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Classifications of acute pancreatitis: to Atlanta and beyond

Review Article

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Abstract: Until Atlanta Classification (AC) made in 1992, there was not any classification of acute pancreatitis (AP). Last twenty years AC let us compare results and papers. But the increasing understanding of the pathophysiology of AP, improvements in diagnostic methods and the development of minimally invasive tools for radiological, endoscopic and surgical management of local complications, several authors have called for the AC to be reviewed. Last months, two new classifications of AP have been published. We made a historical review of AC, the two new classifications and a comparison between them.

Keywords: *Pancreatitis • Classification • Necrotizing • Pseudocyst • Walled-off •Review*

1. Introduction

Until the 1990s, many different classifications were used to define acute pancreatitis (AP), and no single system stood out as the ideal choice [1,2]. The International Symposium on Acute Pancreatitis held in Atlanta in September 1992 proposed a classification system based on clinical data, which provided specific definitions regarding severity, organ failure, and local complications. The Atlanta Classification (AC) quickly gained wide acceptance and has been the classification of choice over the past 20 years [3]. In fact, the vast majority of articles on AP published since then have applied the AC [2,4-6]. The use of this classification has allowed researchers to compare different series and has introduced a degree of uniformity into the information recorded [2].

Despite the wide acceptance of the AC, however, Bollen et al demonstrated in an excellent systematic review that the system is not always strictly applied [2]. Increasingly, other assessment criteria are being used for the early diagnosis of severity: the CTSI (CT Severity Index), Simplified Acute Physiology Score (SAPS), Sequential Organ Failure Assessment (SOFA), APACHE II score and C-reactive protein (CRP) measurement, or clinical and laboratory predictors such as age, obesity, pleural effusion, and elevated hematocrit [2]. Nor are the AC's criteria for organ failure systematically used. Some researchers prefer newer classifications (Marshall, Goris, Bernard, SOFA, APACHE II, etc). Finally, in local complications such as necrosis and pseudocysts the AC's definitions have been applied even less consistently due to the absence of clear radiological criteria [2,7].

With the increasing understanding of the pathophysiology of AP, improvements in diagnostic methods and the development of minimally invasive tools for radiological, endoscopic and surgical management of local complications, several authors have called for the AC to be reviewed [2,4-7]. In January 2013, the journal Gut published a revision of the AC based on a broad international consensus [8].

As noted above, the areas requiring a profound revision are the definition of local complications (especially pancreatic and peripancreatic fluid collections), the demonstration of the importance of organ failure in AP, and the categories of severity [6].

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In the definition of local complications of AP, certain terms dating from the pre-AC period are still in use (e.g., infected pseudocyst), others included in the AC are debatable (e.g., pancreatic abscess), and new terms have been defined since the AC's publication (e.g., walled-off pancreatic necrosis). Therefore, a new updated nomenclature is needed in order to standardize the terminology [9,10].

The AC defined only two categories of AP: mild and severe (1.10). These categories are excessively broad and fail to classify a third group of patients with single organ failure or with pancreatic necrosis without organ failure. Some groups classify this situation as "moderately severe AP" [5,11]. The incorporation of the concepts of early and late phases in AP or transient and persistent organ failure has allowed a better understanding and classification of the condition [5]. In December 2012, another classification was devised for AP based on the determinants of severity, with four groups: mild, moderate, severe and critical. The two parameters that define the groups are pancreatic necrosis and organ failure [1,12].

In this article we present an historical review of the AC and describe the new version. We present the definitions of severity of AP and of local complications, both clinical and radiological, and discuss recommendations from other institutions seeking to optimize the categorization of patients with AP.

2. The Atlanta Classification (1992)

The Atlanta Classification was defined in 1992 and since then has been instrumental in the development of all medical research in AP [3,8]. The main contribution of the AC was the fact that it standardized the definitions of key concepts such as the diagnostic criteria for AP, severity (mild or severe), and systemic and local complications [3,8].

Nonetheless, the AC presents a number of limitations. First, a large group of patients do not fit neatly into its categories. Second, new concepts and therapeutic strategies have appeared since its publication, and third, the AC is unable to predict at onset whether a patient will develop a mild or severe illness, since some of the complications take days or weeks to appear. Attempts to improve the AC in recent years have used a range of diagnostic strategies to predict determinants of severity. Several scales with a high negative predictive value and a low or medium positive predictive value have been used, above all the APACHE II classification [4,7,10,13]. Finally, a new version of the AC has just been published, modifying some of the original concepts and removing others such as pancreatic abscess [3,8].

