Netherlands
The Journal of Medicine

REVIEW

Walled-off pancreatic necrosis

***J.M. Ramia, R. de la Plaza, J.E. Quiñones-Sampedro, C. Ramiro, P. Veguillas, J. García-Parreño**

Hepato-Pancreato-Biliary Surgical Unit, Department of Surgery, Hospital of Guadalajar, Guadalajara, Spain, *corresponding author: tel.: +34 (0)616292056, e-mail: jose_ramia@hotmail.com

ABSTRACT

Acute severe pancreatitits may be complicated by the development of 'walled-off pancreatic necrosis' (WOPN), which is characterised by a mixture of solid components and fluids on imaging studies as a consequence of organised pancreatic tissue necrosis. We present here an overview of the definition, clinical features, and diagnostic and therapeutic management of this clinical condition, which is mostly based on consensus as adequate clinical trials are lacking.

KEYWORDS

Pancreatitis, walled-off, review

INTRODUCTION

The term 'walled-off pancreatic necrosis' (WOPN) was first used in 2005 to define a mixed fluid-solid collection [i.e. a picture that is composed of solid components and fluids], with a similar appearance to pancreatic pseudocyst, which occurs after severe acute pancreatitis.[1-3] Previous designations for the condition are organised pancreatic necrosis, post-necrosis pseudocyst, pancreatic sequestration or necroma.[3-6] In 2006, the term 'walled-off pancreatic necrosis' was officially accepted at the American Gastroenterological Association meeting.[7] However, the new nomenclature had various interpretations and consensus about its radiological characteristics and therapeutic options was lacking. In a PubMed search (June 2011) of "walled-off pancreatic necrosis" we only found 18 entries, but some articles were not totally related to the item, so no more than ten articles about WOPN are currently available.[1-3,6-11] We have performed a comprehensive review of this topic.

DEFINITION OF WOPN

In 1992, the Atlanta Classification added clear terms and definitions for the diagnosis of acute pancreatitis and its complications. This allowed the comparison of the results of different working groups in the medical community and simplified the common management of patients around the world.[12] In recent years, new concepts or terms, such as WOPN, have been postulated and this classification will probably have to be updated.[13]

In 1996, Baron *et al.* first used the term 'organised pancreatic necrosis' to describe a transitional collection between pancreatic necrosis and pancreatic pseudocyst that contained different amounts of fluid and necrotic tissue.[4] This entity was caused by the necrosis and liquefaction of pancreatic and peripancreatic tissue, with or without pancreatic duct communication.[3-5]

A temporary proposed classification of acute pancreatitis postulated the new term 'post-necrotic pancreatic and peri-pancreatic collections'.[14] These collections consisted of different proportions of fluid and solid necrosis and can be identified three to six weeks after the episode of acute pancreatitis. When the collections are fully developed, the presence of a thin wall without epithelium may lead to a misdiagnosis of pancreatic pseudocyst. Once walled-off collections are present, WOPN can be diagnosed.[6,14]

WOPN occurs in 1 to 9% of cases of acute necrotising pancreatitis.[5,6,8] Acute biliary pancreatitis is the most common cause of WOPN (50 to 70%) and other aetiologies are alcohol abuse and idiopathic.[8-10] Only a few cases of WOPN are caused by chronic pancreatitis (4-16%).[1,2,6] No difference in the frequency of WOPN formation between men and women has been clearly demonstrated.[7] The most frequent locations of WOPN are the pancreatic body and tail (80 to 92% of the cases), and extension to the paracolic gutters often occurs.[1,6,8-10] The mean size of published WOPNs is between 11 and 17 cm.[1,2,6,8-10]

