Local complications in acute pancreatitis: what's radiologically new, according to the revised Atlanta classification (2012).

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Learning objectives

1. To review the complex and dynamic pathophysiological process of an episode of acute pancreatitis (AP), underlining the new aspects introduced by revised Atlanta classification (2012). The Atlanta classification is the only widely accepted, clinically-based classification system of AP, initially developed by a consortium of experts in 1992 and then updated in 2012 after incorporating advances in knowledge on pathophysiology and management strategies. This classification should represent a common platform of disease assessment for both clinicians and radiologists.

2. To focus on the new classification of local complications according to the revised Atlanta classification (2012), describing how to recognize them on Contrast-Enhanced Computed Tomography (CECT) and Magnetic Resonance (MR) imaging.
Background

AP

AP is an inflammatory process of the pancreatic gland, characterized by interstitial edema and inflammatory infiltrate. Necrosis occurs in the case of intrapancreatic activation of pancreatic exocrine enzymes, thus leading to parenchymal and peripancreatic tissue damage.

Epidemiology: AP is one of the most frequent gastrointestinal causes for hospitalization, with an annual incidence ranging from 13-45/100,000, with an equal proportion between men and women. Causes of AP include mainly cholelithiasis (38% of cases) and alcohol abuse (36% of cases), followed by hyperlipidemia, hypercalcemia, trauma and drugs. AP is a relatively frequent complication of endoscopic retrograde cholangiopancreatography (ERCP). In 10% to 30% of cases are idiopathic in nature.

Clinical presentation and laboratory:

According to the revised Atlanta classification, AP is clinically diagnosed if at least the first two of the following features are present:

1. Abdominal pain typically persistent, severe, localized in the epigastric region, with possible back irradiation (sometimes associated with nausea and vomiting);
2. Lipase (or amylase) three times greater than the normal range; since the levels of these enzymes declines over 3-4 days, it is important to correlate them with the time of onset of abdominal pain; increase of the inflammatory markers;
3. Characteristic findings on CECT or MR imaging or transabdominal US investigation. Of note, no imaging is required if AP is diagnosed on the bases of the first two points, and there are no signs of SIRS or persistent organ failure.

Prediction of severity

Severity assessment is based on clinical and laboratory parameters. Features that may predict a severe attack within 48 hours of admission to hospital are summarized in TABLE 1. Apache II score is another severity score and is estimated on the base of 12 parameters, such as body temperature, mean arterial pressure, pH, heart and respiratory rates. For the evaluation of organ failure, the modified Marshal scoring system is used (TABLE 2). Three organ systems are assessed, respiratory, cardiovascular and renal; a
score of two or more for one of these three organ systems defines a condition of organ failure.

In agreement with what was said above and based on occurrence of local complications, three grades of severity can be distinguished:

- **Mild acute pancreatitis**: no organ failure or local or systemic complications;
- **Moderate severe acute pancreatitis**: transient organ failure (<48 h), local complication or worsening of co-morbid disease;
- **Severe acute pancreatitis**: persistent organ failure (>48 h); peripancreatic fluid collections, pancreatic or peripancreatic necrosis (sterile or infected) and late local complications.

Of note, patients with organ failure persisting for more than 48 hours were found to have a mortality rate >50%, whereas patients with organ failure resolving within 48 hours had mortality rate of zero.

From the pathological point of view, mild acute pancreatitis is generally an interstitial edematous pancreatitis (IEP), representing the most common form (about 75-85%); it resolves generally within the first week after presentation. The severe form correlates with necrotizing pancreatitis (about 15-25% of all pancreatitis), and is associated with a high mortality rate.

In addition, in this dynamic disease process, the revised Atlanta Classification distinguishes two phases:

- **Early phase**: within the first week; it's characterized by a systemic inflammatory response syndrome (SIRS) because of the cytokine cascade activated by the pancreatic inflammation; in this phase the presence and the duration of organ failure determine clinical severity, which does not correlate with the intra- and peripancreatic alterations;

- **Late phase**: after the first week up to months; it is associated with moderate severe and severe forms of pancreatitis. Persistent organ failure and local complications occur. The imaging is important in this phase for the purpose of identifying local complications and guiding treatment decisions.