The original AC will continue to be used until the new version becomes established. The most important definitions in the old version are the following [3]:

1. Diagnosis: The AC defines AP as an acute inflammatory process of the pancreas with variable involvement of other regional tissue or remote organ systems, associated with raised amylase and/or lipase levels in serum.
2. Severity:

- Mild AP: Associated with minimal organ failure but complete recovery. No presence of pancreatic parenchymal enhancement on CT images. No serious local or systemic complications.
- Severe AP: Associated with organ failure and/or local complications such as necrosis, pancreatic abscess or pseudocyst. Presence of complications.

3. Definition of systemic complications:

- Shock: systolic blood pressure ≤ 90 mmHg
- Pulmonary insufficiency: PaO2 ≤ 60
- Renal failure: creatinine ≥ 177 mmol or ≥ 2 mg / dl after rehydration.
- Gastrointestinal bleeding: 500 ml in 24h
- Disseminated intravascular coagulation: platelets ≤ 100,000/mm, fibrinogen <1g / l
- Severe metabolic disturbances: calcium ≤ 1.87mmol/l, or ≤ 7.5 mg / dl.

4. Local complications:

- Fluid collections: an early complication of AP, located in or near the pancreatic parenchyma; always lack a wall or fibrosis. Spontaneous regression occurs in 50% of patients; in the rest, it progresses to pancreatic abscess or pseudocyst
- Pancreatic necrosis: non-viable pancreatic parenchyma, either localized or diffuse; habitually associated with peripancreatic fat necrosis.
- Pancreatic pseudocyst: collection of pancreatic juice inside a cavity enclosed by a wall formed by granulation tissue and fibrosis. Occurs at least four weeks after the onset of AP symptoms. May occur after AP, chronic pancreatitis or pancreatic trauma.
- Pancreatic abscess: intra-abdominal collection adjacent to the pancreas, with purulent contents; may contain necrosis. Like pancreatic pseudocyst, it occurs at least four weeks after onset of symptoms. It arises as the result of AP or pancreatic trauma [3,4].

3. Revision of the Atlanta Classification (2013)

As noted above, the Atlanta Classification has recently been revised by international consensus and certain changes regarding the concepts of AP, its onset, types, and local complications have been introduced. A concise definition of the radiological terms has also been provided [7].

3.1. New definitions in the AC 2013

Acute pancreatitis is diagnosed in the presence of two of these three features: abdominal pain, increase in serum lipase and/or amylase at least three times the normal value and US and CT findings of an image compatible with AP. CT is only used for confirmatory purposes (see radiological classification below). Another important concept in the definition of local complications is the time of onset of abdominal pain.

The various morphological definitions of AP are:

1. Interstitial or edematous pancreatitis (IEP): Inflammation of the pancreas or peripancreatic tissue, without recognizable tissue necrosis.
2. Necrotizing pancreatitis (NP): inflammation associated with pancreatic and/or peripancreatic necrosis.
3. Acute peripancreatic fluid collection (APFC): peripancreatic fluid collection without necrosis, which occurs within four weeks of onset of IEP.
4. Pancreatic pseudocyst (PP): An encapsulated collection of fluid with a well defined inflammatory wall outside the pancreas, occurring at least four weeks after the beginning of IEP.
5. Acute necrotic collection (ANC): collection with mixed contents occurring within four weeks of onset of NP.
6. Walled-off pancreatic necrosis (WOPN): An encapsulated collection of pancreatic or peripancreatic necrosis that has developed a well-defined inflammatory wall occurring at least four weeks after the onset of an NP.

Table 1 shows a comparison between the terms used in the old and the new versions of the AC.

3.2. Radiological terminology for AP in AC 2013

A clear, specific description of the radiological findings of patients with AP is crucial for their assessment, classification and management [6]. The 1992 Atlanta classification was based on clinical criteria, and some of its

Table 1. Comparison of terminology of AP: Atlanta Classification vs Working Group Classification

