas para reflejar los últimos avances en el campo.

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## Introduction

Optimal management of patients with acute pancreatitis (AP) is essential in order to reduce mortality and morbidity associated with this disease.<sup>1</sup> There was a high mortality rate among AP patients hospitalized in Spanish intensive care units (ICUs) during the 1970s. Eight of every 10 patients (81.2%) died.<sup>2</sup> In 1974 Ranson reported a mortality rate of 100% in SAP patients with more than 7 points<sup>3</sup> and López Benito<sup>4</sup> reported a 77.2% mortality rate in patients with necrotizing pancreatitis.

Recently, the incidence of lethal forms has been significantly reduced<sup>5,6</sup> and this reduction has been attributed to early detection of prognostically unfavourable forms during the first three days after onset of symptoms, to treatment administered in the ICUs, to delaying the operative intervention for as long as possible,<sup>6-8</sup> and to the introduction of minimally invasive draining techniques.<sup>9</sup>

Taking into account the recently emerged evidence in the literature, the Northern Spanish Intensive Care Society (SNMIUC) proposed the development of clinical pathways<sup>10</sup> for AP at its meeting in Pamplona in January 2010.

The main aim of AP pathways is to improve the diagnosis and treatment of patients with AP who are hospitalized and managed by a multidisciplinary team, including but not limited to gastroenterologists, surgeons, intensive care physicians, nutritionists and radiologists. The pathways detail the recommended algorithm of actions and level of care on daily and hourly basis within the first

3 days after hospital admission. The current knowledge based on scientific evidence must be applied by means of multidisciplinary "levels of care" which will include the appropriate succession of clinical management, laboratory tests, radiological investigations, and therapeutic procedures. All these aspects are focused on confirming the AP diagnosis and stratifying the severity by initiating early the most appropriate support treatment for each patient. The previous Spanish guidelines and recommendations for AP management have formed the basis<sup>11,12</sup> for the pathways presented in this document.

All the pathways are presented using a sequential format during the first day of admission and the first three days in the Emergency, Surgery, Gastroenterology Departments or ICU.

## Materials and methods

In preparing the present pathways, we first found a new classification of severity that was proposed by Petrov and colleagues in 2010.<sup>13</sup> This new classification significantly advances the outdated 1992 Atlanta classification.<sup>14</sup> The definitions used for the categories of severity in the new classification are based on the characteristics of "local determinants" (absent, sterile or infected peri/pancreatic necrosis) and "systemic determinants" (an absent, transient or persistent organ failure), as well as the possibility of the determinants factors interacting during the episode of acute pancreatitis. Organ failure (OF) is defined as transient (when it is resolved in a short period of time after having applied adequate support measures, normally in less

than 48 h from the onset of acute pancreatitis) or persistent organ failure (when it is resolved more than 48 h later).

Other clinical entities that are different from these local and systemic factors of severity should be considered as complications and are not used to classify the severity.

The definitions are as follows:

1. Mild Acute Pancreatitis is characterized by the absence of both (peri)pancreatic necrosis and organ failure.
2. Moderate Acute Pancreatitis is characterized as the presence of sterile (peri)pancreatic necrosis or transient organ failure.
3. Severe Acute Pancreatitis is characterized as the presence of infected (peri)pancreatic necrosis or persistent organ failure.
4. Critical Acute Pancreatitis is characterized as the presence of infected (peri)pancreatic necrosis and persistent organ failure.

From a practical standpoint we introduced the concept of "Early severity criteria"<sup>11</sup> that defines a Potentially Serious Acute Pancreatitis (PSAP). A PSAP is defined as an episode of AP with one or more organ failures, i.e. with cardiovascular, respiratory or renal failure or alarm signs (Fig. 1). This is useful for providing early appropriate treatment and for designing future trials.<sup>15</sup> The alarm signs are the symptoms/signs in a patient with AP indicating a potentially negative or severe evolution of the disease.

