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Review

Controversies in endoscopic ultrasonography-guided management of walled-off necrosis

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Walled-off necrosis (WON) develops as local complications after acute necrotizing pancreatitis. Although less invasive interventions such as endoscopic ultrasonography (EUS)-guided drainage and endoscopic necrosectomy are selected over surgical interventions, delayed and step-up interventions are still preferred to avoid procedure-related adverse events. However, there is a controversy about the appropriate timing of drainage and subsequent necrosectomy. The advent of large-caliber lumen-apposing metal stents has also brought about potential advantages of proactive interventions, which still needs investigation in future trials. When step-up interventions of necrosectomy and additional drainage are necessary, a structured or protocoled approach for WON has been reported to improve safety and effectiveness of endoscopic and/or percutaneous treatment, but has not been standardized yet. Finally, long-term outcomes such as recurrence of WON, pancreatic endocrine, and exocrine function are increasingly investigated in association with disconnected pancreatic duct syndrome. In this review we discuss current evidence and controversy on EUS-guided management of WON.

Key words: acute necrotizing pancreatitis, drainage, endoscopic ultrasonography, necrosectomy, walled-off necrosis

INTRODUCTION

WALLED-OFF NECROSIS (WON) develops 4 weeks after acute necrotizing pancreatitis by its definition in the revised Atlanta classification[1] and can be complicated by infection or other gastrointestinal symptoms, which necessitates interventions. While the endoscopic or percutaneous approach is often selected as a first-line treatment over the surgical approach due to its less invasiveness, a delayed and step-up approach is still preferred to avoid procedure-related adverse events. In this delayed and step-up approach, interventions are delayed as long as possible, and necrosectomy are only performed in cases refractory to drainage alone. However, more recently proactive drainage and immediate necrosectomy have been investigated, together with the advent of large-bore lumen-apposing metal stents (LAMS).[2] As for clinical outcomes of WON, long-term outcomes are increasingly discussed, in addition to the management in the early phase of WON. The associations of disconnected pancreatic duct syndrome (DPDS) with recurrence of pancreatic fluid collections (PFCs) and pancreatic endocrine/exocrine insufficiency are also investigated. The management strategies for DPDS have been an unmet need in this field.

Despite these advances in the management of WON, the clinical outcomes of endoscopic treatment have not significantly improved. In the first Japanese multicenter JENIPAN study in 2013,[3] clinical success, adverse event, and mortality rates were 75%, 33%, and 11%, respectively. Ten years later, another Japanese multicenter by the WONDERFUL study group[4] revealed disappointing results: a clinical success rate of 78%, adverse event rate of 25%, and mortality rate of 9.8%. These results strongly suggest that there is room for improvement in the management of WON, in terms of indication and timing of interventions, standardization of endoscopic procedures, as well as long-term management.[5–9]

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In this review we discuss the controversy and unmet needs in various steps of the endoscopic ultrasonography (EUS)-guided management of WON (Table 1).

Table 1 A list of controversies or unmet needs in the management of walled-off necrosis

Drainage
Prophylactic antibiotics, and supportive treatment to prevent infection
Indication: Infection, symptom, or size
Timing: After 4 weeks of onset or after encapsulation
Stent selection: LAMS vs. plastic stent, the size of LAMS
Step-up: Necrosectomy first or additional drainage first
Additional drainage: Multigateway or dual modality (endoscopic and percutaneous)
DEN
Indication: Infection, upfront, necrotic components
Timing: Upfront or step-up necrosectomy
Irrigation: Timing, amount, saline or hydrogen peroxide
Device selection
Modality: Endoscopic vs. percutaneous/surgical, VARD vs. open necrosectomy
Long-term outcomes
Timing of stent removal
Diagnosis and management of DPDS
Effects on pancreatic endocrine, and exocrine function

DEN, direct endoscopic necrosectomy; DPDS, disconnected pancreatic duct syndrome; LAMS, lumen apposing metal stent; VARD, video-assisted retroperitoneal debridement.