	ATLANTA 1992	ATLANTA 2013
Subtypes of AP	**- Interstitial pancreatitis**	**- Interstitial oedematous pancreatitis**
	- Necrotising pancreatitis - sterile - infected	**- Necrotising pancreatitis** - sterile - infected - site: peri/pancreatic
Fluid Collections < 4 weeks after onset AP	**- Acute Fluid Collections**	**- Acute Peripancreatic Fluid Collections (APFCs)** peripancreatic fluid associated with interstitial oedematous pancreatitis without necrosis -sterile -infected
	- Pancreatic Necrosis **- Infected Necrosis**	**- Acute Necrotic Collection (ANCs)** collection of fluid and necrosis associated with necrotising pancreatitis of (peri)pancreatic tissue -sterile -infected
Fluid Collections > 4 weeks after onset AP	**-Pseudocyst**	**- Pseudocyst** encapsulated collection of fluid with well defined inflammatory wall, usually outsider of the pancreas -sterile -infected
	- Pancreatic Abscess	
		- Walled-OFF pancreatic necrosis (WOPN) encapsulated Collection of (peri)pancreatic necrosis with a well defined inflammatory wall -sterile -infected

AP: Acute pancreatitis

definitions (especially the radiological ones) were confusing. This led to problems of communication not only between clinicians and radiologists, but also between radiologists themselves [4,7]. The poor radiological agreement was demonstrated in a study by Besselink et al, who showed CT corresponding to 70 patients with severe AP to five radiologists; agreement was reached in only three of the 70 cases [13]. Because of these difficulties, new classifications and definitions of the AP and its complications have been proposed, based mainly on morphological criteria obtained in contrast-enhanced CT [4,6,7,14].

The clinical-radiological definitions in the new AC 2013 are shown below:

3.2.1. Types of AP

Two subtypes of AP have been described, based on morphological characteristics: a) IEP, called Interstitial Pancreatitis in the 1992 Atlanta Classification [3], b) and NP [4,6-8,14]:

2. IEP: A localized or diffuse increase in the pancreas, due to interstitial or inflammatory edema with normal contrast enhancement of the pancreatic parenchyma. Peripancreatic tissue occurs without alterations or mild inflammatory changes and there may be a variable amount of liquid [4,7,14].

3. NP: characterized by the absence of contrast enhancement in all or part of the pancreatic gland in the CT, corresponding to areas of necrosis [6,7]. The necrosis needs some time to develop; as demonstrated by Knoepfli et al's multicenter study [15], CT performed in the early hours of the AP may understage necrosis. NP is classified according to whether the necrosis is infected, its location, and its percentage:

2.1. According to the presence of infection: NP is defined as sterile or infected [4,7,14]. The presence of gas in the necrosis is highly indicative of infection. In case of doubt fine needle aspiration may be performed to confirm the diagnosis [7]. This distinction is important because the presence of infection marks the natural history, treatment and prognosis of AP [4]. Also, as mentioned above, in the new classification published by the IAP the presence or absence of necrosis infection is a determinant of severity [12].

2.2 Location: Depending on the location, necrosis is divided into: necrosis of the pancreatic parenchyma (5% of patients with AP); peripancreatic necrosis, normally located in the retroperitoneal area or lesser sac (20% of cases), and pancreatic and peripancreatic necrosis (75-80% of AP) [4,6,7,14]. Peripancreatic necrosis (ExPN), defined in 1989 by Howard [16], refers to necrosis of peripancreatic fat but not of the pancreatic parenchyma [4]. In 1999, Sakorafas et al suggested that patients with ExPN had a better prognosis and lower severity [17]. A German study comparing 315 patients with ExPN and 324 pancreatic necrosis found more organ failure and persistent multiple organ failure, risk of infection, need for intervention and mortality in patients with pancreatic necrosis. However, when the ExPN is infected, the results in terms of complications and mortality are similar in the two groups [18].

2.3 Percentage of necrosis: traditionally, NP was classified into three categories according to percentage: <30%, 30% -50% and> 50% of pancreatic tissue [4,6,14].

3.2.4. Peripancreatic collections (Table 2)

Peripancreatic collections have also been redefined. Four different types are now proposed depending on the type of AP, content, location, time of evolution and the presence/absence of a capsule [4,6-8,14]. Other terms such as pancreatic phlegmon and pancreatic abscess are obsolete and are not included in the new classification [6]:

- Acute peripancreatic fluid collection (APFC): fluid collections that develop in the early phase of IEP. CT shows a homogeneous image without a defined wall, limited by normal fascial planes in the retroperitoneum. The collections may be multiple. Most remain sterile and