Each one of them has been presented in the following pathways: The AP Pathway (intended for the medical specializations involved in the first patient treatment, especially Emergency and Digestive Care or Surgery), and the PSAP Pathway (Table 2) or post-surgical phase (Table 3). The "levels of care" are shown in the first column and listed in the following order:

1°. Assessment.—2°. Medical intervention.—3°. Laboratory tests.—4°. Imaging.—5°. Catheters/Monitoring/Surveillance.—6°. Medication/Treatments.—7°. Nutrition/Fluids.—8°. Biliary AP.—9°. Information/Teaching.—10°. Discharge; hospitalized.—11°. Medical Objectives/Nursing.—12°. Early Severity Criteria or Alarm signs. (They determine which patients require most detailed medical attention, where the AP algorithm is applied.)—13°. ICU Call Criteria, Assessment and ICU admission. (They are based on the evaluation of three organ failure parameters.)

The other four columns correspond to initial assessment (Day 0) in Emergency, Digestive, or ICU Services, and the following columns show the chronology of the first three days in the hospital (Date: Day 1, Day 2 and Day 3 in Emergency, Digestive or ICU Services). The actions, attitudes and measures conforming to the previous recommendations<sup>11</sup> are subsequently developed.

Lastly, the algorithms for AP and PSAP are developed as a result of these pathways (Figs. 1 and 2).

## Legal and ethical aspects

In accordance with Spanish Law 15/1999 covering the Protection of Personal Data and Royal Decree 994/1999, this

document should not be considered a health data file. It shall be considered a guide or a "pathway" (as its name suggests) for treating AP patients hour-by-hour and day-by-day.

## Reviewer requests

In February 2010, the Scientific Committee of the Sociedad Española de Medicina Intensiva y Unidades Coronarias (SEMICYUC) endorsed the development of AP pathways. The first draft was prepared by the Northern Spanish sponsoring Group (Intensive care physicians and specialists in Emergency and Digestive Care, Surgery, Laboratory Tests and Radiology) and then was open to criticism, corrections, amendments and additions.

The SEMICYUC subsequently asked physicians to volunteer and actively participate as REVIEWERS-SUPERVISORS, one for each participating ICU. In addition, intensive physicians from Spain, South America and other regions of the world were invited to participate (see list of Reviewers).

The reviewer's task consisted of "reviewing the first draft on the basis of the available scientific evidence", in collaboration with the reviewers or heads of the care services in each hospital (Emergency and Digestive Care, Laboratory, Surgery and Radiology).

The most important part of the pathways is for each clinical or therapeutic level to be suitable to the guidelines and recommendations. Consequently, each participating expert REVIEWER or person acquainted with these recommendations carefully analyzed each problem that was raised and completed the levels of care in a very critical way. It is evident that feedback to this document was the most important factor in its development.

## Target population

Patients suffering from AP, who are admitted to Emergency or Digestive Care, ICU or Surgery. In other words,<sup>16</sup> the group of patients who may potentially benefit from these pathways are those whose evolution is reasonably foreseeable. In this case, these patients suffer from AP that could become mild, moderate, severe or critical.<sup>13</sup> It has been shown that application of pathways may reduce variability in the clinical practice, and improve the outcomes.<sup>17,18</sup>

## Quality control

The development of these pathways has been overseen by the Scientific Committee of the SEMICYUC and the Working Group on Infectious Diseases (GTEI-SEMICYUC).

## Results

Table 1 represents the pathway for acute pancreatitis. It displays the specific aspects of clinical care in the first column and how it should be implemented on the day of hospital admission (day 0) and the following 72 h.

This pathway is based on the best available evidence, including the new determinants-based classification of acute pancreatitis severity and a complex of therapeutic treatments known under the acronym P.A.N.C.R.E.A.S. Besides, the Alarm Signs are shown as the last two aspects of care (Table 1) and they define the patients requiring most detailed medical attention. These signs are also shown in the AP algorithm (Fig. 1).