**NOTES ON THERAPY**

**SUPPORTIVE THERAPY**: early fluid resuscitation and oxygen supplementation in order to prevent systemic complications, pharmacological control of pain, correction of hyperglycemia, enteral nutrition through a nasogastric tube;
PROPHYLACTIC ANTIBIOTICS: its utility is still debated; generally it is administered in severe pancreatitis with evidence of necrosis, in order to prevent infection (especially when the pancreatic necrosis is 30% or more because the risk of infection is greater). It should last 7 -14 days (the treatment can be extended only in cases of evidence of bacterial contamination by culture).

ERCP: this procedure should be carried out within 72 hours after the onset of pain in AP, caused by gall stones, in which the criteria for a predicted or actual sever attack are satisfied; other cases necessitating an urgent ERCP are jaundice, cholangitis or a dilated common bile duct;

CHOLECISTECTOMY: It is preferred perform it during the same admission at hospital. A potential fatal recurrent AP is the risk of a surgical delay. This procedure should be delayed in patients with severe AP until the systemic complications are resolved;

MANAGEMENT OF NECROSIS: it is different depending on if the necrosis is sterile or infected. In the first case a CECT follow-up is performed every 7-10 days in order to control the evolution of necrosis and to exclude the presence of air bubbles indicating infection. FNA (fine needle aspiration), to exclude necrosis infection, is needed in cases of clinical instability in the absence of radiological evidence of infection. If the suspicion is confirmed, treatment is necessary and it is performed surgically (necrosectomy) together with antibiotic therapy. If the patient is unstable, percutaneous drainage can be performed initially, by removing the more liquefied material, until the stabilization of the clinical status;

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MANAGEMENT OF LOCAL COMPLICATIONS: they can require surgical, endoscopic or radiological intervention; the approach depends on many elements, such as patient's conditions or local expertise. In general a multidisciplinary approach is needed.
Table 1

<table>
<thead>
<tr>
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<th>Elements predicting a severe attack of AP within 48 hours of admission to hospital</th>
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</table>
| **Initial assessment** | BMI > 30  
                          | Chest radiograph documenting pleural effusion  
                          | APACHE II score > 8 |
| **24 h after admission** | APACHE II score > 8  
                          | Glasgow Score 3 or more  
                          | Persisting organ failure  
                          | C reactive protein > 150 mg/l |
| **48 h after admission** | Glasgow score 3 or more  
                          | C reactive protein > 150 mg/l  
                          | Persisting organ failure for 48 H  
                          | Multiple or progressive organ failure |

Table 2

<table>
<thead>
<tr>
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<th>Modified Marshall scoring system for organ dysfunction</th>
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<tbody>
<tr>
<td><strong>SCORE</strong></td>
<td>0</td>
</tr>
<tr>
<td>Respiratory (PaO2/FIO2)</td>
<td>&gt;400</td>
</tr>
<tr>
<td>Renal (serum creatinine mg/dl) (serum creatinine, micromol/L)</td>
<td>&lt;1.4</td>
</tr>
<tr>
<td>Cardiovascular (systolic blood pressure, mm Hg)</td>
<td>&gt; 90</td>
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A score of 2 or more indicates an organ failure.
Findings and procedure details

IMAGING TECHNIQUES FOR AP

Ultrasound: it is indicated in an early episode of acute pancreatitis to evaluate the presence of colelithiasis/coledocolithiasis. The assessment of the pancreatic region is often limited by the presence of intestinal bloating; pancreatic swelling can be showed. The evaluation of the peripancreatic collection is usually difficult.

Computed Tomography: according to the revised Atlanta classification, CECT is the primary tool for assessing a potential episode of AP, thanks to its wide availability, panoramicity and high degree of accuracy. The assessment should be made after 48-72 h of the onset of symptoms, i.e. the time needed to develop necrosis. CT protocol is based on a pre-contrast scan, followed by the injection of a bolus of contrast medium at high injection rate (3-4 ml/s). Post contrast study should include late arterial phase acquired about 40 sec from the injection start (better contrast between viable parenchyma and necrotic areas), venous phase at 65-70 sec (for evaluating patency of the peripancreatic veins and peripancreatic regions). Thin collimation is needed.