DRAINAGE: INDICATIONS, TIMING, AND SELECTION OF STENTS OR APPROACH

THE CURRENT STANDARD algorithm of short- and long-term management of WON is shown in Figures 1 and 2. Drainage for WON is indicated when it causes symptoms such as infection, pain, and biliary/gastrointestinal obstruction. Routine percutaneous aspiration or endosonography-guided fine-needle aspiration of WON to confirm infection is not recommended because of a considerably high false-negative rate of 20–29%.[10,11] In cases with clinically or radiologically uncertain infection, however, aspiration of WON contents for culture might be useful if interventions are performed based on its results. While infection is the absolute indication of intervention for WON, it is unclear whether symptomatic but sterile WON should be routinely drained or can be conservatively managed. In a retrospective study of EUS-guided drainage of symptomatic sterile WON, 73% developed iatrogenic infection, although symptom resolution was eventually obtained in 87%.[12] When treatment outcomes were compared between infected and sterile WON,[13] adverse events other than spontaneous fistula were comparable, but higher mortality (4.1% and 0.9%) and longer hospital stay (29.8 and 17.3 days) were observed in infected WON. A natural history of asymptomatic WON has not been fully elucidated either. The reported rates of asymptomatic WON getting symptomatic were 26.6–56%.[14–16] Given the

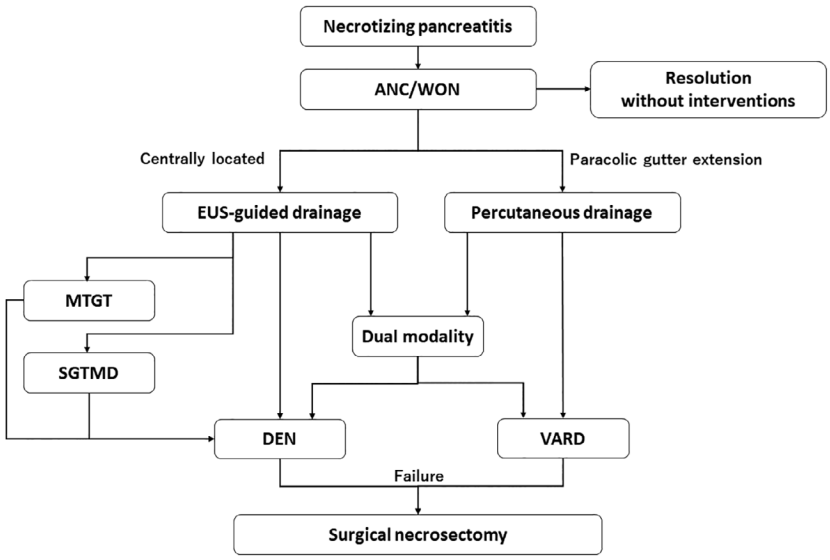

Figure 1 Flowchart of endoscopic and percutaneous treatment of walled-off necrosis (WON). ANC, acute necrotic collection; DEN, direct endoscopic necrosectomy; EUS, endoscopic ultrasonography; MTGT, multiple transluminal gateway; SGTMD, single transluminal gateway transcystic multiple drainage; VARD, video-assisted retroperitoneal debridement.

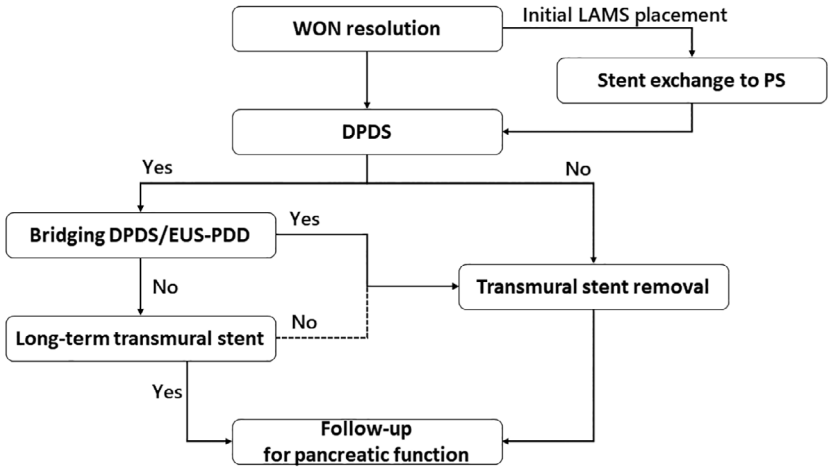

Figure 2 Flowchart after resolution of walled-off necrosis (WON). DPDS, disconnected pancreatic duct syndrome; EUS-PDD, endoscopic ultrasonography-guided pancreatic duct drainage; LAMS, lumen-apposing metal stent; PS, plastic stent.