Table 2 and Fig. 2 represent the pathway for potentially severe acute pancreatitis (PSAP) and the respective algorithm. The "ICU call criteria" are shown in the first row. The management in Intensive Care (a more detailed P.A.N.C.R.E.A.S. protocol) and the "final classification" of the PSAP patients admitted to an ICU are described in the last two rows.

Analytical panels have been designed with the appropriate laboratory tests to be ordered in patients with AP (see Attachment 1). These patients are usually admitted to the Emergency or Digestive or Surgical Department or ICU at this stage.

The pathways are designed to be used on a sheet of paper (printed on both sides) in order to be placed at the head of the patient's bed for easy consultation on the part of all the medical specialists involved in the patient's care.

## Discussion

Identification of unfavourable signs in patients with AP during the first three days after admission improves the prognosis and reduces the probability of death.<sup>3,8,14,17,19–22</sup> This document presents the multidisciplinary clinical care pathways that aim to improve and standardize early management of patients with AP.

One of the most important recent developments that has been reflected in the pathway is the determinants-based classification of acute pancreatitis severity, originally proposed by Petrov in 2012.<sup>23</sup> This new classification of AP severity is based on two fundamental principals. First, it is based on real severity factors instead of factors that predict severity. The use of systems with multi-factor scoring (for example, APACHE II, Ranson criteria, Imrie-Glasgow criteria, etc.) for predicting severity were incorporated into the original Atlanta classification and it was an important development 20–30 years ago<sup>14</sup> but time proved that all of them suffer from at least 30–40% misclassification error. The direct implication is that patients are often admitted to ICU too late, when the opportunities of intensive care to alter favourably the natural course of AP are quite limited. Therefore, it is important to identify the early markers of persistent organ failure<sup>24</sup> and the risk factors that trigger the alarm.<sup>22</sup> Second, the new classification defines the severity only on the basis of factors that have a causal relation to this severity. In acute pancreatitis these factors are (peri) pancreatic necrosis and organ failure. On the basis of published studies there are three organs that should be considered in diagnosing OF: cardiovascular, renal, and respiratory.<sup>25,26</sup>

When these two principles were applied, four categories of severity appeared: Mild AP (MiAP); moderate AP (MoAP); severe AP (SAP); and critical AP (CAP). The exact definitions are provided in Fig. 2 and Table 2. It is also worth mentioning that these four categories of severity have very different outcomes. In our cohort of patients admitted to ICU, the mortality was 0% among patients with moderate AP, 21.2% in SAP patients and 25% in CAP patients.<sup>2</sup>

At the same time, some of the previously published severity criteria<sup>11,14,22</sup> could still be used as "early" criteria that predict which patients will have an unfavourable course of the disease and will require more attention. These criteria are described as "alarm signs" in the AP pathways (Figs. 1 and 2) and in Table 1.

It is also necessary to point out that this classification is dynamic and evolving, so that the accurate assignment of a severity category (particularly, SAP and CAP) will require at least 48 h after hospital admission. This is a potential disadvantage of the new classification as it is impossible to "diagnose" SAP or CAP at the time of hospital admission. At most, we are able to diagnose a moderate AP only.<sup>27</sup> For this reason, we suggest to term an AP patient who has at least one organ failure or signs of alarm upon admission and within first 48 h "Potentially Serious Acute Pancreatitis" (PSAP) and this is the type of patient who may require management in the ICU, as described in Table 1 and Figs. 1 and 2.

The pathways presented in this document incorporate the acronym P.A.N.C.R.E.A.S.,<sup>28</sup> in which all the therapeutic modalities currently advocated in patients with AP are summarized. There are "eight" easy therapeutic measures for remembering the acronym: Perfusion; Analgesia; Nutrition; Clinical; Radiology; ERCP; Antibiotics; and Surgery<sup>28</sup>:

1. **Perfusion:** The sequestration of fluids in the interior of the third abdominal space can become so significant that it could account for a third of the total plasma volume. Rapidly restoring and maintaining intravascular volume in the first 48 h after patient admission is essential and the cornerstone for initial resuscitation. However, both excessive rehydration and the scarce supply of fluids in the first 48 h are associated with an increased morbidity and mortality.<sup>29</sup> In addition, a greater need of fluids associated with oliguria<sup>30</sup> is a sign of alarm and consequently requires greater and continuous hemodynamic control<sup>31,32</sup> or even the employment of vasopressor drugs in accordance with the initial severity.<sup>29</sup> Oxygenation is needed for adjusting the saturation >95% in severe and critical AP.<sup>33</sup>
2. **Analgesia:** Controlled patient analgesia; or analgesia on demand, including with opioids.<sup>34</sup>
3. **Nutrition:** There is a growing body of evidence that mortality is reduced in those patients with acute pancreatitis who receive enteral nutrition. Enteral nutrition in the first 48 h via nasojejunal tube is advocated if the gastric route is not tolerated.<sup>35,36</sup>

4. Clinical: Scores for evaluating and stratifying cases such as BISAP,<sup>37</sup> the APACHE II<sup>38</sup> or the APACHE-O<sup>39</sup> are available. These scoring systems are not mandatory in most emergency and digestive care areas. This clinical evaluation should be performed especially in intensive care units according to the severity of the pancreatitis.<sup>40</sup>
5. Radiology: Ultrasound (US) for detecting gallstones, choledocholithiasis, and local complications (free peritoneal fluid). Contrast-enhanced Computed Tomography (CECT) after the first 72 h following the onset of pain is useful for determining the extension and magnitude of the necrosis.<sup>41</sup> Percutaneous catheter drainage guided by ultrasound or CT is useful for managing infected fluid collections or necrosis and also as a part of the step-up approach.<sup>9,42</sup>
6. ERCP: If cholangitis is present ERCP should be performed during the first 24 h or in the case of AP with common bile duct obstruction in the first 48 h.<sup>43</sup>
7. Antibiotics: There is little evidence to support the prophylactic role of antibiotics in the prevention of infected necrosis.<sup>24</sup> As a general rule, treatment with empirical antibiotics can begin after 14 days if there is suspicion of infection, following culture collection. However, the appearance of SIRS after the first week in the case of AP with necrosis raises the suspicion of infection and it would be the appropriate time to indicate an antibiotic after obtaining culture samples. The intra-abdominal pressure assessment (IAP) is essential in this sense, because it is one of the markers indicating that (peri)pancreatic inflammation has become an infected entity. It is evident that obtaining purulent material and/or culture and antibiogram of suctioned material, by means of percutaneous US or CT guided fine needle aspiration (FNA), should be useful for guiding the administration of antibiotics.<sup>44</sup>
8. Surgery: Should be considered in patients with: (a) multi-organ failure with necrosis that does not respond to conservative treatment; (b) compartmental syndrome (IAP >25 mmHg) with persistent organ failure; (c) infected necrosis; and (d) mesenteric ischaemia and/or perforation of the intestine.<sup>9,33,34</sup> In this case monitored measurements of IAP in a critical patient with AP is essential,<sup>45,46</sup> because it indicates the evolution of process to an abdominal compartmental syndrome, regardless of whether it is infected or not, and it indicates complementary exploration (repeat CT if applicable) and surgery. Take into account the role of new surgical techniques: Minimal invasive pancreatic necrosectomy or step-up (open necrosectomy after the failure of minimal invasive surgery).<sup>9</sup> The important message is to try to "gain time" before performing early surgery as "necrosectomy in itself could be less important than obtaining adequate drainage".<sup>47</sup> Pseudo-aneurysm of surrounding vessels with or without haemorrhage can be treated with embolization techniques.

To conclude, this document proposes the pathways for AP, PSAP, Peri-surgical phase and the algorithms for clinical care during the first 72 hours after hospitalization based on

various approaches, levels of care, analytical tests, medical and surgical indications that are supported by current scientific evidence. The second conclusion is to propose a revision of the previous Recommendations for treatment of Severe and Critical AP.

## Conflict of interest

The authors have no conflicts of interest to declare.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.medic.2012.02.008](https://doi.org/10.1016/j.medic.2012.02.008).

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