CT findings help clinicians to discriminate among mild, moderate, and severe forms of pancreatitis, as exemplified by the modified CT severity index (TABLE 3). According to this score, the severity of pancreatitis is categorized as mild (0-2 points), moderate (4-6 points) or severe (8-10 points). In patients with a score between 0 and 2 no further CECT is required, unless there is a worsening in clinical status suggesting a complication. In case of CT severity index of 3-10, CECT follow-up is recommended if clinical status deteriorates or there are no signs of improvement.

Magnetic Resonance Imaging: In an initial phase of AP, MR can play a role in cases in which CECT is contraindicated. However, minor accessibility, costs, long acquisition time and possible artefacts from reduced respiratory collaboration limit its use in the clinical routine. The core of an MRI study for AP should be 2D and/or 3D Magnetic Resonance Cholangiopancreatography (MRCP), with the aim to identify small biliary calculi undetected on US and/or CT. More importantly, MRCP can assess whether parenchymal necrosis transected (or not) the main pancreatic duct; secretin stimulation is of help in excluding pancreatic fluid leakage within intra- or peripancreatic collections. Finally, high soft-tissues contrast of MRI can be of help in detecting causes of AP (e.g., small tumors) or characterizing the content of abdominal collections.

IMAGING FINDINGS
**INTERSTITIAL EDEMATOUS ACUTE PANCREATITIS (IEP):** it is characterized by a diffuse (or focal) enlargement of the pancreas due to inflammatory edema. Both CECT and MRI show an homogeneous (or slightly patchy) post-contrast pancreatic enhancement; there may be also mild peripancreatic fat stranding in association with fluid (FIG. 1).

**NECROTIZING PANCREATITIS:** some cases (15-25% of patients with an episode of AP) can develop a necrosis of pancreatic parenchyma and/or peripancreatic fat. Revised Atlanta classification distinguishes three forms of acute necrotizing pancreatitis, based on necrosis extension:

- **Pancreatic necrosis alone:** in less than 5% of cases with a necrotizing AP; in the modified CTSI two categories are present, based on the extension of necrosis: less than 30% or greater than 30%, as TABLE 3 shows;
- **Peripancreatic necrosis alone:** seen in 20% of patients; this entity is difficult to confirm on imaging; typical sites are the retroperitoneum and the lesser sac; patients with peripancreatic necrosis alone have better prognosis than patients with coexistence of pancreatic necrosis;
- **Pancreatic parenchymal necrosis with peripancreatic necrosis:** the most common type (75-80%).

All three types of necrosis can be sterile or infected.

Necrotic parenchymal changes are represented, both on CECT an MR, by areas of diminished or non-enhancing pancreatic parenchyma. In the first few day from the onset, CECT (or MR) may underestimate the real extension of necrosis, because it needs some days to manifest clearly on imaging. In this hyperacute phase, pancreatic parenchyma may demonstrate an heterogeneous enhancement that might represent both IEP or necrosis (FIG. 2). A CECT performed after few days (5-7 days) can characterize it definitely.

**LOCAL COMPLICATIONS**

Previous Atlanta classification included three types of local complications: acute fluid collection, pancreatic pseudocyst and pancreatic abscess. This classification was a source of confusing interpretation of surgical and radiological findings, and has been updated in 2012 based on novel pathophysiologic knowledge and management techniques. According to revised Atlanta classification, local complications can be divided into:
ACUTE PERIPANCREATIC FLUID COLLECTION (APFC): it means the presence of peripancreatic fluid, associated to interstitial edematous pancreatitis and absence of peripancreatic necrosis. It usually occurs within 4 weeks after the onset of an IEP and most of the time is reabsorbed in a few weeks. It is due to pancreatic/peripancreatic inflammation or to the rupture of small peripheral duct branches. It usually develops next to the pancreas and it is confined within peripancreatic fascial planes, with no intrapancreatic extension. The density (or signal on MR) is homogeneous, fluid, with no definable wall (FIG. 3)