Table 2. Atlanta 2013: Fluid Collections in Acute Pancreatitis

	APFC	PSEUDOCYST	ANC	WOPN
Content	Fluid	Fluid	Fluid and necrosis	Fluid and necrosis
Appearance	Homogeneous	Homogeneous	Heterogeneous	Heterogeneous
Wall	No	Yes	No	Yes
Location	Peripancreatic	Peripancreatic	Intrapancreatic and/ or peripancreatic	Intrapancreatic and/ or peripancreatic
Type AP associated	Interstitial Oedematous Pancreatitis	Interstitial Oedematous Pancreatitis	Necrotising Pancreatitis	Necrotising Pancreatitis
Time alter onset	< 4 weeks	> 4 weeks	< 4 weeks	> 4 weeks

APFC: acute peripancreatic fluid collection; ANC: acute necrotic collection; WOPN: walled-off pancreatic necrosis

resolve spontaneously within 2-4 weeks, but they may become infected and require drainage. If they do not resolve within 4 weeks, they evolve into pseudocysts [4,6-8,14]

- Acute necrotic collection (ANC) (Figure 1): collections resulting from the liquefaction of necrotic tissue, occurring within the first four weeks of evolution of the NP. Collections may be located in the pancreatic parenchyma or peripancreatic tissue. CT performed after the first week shows a heterogeneous image containing fluid and necrosis; there is no defined wall, they may be multiple and have a loculated appearance. They may be sterile, in which case conservative treatment will be performed, or infected, in which case drainage is required [4,6-8,14]. This term was not defined in the 1992 Atlanta Classification; there the term "acute fluid collection" was used, covering the current terms APFC and ANC [7].
- Pseudocyst: fluid collections in the peripancreatic tissue, surrounded by a well-defined wall, which may appear after an IEP. They require more than four weeks' duration for development and may be sterile or infected. In the presence of infection the CT image of the wall is thicker and irregular [4,6-8,14].
- Walled-off pancreatic necrosis (WOPN) (Figure 2): a new term introduced to describe the evolution of ANC. This condition previously received other names: necroma, organized pancreatic necrosis, pancreatic sequestration and pseudocyst associated with necrosis. It is an encapsulated collection of pancreatic or peripancreatic necrosis with a well-defined wall, which usually occurs four weeks after an NP [4,6-9,14]. If sterile and asymptomatic its management is controversial, but in the case of infection endoscopic drainage is recommended as first choice, or surgical drainage in selected cases of > 15 cm or with involvement of both paracolic gutters. Percutaneous drainage is not recommended because the solid component of the collection limits the resolution rate [9].

Bollen proposes a fifth type of collection that is not included in the classification, which he terms post-necrosectomy pseudocyst. This occurs in patients with prior necrosectomy due to NP or WOPN in the central area of the pancreas with a viable pancreatic tail, causing what is known as "disconnected duct syndrome", in which the residual cavity post-necrosectomy in the center of the pancreas is filled with pancreatic fluid produced by the pancreatic tail [4]. This condition is recurrent and occurs months or years after the episode of AP. Banks includes it in the category of pseudocysts [8].

4. IAP Classification (IAP: International Association of Pancreatology)

In December 2012, the IAP promoted a classification of AP based on determinants of severity, defined as factors that are causally associated with the severity of AP. The two factors that have been identified as major determinants of severity are systemic complications, focusing on organ failure (OF), and local complications, focusing on necrosis [12,19,21] (Table 3).

The IAP defines OF based on the SOFA score of 2 or higher (inotropic agent requirement, creatinine ≥ 2mg/dL, PaO2/FiO2 ≤ 300 mmHg) (Vincent) and like previous studies [10,20] differentiates between transient (<48h) and persistent OF (≥ 48h) [12]. The definition of necrosis refers to non-viable tissue located in the pancreas, pancreatic gland and peripancreatic tissue, or in the peripancreatic tissue alone. For the IAP the difference between sterile or infected (peri) pancreatic necrosis is important and influences the classification [12].