CLINICAL FEATURES

WOPN typically occurs later in the course of pancreatitis, several weeks (>3-6 weeks) after the start of the attack.[7] After the first episode of acute pancreatitis, WOPN patients might be asymptomatic (50%) or present with symptoms (50%) such as abdominal pain, malaise, relapsing or recurrent pancreatitis, feeding intolerance or weight loss.[1,6] In severe cases, WOPN can obstruct the gastrointestinal tract, fistulise to adjacent anatomic strictures, and compress or erode into blood vessels or the bile duct. [11] WOPN can be infected or aseptic. [1,6] A third of the patients have infected WOPN, sometimes after percutaneous drainage or endoscopy treatment, which could be the source of infection. There is no clear correlation between the symptoms and WOPN infection. If infection is present, gas can be observed on the computed tomography (CT) but only a positive test after percutaneous puncture and gram staining will confirm the infection. The most commonly isolated bacteria in WOPN are *E. coli*, *K. pneumoniae*, *E. faecalis* and *S. aureus*.[6,7] Splenic vein thrombosis is seen in 40% of cases.[6]

DIAGNOSTIC METHODS

No specific clinical chemistry tests define WOPN.[7] The degree of pancreatic enzyme elevation does not correlate with the degree of necrosis.[7] WOPN can be identified with the use of initial and subsequent CT scans that show progression of the initial early necrosis to WOPN which occupies and expands the initial necrotic areas. On CT, WOPN appears as a mostly heterogeneous collection (mixture of fat, fluid and solids) usually without gas.[3,11] Gas within a WOPN collection does not always mean infection. For the most part it is due to fistulisation to the stomach or more commonly the duodenum, in which case it may be sterile. When WOPN fistulises to the colon it is always infected. CT accuracy in the differential diagnosis between WOPN and pseudocyst is about 79 to 84%.[3] A correct diagnosis is crucial because it influences the management of the pancreatic collection. Magnetic resonance imaging (MRI) and endoscopic ultrasound scans provide a better definition of the solid component inside necrotic collections.[3,13,14]

MANAGEMENT OF WOPN

This new term (WOPN) creates a challenge for identifying the most appropriate management. WOPN rates have probably been underestimated in the past because of an unclear definition, multiple names and incorrect diagnosis. The management of asymptomatic patients is unclear. Discussions centre on the need for, time and duration of management.[2,6] In symptomatic patients, infection evidenced by fever, leukocytosis and/or sepsis syndrome is the most common indication for the treatment of WOPN.[6] Other indications are: progressive increase in size, pain, gastric or duodenal outlet obstruction that interferes with feeding or causes persistent nausea or vomiting, biliary obstruction, portal thrombosis, fistulous connection between WOPN and adjacent strictures or clinical deterioration.[1,10,11] The start of WOPN treatment has ranged from 42 to 72 days (range 20 to 300 days) after the onset of acute pancreatitis.[1,2,6] However, there is no absolute time frame and intervention is based upon the severity of clinical symptoms and degree of organisation. There are several treatment options: percutaneous drainage, endoscopic drainage, laparoscopic drainage, surgical necrosectomy and mixtures of these techniques.[1,2,11] WOPN was historically believed to be less amenable to endoscopic or percutaneous treatment because of non-viable solid components. More recently, there has been a paradigm shift in the management of WOPN toward less invasive approaches.[8] The goal of these techniques is to provide minimal access necrosectomy equivalent to open necrosectomy.[8] The therapeutic options are:

- Percutaneous drainage (PD) and combined endoscopy plus PD

The solid component of WOPN limits the management of patients with percutaneous drainage, so the resolution rate is low.[2,9] Percutaneous therapy alone had a worse success rate and more prolonged length of stay, complications, need for surgery and deaths compared with combined therapy.[11] Percutaneous therapy is only effective if multiple large drains are used with frequent upsizing, removal of solid debris and aggressive irrigation. The main indications for PD are: PD combined with endoscopic procedures and puncture to rule out infection.[2,10]

Gluck *et al*. proposed combined therapy (percutaneous drainage and endoscopy). They first inserted a percutaneous drainage tube. If effective, they waited for the clinical outcome; if not, they immediately performed endoscopic therapy plus ERCP in selected cases.[11]

- Endoscopy

Baron described the endoscopic treatment of WOPN in 1996.[4,8,9] The main advantage of endoscopic therapy is the avoidance of surgical necrosectomy, because this procedure is associated with high morbidity and mortality. In addition, endoscopic necrosectomy is associated with a lower risk of pancreatic-cutaneous fistula compared with percutaneous drainage or surgical procedures.[10,11] A few articles about per-oral transgastric necrosectomy in infected pancreatic necrosis have been published, but we are going to focus on articles dedicated to WOPN.[15-18]