possible adverse events of interventions, including the abovementioned iatrogenic infection, drainage is indicated only in symptomatic WON, and routine drainage is not recommended in asymptomatic WON. It should be further evaluated whether we should intervene early in cases with minimally symptomatic WON.

The role of prophylactic antibiotics has been investigated in severe acute pancreatitis, with conflicting results. In terms of infection of WON, early (<48 h of hospital admission) enteral nutrition was reported to be associated with reduced pancreatic infection with a risk ratio (RR) of 0.55.[17] However, the difference was not statistically significant in another meta-analysis, including studies irrespective of timing of antibiotics.[18] The role of prophylactic antibiotics in asymptomatic WON should be further investigated. Enteral nutrition can also reduce bacterial overgrowth and reduce infectious complications, with an RR of 0.46 if administered <48 h in acute pancreatitis.[19] In cases with severe acute pancreatitis complicated by disseminated intravascular coagulopathy, the use of recombinant human soluble thrombomodulin was associated with less development of WON, which was only reported in a single, retrospective study, however.[20] In addition to the improvement in interventions for WON, the role of supportive treatment needs to be recognized for further improvement in clinical outcomes of WON.[21]

The timing of drainage is a matter of debate in WON. A delayed approach is the current standard treatment of WON since the landmark article of 639 cases with necrotizing pancreatitis was published by the Dutch Pancreatitis Study Group in 2011.[22] The study showed that the mortality and adverse event rates decreased as the time between admission and intervention was longer: Mortality rates were 56% in <2 weeks, 26% in 2–4 weeks, and 15% in >4 weeks ($P < 0.001$), and adverse event rates were 72% in <2 weeks, 57% in 2–4 weeks, and 39% in >4 weeks ($P = 0.007$). Along with the threshold of 4 weeks in the revised Atlanta classification,[1] therefore, drainage for WON is often delayed until 4 weeks of the onset of acute pancreatitis. However, early drainage of WON might be necessary when infection is suspected within 4 weeks, and three meta-analyses including ours,[23–25] have been published, comparing early and delayed interventions. In those meta-analyses, most clinical outcomes did not show statistically significant differences but mortality and adverse event rates tend to be high in the early intervention group. Despite the potential bias of the early intervention group, including those in poor general conditions, these results would argue against the routine early drainage of WON. In a recent randomized controlled trial (RCT), the POINTER trial,[26] the immediate-drainage group was not superior to the postponed-drainage group in terms of safety, including mortality, with the number of interventions higher in the immediate-drainage group (4.4 and 2.6 sessions), also supporting the delayed approach for WON. However, we sometimes encounter deterioration by infection in severe acute pancreatitis, and selection of patients who need and benefit from early drainage of WON should be further explored.

Endoscopic drainage has its advantages in terms of less pancreatic fistula than percutaneous drainage of WON.[27] Percutaneous drainage might be selectively preferred

in cases with unstable conditions who cannot tolerate endoscopic procedures or with paracolic extension, where the endoscopic approach is difficult. Furthermore, percutaneous drainage is also recommended in cases who need early (<3–4 weeks) drainage for infected necrotizing pancreatitis without encapsulation.[28] EUS-guided drainage in those cases without encapsulation might cause contamination by gut microorganisms and lead to peritonitis. In addition, in cases with complex and widespread WON, dual modality (endoscopic and percutaneous) approach or a multigateway endoscopic approach can be selected (Fig. 1), but selection has not been standardized.