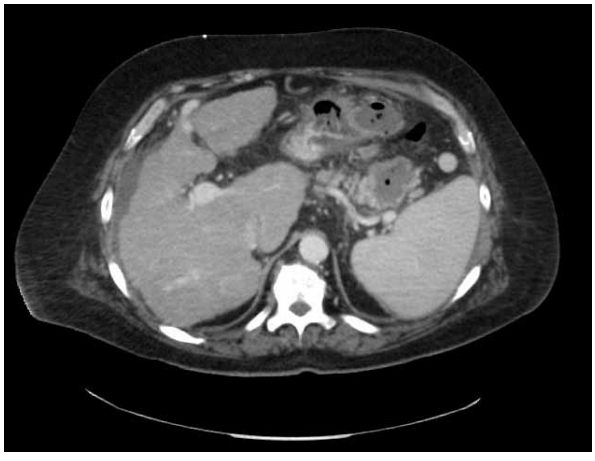

Figure 1. CT: walled off pancreatic necrosis

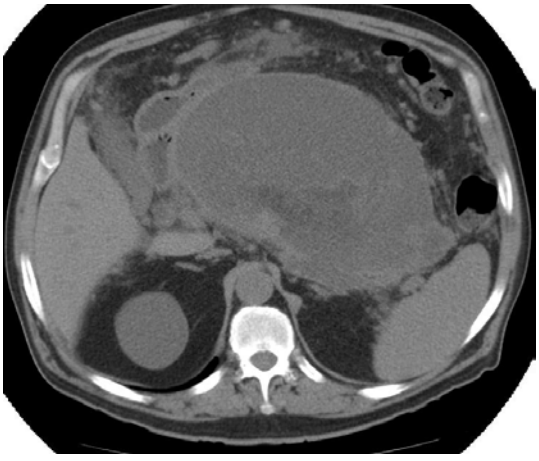

Figure 2. CT: acute necrotic collection

The cause-effect relationship between these two determinants was demonstrated in a multicenter study in which the absolute influence of OF and infected pancreatic necrosis was comparable and in which the relative risk of mortality doubled when both were present, indicating an extremely severe AP [19]. For this reason a fourth group has been introduced in the classification of AP severity, termed "critical AP", originally proposed by Petrov in 2010 [20] and now accepted by the IAP. The definitions used for categories of severity proposed are based on the attributes of local determinants (absent, sterile or infected (peri) pancreatic necrosis) and systemic determinants (absent, transient or persistent OF) and the possibility of interaction between them during the same episode of AP [12] (Table 4). The IAP supports this classification because it uses unambiguous language, facilitates communication between professionals and promotes standardization for data comparison in clinical trials [12,20].

To conclude: in its day, the AC represented a breakthrough in daily clinical practice. It allowed comparison of the results of published series and established a terminology that has lasted for 20 years. Advances in the last two decades have led to the revision of the AC that proposes three types of AP, incorporates new pathophysiological concepts and provides highly specific definitions of the local complications that occur in AP. The IAP's new classification, which appeared at the same time, divides AP into four subtypes according to the presence of determinants of severity (pancreatic necrosis and OF). Radiologists, ICU specialists, gastroenterologists, and surgeons involved in the care of acute pancreatitis should be familiar with these new classifications and definitions, and should gradually abandon the terms and concepts used in the old AC and earlier classifications.

Table 3. Determinant-Based Classification of AP (12)

	MILD AP	MODERATE AP	SEVERE AP	CRITICAL AP
(Peri)pancreatic necrosis	No	Sterile	Infected	Infected
	AND	AND/OR	OR	AND
Organ Failure	No	Transient	Persistent	Persistent

Table 4. Comparison of Classification Schemes of AP: Atlanta Classification vs Working Group Classification vs Determinant-Based Classification

	Atlanta Classification (Bradley.1993.Arch Surg)	**Working Group** (Banks 2012.Gut)	**Determinant-Based Classification** (Dellinger.2012.Ann Surg)
Severity assessment	- Organ Failure: Shock, pulmonary insufficiency, renal failure or gastrointestinal bleeding	- Organ failure (score of ³ 2 in modified Marshall scoring system*) - transient: organ failure in the same organ system for < 48h - persistent: organ failure in the same organ system for ³ 48h	- Systemic determinants: Organ failure (score of ³ 2 in SOFA**) - transient: organ failure in the same organ system for < 48h - persistent: organ failure in the same organ system for ³ 48h
	- Systemic complications: DIC, severe metabolic disturbance (calcium£7.5mg/dL)	- Systemic complications: exacerbations of underlying co-morbidities related to the acute pancreatitis	
	- Local complications: necrosis, abscess, pseudocyst	- Local complications: (peri)pancreatic fluid collections	- Local determinants: (peri) pancreatic necrosis - sterile - infected
	- Prognostic signs: Ranson's socre ³ 3, Apache II ³ 8		

AP: acute pancreatitis; DIC: disseminated intravascular coagulation, SOFA: Sepsis-related Organ Failure Assessment

Conflict of interest statement

Authors state no conflict of interest.

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