One problem of endoscopic treatment is that it is inconvenient for patients because it takes at least three sessions.[6,8,9,11] The endoscopic procedure is also a major interventional procedure associated with major morbidity in 10 to 26% of cases (most commonly bleeding and perforation), mortality of 2 to 7% and need for laparotomy in 0 to 23%.[1,2,6,8-10] Moreover, endoscopy is not feasible in patients with WOPN located more that 1.5 cm from the gastrointestinal lumen or coagulopathy.[11] The transgastric route is the most frequent access used (73 to 85%), but the duodenal route is also employed.[8-10] Endoscopic ultrasound guidance is often used, but not always.[8,9]

Figure 1. *Abdominal CT: Mixed solid-liquid collection (WOPN) Star: solid component*

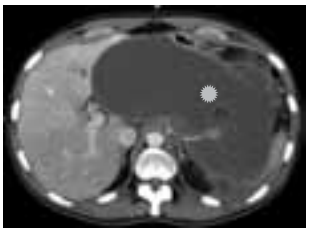

Figure 2. *Abdominal CT: Patient from figure 1: check-up one year after open surgical necrosectomy*

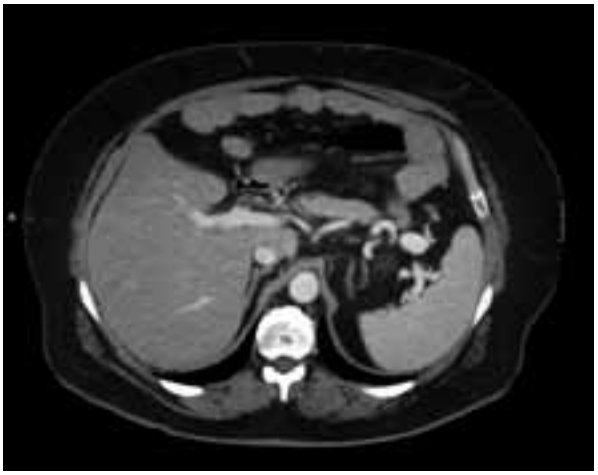

Figure 3. *Abdominal CT: Mixed solid-liquid collection (WOPN)*

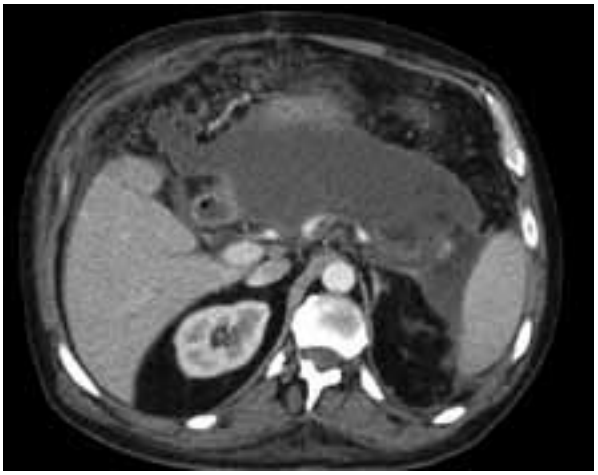

Table 1. *Messages*

WOPN is a new name for an old entity (necroma, organised pancreatic necrosis,..)
WOPN is a transitional collection after pancreatic necrosis that contained various amounts of fluid and necrotic tissue, occurring 6 weeks after an acute pancreatitis attack
CT and MRI are the best diagnostic methods; differential diagnosis with pseudocyst is crucial
Asymptomatic patients would probably not be treated
Transmural endoscopic debridement of WOPN should be the first therapeutic technique performed in symptomatic patients
Surgery should be done only in selected cases (WOPN over 15 cm or affecting both paracolic gutters) after the failure of endoscopic techniques