Encapsulation of PFCs is increasingly discussed, along with the timing of interventions. As per the revised Atlanta classification,[1] acute necrotizing collection after necrotizing pancreatitis becomes walled-off around 4 weeks after acute pancreatitis onset. This encapsulation allows safe drainage without a risk of peritonitis, even in the early phase of acute pancreatitis.[29] However, the timing of this encapsulation differs case by case. The rates of complete or full encapsulation were higher in the delayed intervention groups: 6.8% and 42.5% by Trikudanathan *et al.*,[30] and 42.1 and 89.5% by Oblizajek *et al.*,[31] in the early and delayed intervention groups, respectively. Another advantage of the delayed approach is liquefaction of WON contents, which might allow better drainage effects and reduce the necessity of necrosectomy after EUS-guided drainage. The rate of liquefaction was reportedly higher (5.3% vs. 25.6%) in the delayed intervention group.[30] Thus, it should be further investigated whether an encapsulation-oriented approach, rather than the traditional 4-week approach, is more relevant in terms of safety and effectiveness of EUS-guided drainage of WON.

Stent selection for EUS-guided drainage has been discussed since the advent of LAMS. LAMS, with its large bore, might potentially facilitate drainage and reduce the necessity of direct endoscopic necrosectomy (DEN). Furthermore, scope insertion to the WON cavity is technically easy if large-bore LAMS are placed. Comparison of LAMS and plastic stent (PS) has been investigated both for WON and pseudocysts, with conflicting results. A recent meta-analysis of three RCTs comparing LAMS and PS for WON[32] revealed no significant differences in clinical outcomes other than the short procedure time in LAMS, with the pooled rates of necrosectomy (38.5% vs. 41.2%), treatment success (90.7% vs. 94.5%), recurrence (4.6% vs. 0.6%), adverse events (23.6% vs. 19.2%), bleeding (11.0% vs. 10.7%), new-onset organ failure (10.6% vs. 14.6%), and mortality (8.5% vs. 9.8%) in the LAMS and PS groups. The same group in the meta-analysis, however, claimed that the use of PS in addition to the presence of >33% of necrosis was associated with systemic inflammatory response syndrome and new organ failure after EUS-guided drainage, and recommended the use of LAMS in sick patients and those with >33% necrosis.[33] Of note, when each data of three RCTs[34–36] included in the meta-analysis were compared (Table 2), patient characteristics including severity differed significantly between studies and might affect the study results. Although the only difference between LAMS and PS was the procedure time,[32] the simple step of LAMS placement is readily available in nonexpert centers. In addition, the short procedure time would allow safe EUS-guided drainage even in cases with deteriorated conditions or to facilitate advanced procedures through LAMS such as immediate DEN in the same session. Thus, even with significant but small differences in the procedure time, the advent of LAMS can possibly change the treatment strategy for WON.

There has been a debate about the most suitable types of LAMS for the management of PFCs. When two sizes of LAMS (20 mm and 15 mm) were compared,[37] a larger (20 mm) LAMS might facilitate better drainage and lead to fewer DEN sessions (1.3 vs. 2.1) without significant increased risks of adverse events (21.6% vs. 15.2%) or bleeding (4.9% vs. 3.4%). A risk of bleeding was considered a potential disadvantage in LAMS. An early study of LAMS for PFCs[38] claimed that LAMS placement >3 weeks would increase the risk of delayed bleeding, and early exchange to PS was recommended. Placement of coaxial PS within LAMS might also reduce the risk of adverse events (20.7% and 51.5% in LAMS with and without coaxial PS, respectively) and stent occlusion (14.7% and 26.3% in LAMS with and without coaxial PS, respectively).[39] The rate of bleeding was low (5.9% and 12.1%) with coaxial PS placement, but without statistical significance. In a recent comparative study,[40] a new, commercially available LAMS with flexible flanges might be associated with less bleeding: the rates of overall adverse events and bleeding were 9.8% vs. 3.0% (P = 0.04) and 6.8% vs. 1.5% (P = 0.03) in conventional LAMS vs. new LAMS with rounded edges and foldable flanges. In summary, LAMS does not have significant drawbacks in comparison with PS, but it should be further clarified whether LAMS should be routinely or selectively used for EUS-guided drainage of WON.