ACUTE NECROTIC COLLECTION (ANC): this collection contains both fluid and necrosis and it is a complication of a necrotizing pancreatitis; it develops within the first 4 weeks from the onset. In the first week after the onset of symptoms it is difficult to distinguish an ANC from an APFC; then, gradually, in case of an ANC, non-liquefied material (in general haemorrhage, fat or necrotic fat) appears, giving it an inhomogeneous aspect on imaging (MR can show it better); no definable wall is present; it can be intra- and/or extrapancreatic (FIG 4)

PANCREATIC PSEUDOCYST (PP): it is represented by a fluid collection of pancreatic juices, encapsulated in an inflammatory well-defined wall (formed by a fibrous membrane) with minimal or no necrosis or solid components. It is usually outside the pancreas (occasionally intrapancreatic) and develops 4 weeks after the onset of an IEP from a previous APFC. Both CECT and MR show a round or oval collection, surrounded by a wall, of variable thickness, characterized by a slightly enhancement of contrast media. The content is mainly homogeneous; better content definition is achieved on MRI (FIGS. 5, 6)

WALLED-OFF NECROSIS (WON): It means a mature encapsulated collection of pancreatic and/or peripancreatic necrosis with a well-defined reactive wall; like the pseudocyst, it is a late local complication (beyond 4 weeks) evolving from previous ANC. On CECT, WON appears as a heterogeneous collection with liquid and non-liquid density (necrotic debris) within or around the pancreas, surrounded by an enhancing wall. It may be multiple and may be distant from the pancreas. MR identifies more accurately than CECT the internal necrotic debris that favors the presence of a WON. It is important to differentiate a WON from a pseudocyst because the management is different: in general, WON need a more aggressive treatment. (FIGS. 7, 8)
DISCONNECTION OF THE PANCREATIC DUCT (FIG. 8): it is a potential complication of necrotizing AP (30-50 % of cases) in which a viable segment of the pancreatic body or tail is isolated from the gastrointestinal tract with a complete discontinuity of the pancreatic duct. The result is that the secretions of the pancreas distal to the disruption are drained into the peripancreatic spaces. The consequences are a persistent fistula and an inflammatory collections.

CT or MR imaging can show a large intrapancreatic collection or necrotic area (of at least 2 cm of length) combined with a viable segment of the distal body or tail. The diagnosis is confirmed by ERCP. At present, secretin enhanced MR cholangiopancreatography has been proposed as an alternative to ERCP.

Initial management is achieved by positioning an endoscopic stent to drain collections. Unfortunately, there is a significant risk of recurrence and a surgical intervention is frequently needed.

OTHER COMPLICATIONS OF AP: VASCULAR COMPLICATIONS

Pseudoaneurysm: it develops as a result of an arterial wall digestion by proteolytic enzymes that leads to the formation of an encapsulated hematoma; the external wall consists of adventitia, perivascular tissue, fibrosis or clot. It usually occurs in the proximity of a pseudocyst. The most commonly vessel involved is the splenic artery, followed by the gastroduodenal and the pancreaticoduodenal arteries (rarely superior mesenteric artery and proper hepatic artery) (FIG.10).

Portomesenteryc vein trombosis: it is an uncommon complication of a severe episode of AP (1-2% of cases); the splenic vein is more commonly involved due to its proximity to the pancreas (in 10-40% of cases of AP). Thrombosis of the portal and superior mesenteric veins may also occur.
**Table 3**

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**Modified CT Severity Index**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Score</th>
</tr>
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<tbody>
<tr>
<td>Normal pancreas</td>
<td>0</td>
</tr>
<tr>
<td>Intrinsic pancreatic abnormalities with or without inflammatory changes in paripancreatic fat</td>
<td>2</td>
</tr>
<tr>
<td>Pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis</td>
<td>4</td>
</tr>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>&lt; α = 30%</td>
<td>2</td>
</tr>
<tr>
<td>&gt; 30%</td>
<td>4</td>
</tr>
<tr>
<td>Extrapancreatic complications (one or more pleural effusion, ascites, vascular complications, parenchymal complications or gastrointestinal tract involvement)</td>
<td>2</td>
</tr>
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**Table 4**