Simple endoscopic drainage of WOPN has been found to be less effective than transmural endoscopic debridement (NED). [8,10]. NED is successful in approximately 90% *vs* 50% with standard endoscopic drainage.[1,8-10] This outcome is probably due to the fact that standard endoscopy does not allow correct drainage of solid debris. The wider tract fistula and direct cleaning performed in NED improve the results of endoscopy.[8,10]

Papachristou *et al.* described 53 WOPN patients initially managed by endoscopic drainage. Endoscopy alone solved the situation in half of the cases, endoscopy and percutaneous drainage in 25% and surgical management was required in 25%.[1] Two later studies compared only irrigation-based debridement with NED, demonstrating that NED achieves better outcomes (high successful resolution rate and low rates of surgical rescue, percutaneous drainage and recurrent collection).[8,10] In 2011, Gardner *et al.* published a multicentre study of 104 patients with WOPN treated with NED. All the patients were symptomatic. Successful resolution of WOPN was achieved with NED in 95 of 104 patients (91%). Recurrent collection and recurrent pancreatitis were the main causes of failed NED. The mean time to resolution of WOPN was 4.1 months. BMI >32 was a risk factor for failed NED. In conclusion, Gardner *et al.* stated that NED is the most efficacious technique for treating WOPN with an acceptable safety profile.[9]

Varadarajulu *et al.* described a new EUS-based approach to WOPN management consisting of creating multiple transluminal gateways to facilitate effective drainage of the necrotic contents with fewer procedures than conventional endoscopy. The associated success rate was 91.7%.[10]

Fischer *et al.* described six patients treated with a novel endoscopic laparoscopic drainage technique. Only one

patient required surgery. An average of six endoscopic sessions was needed (range 4-11).[2]

- Surgery

The classical indications for surgical therapy of WOPN are infection, complications or failed non-surgical therapies.[11] Surgical minimally invasive necrosectomy is technically feasible and acceptable outcomes are achieved.[18] The laparoscopic approaches to pancreatic necrosectomy can be classified by access route (transperitoneal, retroperitoneal, transgastric) and type of scope (endoscope, laparoscope or nephroscope).[6,19] The main pitfall of the laparoscopic approach is incomplete or unsuccessful drainage.[2] Laparoscopic and hybrid techniques that utilise wide external drainage have high rates of pancreatic fistula formation.[6]

An open approach should be used when endoscopic or laparoscopic treatment fails.[1,2] Operative management of WOPN involves open debridement, lavage of the cavity followed by closed packing and/or drainage.[6] Open debridement for necrotising acute pancreatitis is associated with a high morbidity (55%) and mortality (14%); no data about surgical necrosectomy for WOPN are available but will probably be lower.[11] Several complications have been reported: pancreatocutaneous fistula (up to 53%), enteral fistulae (16%) and abdominal wall hernias.[6,9] Necrosectomy in WOPN patients is not easy but is less technically demanding than necrosectomy performed in necrotising acute pancreatitis.[9]

Three prognostic factors for which WOPN requires a surgical approach have been proposed: preoperative diabetes mellitus, size bigger than 15 cm and WOPN on both sides of the abdomen.[1,8]

Munene *et al.* treated ten patients with open transgastric debridement and internal drainage for symptomatic non-infected WOPN. No mortality was observed, morbidity was 20%, and no pancreatic fistula occurred. Symptoms resolved in 90% of patients.[6] The limitations of this technique are: lack of opposition of the gastric wall to WOPN and extension via paracolic gutters. The main problem of internal WOPN drainage is that it could lead to continuous retroperitoneal contamination. The advantages of this surgical technique compared with the endoscopic approach are similar morbidity, no mortality, reduced length of hospital stay and fewer procedures.[6]

CONCLUSION

WOPN is a new term for an established pancreatic condition. There have been very few studies of WOPN. Indications and management guidelines remain unclear and no randomised clinical trial about WOPN has been conducted. Asymptomatic patients probably would not be treated. Transmural endoscopic debridement of WOPN is efficacious with an acceptable safety profile and probably should be the first therapeutic technique to be performed in symptomatic patients. Surgery should only be performed in selected cases: WOPN over 15 cm or affecting both paracolic gutters after endoscopic techniques have failed.

