

## Walled-off pancreatic necrosis: where are we?

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Walled-off pancreatic necrosis (WOPN) is a well-circumscribed area of necrosis which occurs as a late complication of acute pancreatitis, generally after four weeks from the initial attack. The term “walled-off necrosis” was introduced for the first time in 2006. Approximately 15% of patients with severe acute pancreatitis will develop a WOPN [1]. The impact of the onset of pancreatic necrosis and other complications after an episode of acute pancreatitis may have deep repercussions on the quality of life of the single patient that can persist for years or even lifelong. For instance, exocrine and endocrine insufficiency following pancreatic necrosis may cause lifelong morbidity. Exocrine and endocrine insufficiency is probably related to the extent of necrosis into the pancreatic parenchyma, or as recently suggested by Rana *et al*, by the type of approach [2] adopted to clean the necrosis: surgery versus endoscopy.

For the first time Rana *et al* evaluated the structural and functional changes in the pancreas comparing endoscopic to surgical debridement of pancreatic necrosis. In this study, the morphological changes in the pancreas in patients treated endoscopically were evaluated by magnetic resonance, computed tomography (CT) and/or endoscopic ultrasound (EUS). Furthermore, these patients were followed with blood glucose controls and fecal fat measurement. The authors compared the results with an historical group of 25 patients had undergone surgery in the past and found slightly reduced impairment of pancreatic function in patients treated endoscopically compared to those treated surgically. The study was retrospective but the follow-up period was long.

Minimally invasive approaches, especially endoscopic drainage/debridement of WOPN, were developed to reduce the trauma of surgery to the vital pancreatic parenchyma. Nevertheless, at present no randomized trial has proven the superiority of this approach compared to open necrosectomy in terms of onset of pancreatic endocrine and exocrine insufficiency. As far as infection is concerned, Gupta *et al* in 2009 found a higher frequency of pancreatic insufficiency when the pancreatic necrosis was infected, in comparison to sterile necrosis [3]. Furthermore, if the functional impairment of the pancreas will be persistent, or only be temporary it is still unknown.

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When and which pancreatic necrosis should be drained? The recommendation of the recently revised guidelines [4,5] of the International Association of Pancreatology, the American Pancreatic Association and the American Gastroenterological Association state that there is no need of intervention in asymptomatic patients without infected necrosis, regardless of its size, location, and extension. In case of infected (confirmed on CT scan or EUS liquid aspiration), but asymptomatic necrosis, it is advisable to delay any surgical, radiologic or endoscopic approach for more than four weeks in order to facilitate the formation of WOPN with liquefaction of the contents [4,5]. Infected and symptomatic necrosis requires immediate drainage in order to avoid fatal complications [4,5]. In these cases, minimally invasive methods of necrosectomy should be preferred to open surgery [4,5]. The above-mentioned guidelines suggest that it is not indicated to perform routine percutaneous or endoscopic fine needle aspiration (FNA) of pancreatic and peripancreatic collections for the detection of infection [5]. Infection in these cases should be assessed clinically. In any case, infection can be confirmed by FNA, and this can be useful for bacterial culture and to assess the best antibiotic therapy.

Can there be a *restitutio ad integrum* of the pancreatic parenchyma after WOPN drainage? In daily clinical practice it is assumed that exocrine and endocrine pancreatic functions recover completely after a mild episode of acute pancreatitis. The grade of pancreatic exocrine and endocrine insufficiency depends on the extension of the necrosis [6-8], and is strictly related to the severity of the attack of acute pancreatitis [7,8].

It is known that vital pancreatic tissue can be lost during surgical debridement of pancreatic necrosis [9-11]. Actually there often is a poor demarcation between the necrotic areas and the remnant vital pancreatic parenchyma. But can surgery be avoided? Uomo *et al* found that endocrine and exocrine functions recover completely in the vast majority of patients, if these undergo conservative treatment, avoiding surgery [12]. But how can we decide which patients should be treated conservatively? And if needed, which is the best way to clean the pancreatic necrosis, especially if infected, in order to induce less traumatism to the pancreas? Surgery with open necrosectomy (an anterior or retroperitoneal approach) is associated with longer convalescence, higher morbidity, development of abdominal wall hernias, external fistulae and has increased costs, often influenced by the need of re-interventions [13-15].

Alternatives to traditional surgery are other “minimal access techniques” that permit access to the areas of necrosis. These are: percutaneous catheter drainage with interventional radiology, percutaneous laparoscopic necrosectomy, focused

operative necrosectomy [16], sinus tract endoscopy [17,18], and the video-assisted retroperitoneal debridement [19]. These techniques can be applied only to very restricted areas, but permit direct approach to necrosis allowing the so-called “functional necrosectomy”.

In the past two decades endoscopy has emerged as an alternative to other major procedures. Endoscopic drainage of WOPN can be transgastric or transduodenal. The transpapillary endoscopic drainage of WOPN is not feasible and is generally reserved to pancreatic pseudocysts and other fluid collections that do not contain massive solid components. Unlike WOPN, pseudocysts are mostly liquid, and generally require small-caliber stents to allow an effective drainage. Since generally WOPN contains solid debris, there is often a need of large transmural tracts, that will allow the spontaneous passage of the necrotic material, usually with irrigation with saline or as recently suggested, with hydrogen peroxide. Large transmural tracts are also useful to directly access the cavity with a gastroscope in order to actively remove necrotic debris. These procedures may be long-lasting and often necessitate of many sessions. Generally, plastic pigtail stents are placed between the WOPN and the stomach or duodenum, in order to maintain the transmural tract open. Plastic stents in WOPN allow only drainage of the liquids and can easily clog. Recently, covered metal stents have been used for spontaneous debridement clearance and to easily access the necrosis [20]. Results of the use of these stents are promising [20].

At the moment we are waiting for new biomarkers that will be able to predict complications of acute pancreatitis, as well as for new randomized trials that will test the superiority of minimally invasive approaches over open necrosectomy, in terms of preserving pancreatic vital parenchyma. Today we know how to clean a pancreatic necrosis using minimally invasive approaches that allow us to spare the pancreatic vital parenchyma. What is needed now are new less invasive devices that will facilitate pancreatic necrosectomy, avoiding endless procedures. WOPN represents a challenging critical problem with still high burden of mortality and morbidity: even if today we have “different ways to skin a cat” the best individual treatment should always be chosen on multidisciplinary basis involving surgeons, endoscopists, radiologist and intensive care specialists.

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