**Acute Pancreatitis**

<table>
<thead>
<tr>
<th>≤ 48 h</th>
<th>4 weeks</th>
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<tbody>
<tr>
<td>ACUTE PERIPANCREATIC FLUID COLLECTION</td>
<td>PSEUDOCYST</td>
</tr>
<tr>
<td>ACUTE NECROTIC COLLECTION</td>
<td>WALLED-OFF NECROSIS</td>
</tr>
<tr>
<td>INTERSTITIAL EDEMATOUS ACUTE PANCREATITIS</td>
<td>Sterile or infected</td>
</tr>
<tr>
<td>NECROTIZING PANCREATITIS</td>
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**Fig. 1:** Post-ERCP IEP on portal venous phase CT. The pancreatic boundaries are ill-defined, with peripancreatic fat stranding, associated with minimal amount of peripancreatic fluid. A biliary stent is in site (arrows).
**Fig. 2:** Necrotizing pancreatitis on portal venous phase CT. Necrotic area showing no contrast enhancement affecting less than 50% of pancreas, located at the pancreatic isthmus (blue arrows). Gross peripancreatic fat stranding is observed (white arrow).

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**Fig. 3:** Acute peripancreatic fluid-collection (APFC); portal venous phase CT shows a slightly patchy pancreatic parenchyma with peripancreatic fat stranding and a minimal amount of fluid adjacent to the pancreatic tail (blue arrows).

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Fig. 4: FIG. 4 a, b and c: extrapancreatic ANC: a 95-year-old female patient: a, b) portal venous phase CT shows inhomogeneous peripancreatic fluid with areas of fat inside (blue arrows); the component located behind the pancreas has a very ill-defined wall; c) CT control after two weeks demonstrates a progressive formation of a wall, delimiting the boundaries of the collection (a walled-off necrosis, WON).

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**Fig. 5:** FIG. 5: pancreatic pseudocyst: portal venous phase CT shows a round, low-attenuated, homogeneous fluid collection adjacent to the pancreatic isthmus with a well-defined enhancing wall; there are no areas of greater attenuation which might suggest non-liquid components.

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**Fig. 6:** FIG. 6: pancreatic pseudocyst (PP): a) portal venous phase CT shows a round fluid collection, encapsulated by a well-defined enhancing wall; b) HASTE T2w sequence, c, d) GE 3D FAT SAT T1w sequence pre- (c) and post-contrast (d; 70 seconds after the injection of contrast media) confirm the presence of the collection with a homogeneous water-intensity content.

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Fig. 7: walled-off necrosis (WON): a 63-year-old female patient one month after the onset of a necrotizing AP with hemodynamic instability: portal venous phase CT shows multiple inhomogeneous collections with well-defined wall, surrounding the pancreas; the boundaries of pancreas are ill-defined.

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Fig. 8: Fig. 8: walled-off necrosis (WON): a 70-year-old male patient with epigastric abdominal and an increase of the amylase two months after the onset of a necrotizing AP. MR shows a voluminous collection with well-defined wall, placed in the context of the pancreatic body, with predominant fluid signal intensity (a, b); there are also some components of low signal intensity suggesting the presence of necrotic debris (b); on HASTE sequence and T2w 3D TSE sequence (coronal planes)(c, d) it seems to be in continuity with the main pancreatic duct (disconnected pancreatic duct syndrome) (blue arrows); e) MIP reconstruction.

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Fig. 9: Fig. 9: walled-off necrosis (WON): MR imaging shows a gross, irregular and inhomogeneous collection with well-defined wall, surrounding the pancreas, which is thin and barely recognizable (white arrow).

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Fig. 10: pseudoaneurysm of the gastroduodenal artery in a 68 years old male patient with relapsing episodes of AP: a) arterial phase CT; b) MIP (axial and coronal planes) and VR reconstructions; c) post-embolization MIP reconstructions in axial and coronal planes (blue arrow).

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Conclusion

AP is a complex and dynamic process and it is very important that also radiologists have a panoramic overview of its several aspects; the revised Atlanta classification clarify these points and, in particular, introducing new standardizing terminology for pancreatic fluid collections, will improved the communication between radiologists and clinicians, facilitating a comparison among different institutions and the choice of the best treatment option.
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