REFERENCES

1. Papachristou GI, Takahashi N, Chahal P, Sarr MG, Baron TH. Peroral endoscopic drainage/debridement of walled-off pancreatic necrosis. Ann Surg. 2007;245:943-51.
2. Fischer A, Schrag HJ, Keck T, et al. Debridement and drainage of walled-off pancreatic necrosis by a novel laparoendoscopic rendezvous maneuver. Experience with 6 cases. Gastrointest Endosc. 2008;67:871-8.
3. Takahashi N, Papachristou GI, Schmit GD, et al. CT findings of walled off pancreatic necrosis: differentiation from pseudocyst and prediction of outcome after endoscopic therapy. Eur Radiol. 2008;18:2522-9.
4. Baron TH, Thaggard WG, Morgan DE, Stanley RJ. Endoscopic therapy for organized pancreatic necrosis. Gastroenterology. 1996;111:755-64.
5. Ramos-De la Medina AM, Reid-Lombardo KM, Sarr MG. Strategies for surgical treatment of pseudocysts after acute pancreatitis. Chapter 30. In: The Pancreas: An Integrated Textbook of Basic Science, Medicine, and Surgery. Edited by H. G. Beger, A. L. Warshaw, M. W. Büchler, et al. 2008 Blackwell Publishing Limited. 2ffl Edition.
6. Munene G, Dixon E, Sutherland F. Open transgastric debridement and internal drainage of symptomatic non-infected walled-off pancreatic necrosis. HPB. 2011;13:234-9.
7. Stamatakos M, Stefanaki C, Kontzoglou K, et al. Walled off pancreatic necrosis. World J Gastroenterol. 2010;16:1701-12.
8. Gardner TB, Chahal P, Papachristou GI, et al. A comparison of direct endoscopic necrosectomy with transmural endoscopic drainage for the treatment of walled-off pancreatic necrosis. Gastrointest Endosc. 2009;69:1085-91.
9. Gardner TB, Coelho N, Gordon SR, et al. Direct endoscopic necrosectomy for the treatment of walled-off pancreatic necrosis: results from a multicentre US series. Gastrointest Endosc. 2011;EPub.
10. Varadarajulu S, Phadnis MA, Christein JD, Wilcox CM. Multiple transluminal gateway technique for EUS-guided drainage of symptomatic walled-off pancreatic necrosis. Gastroint Endosc. 2011;EPub.
11. Gluck M, Ross A, Irani S, et al. Endoscopic and percutaneous drainage of symptomatic walled-off pancreatic necrosis reduces hospital stay and radiographics resources. Clin Gastroenterol Hepatol. 2010;8:1083-8.
12. Bradley EL. A clinically based classification system for acute pancreatitis. Arch Surg. 1993;128:586-9.
13. Bollen TL, Besselink MGH, Santvoort HC, et al. Toward an update of the Atlanta classification on acute pancreatitis. Pancreas. 2007;35:107-13.
14. Sarr MG. Proposed revision of the Atlanta Classification of acute pancreatitis. Acute Pancreatitis Classification Working Group. http://www.suizou.org/Atlanta_Classification.pdf.
15. Friedland S, Kaltenbach T, Sugimoto M, Soetikno R. Endoscopic necrosectomy of organized pancreatic necrosis: a currently practiced NOTES procedure. J Hepatobiliary Pancreat Surg. 2009;16:266-9.
16. Voermasn RP, VeldKamp MC, Rauws EA, et al. Endoscopic transmural debridement of symptomatic organized pancreatic necrosis. Gastroint Endosc. 2007;66:909-16.
17. Escorrou J, Shehab H, Buscail L, et al. Peroral transgastric/transduodenal necrosectomy. Success in treatment of infected pancreatic necrosis. Ann Surg. 2008;248: 1074-80.
18. Babu BI, Siriwadena AK. Current status of minimally invasive necrosectomy for post-inflammatory pancreatic necrosis. HPB. 2009;11:96-102.
19. Windsor JA. Minimally invasive pancreatic necrosectomy. Br J Surg. 2007;94:132-3.