NECROSECTOMY: TIMING AND ALGORITHM-BASED APPROACH

AFTER ENDOSCOPIC OR percutaneous drainage of WON, a step-up approach is applied for necrosectomy either by DEN (Fig. 3) or video-assisted retroperitoneal debridement (VARD). However, the timing of step-up necrosectomy has not been standardized. In the international

Table 2 Comparison of patient characteristics and clinical outcomes of lumen-apposing metal stents (LAMS) and plastic stents (PS) for walled-off necrosis in three randomized controlled trials

Author, reference	Bang *et al.*[34]	Boxhoorn *et al.*[35]	Karstensen *et al.*[36]
Number of patients	60 (LAMS 31, PS 29)	104 (LAMS 53, PS 51)	44 (LAMS 22, PS 20)
SIRS			
LAMS	9 (29.0)	47 (89)	12 (60.0)
PS	13 (44.8)	33 (65)	15 (68.2)
Organ failure			
LAMS	2 (6.5)	12 (23)	6 (30.0)
PS	4 (13.8)	4 (13.8)	4 (13.8)
Size, median (IQR), cm			
LAMS	9.2 (6.4–12.0)	NA	29.7 (18.7–31.4)
PS	7.8 (6.0–13.1)	NA	21.5 (19.9–28.3)
Infected necrosis			
LAMS	27 (87.1)	19 (36)	13 (65.0)
PS	26 (89.7)	23 (45)	14 (63.6)
Necrosis ≥30%			
LAMS	25 (80.6)	30 (56.6)	NA
PS	28 (96.6)	25 (49.0)	NA
DEN			
LAMS	4 (12.9)	34 (64.2)	8 (40.0)
PS	6 (20.7)	27 (52.9)	11 (50.0)
Number of sessions, mean (SD)			
LAMS	0.13 (0.43)	2.4 (3.1)	5.3 (3.4)
PS	0.28 (0.65)	1.8 (2.5)	4.5 (3.1)
Treatment success			
LAMS	29 (93.5)	NA	18 (90.0)
PS	28 (96.6)	NA	21 (95.5)
Mortality			
LAMS	1 (3.2)	6 (11.3)	1 (5.0)
PS	1 (3.4)	9 (17.6)	1 (4.5)
Adverse events			
LAMS	13 (41.9)	13 (24.5)	1 (5.0)
PS	6 (20.7)	11 (21.6)	2 (9.1)

Data are shown in *n* (%), unless otherwise described.
DEN, direct endoscopic necrosectomy; IQR, interquartile range; NA, not available; SD, standard deviation; SIRS, systemic inflammatory response syndrome.

consensus survey, 86.4% of endoscopists did not recommend immediate (the same session) DEN, but the optimal interval ranged from 3 to 21 days even within experts.[41]

Since about half of patients needed DEN after EUS-guided drainage of WON, early or immediate DEN might lead to early clinical success, especially in cases who need DEN such as PFC size of ≥10 cm (odds ratio [OR] 8.91; 95% confidence interval [CI] 3.36–23.61), paracolic extension (OR 4.04; 95% CI 1.60–10.23), and ≥30% solid necrosis (OR 4.24; 95% CI 1.48–12.16).[42] A recent study proposed QNI classification for risk stratification.[43] Q (quadrant) represented an abdominal quadrant distribution; N (necrosis) denoted by the percentage of necrosis of WON; and I (infection) denoted as positive blood culture and/or systemic inflammatory response syndrome reaction with a positive WON culture. QNI scores were associated with more sessions of necrosectomy, a longer hospital stay and time to resolution, and a higher mortality rate. Given the need for DEN in cases with high QNI scores, those cases might benefit from early or immediate DEN. Conflicting data, however, were reported on immediate DEN at the initial EUS-guided drainage of WON. While one study[44] showed immediate DEN led to the resolution of WON, it necessitated more DEN sessions and a longer hospital stay in the other study.[45] A recent RCT, DESTIN, by the United States Pancreatic Disease Study Group[46] demonstrated the number of reinterventions was lower in the upfront necrosectomy (1 vs. 2) without an increase in the mortality

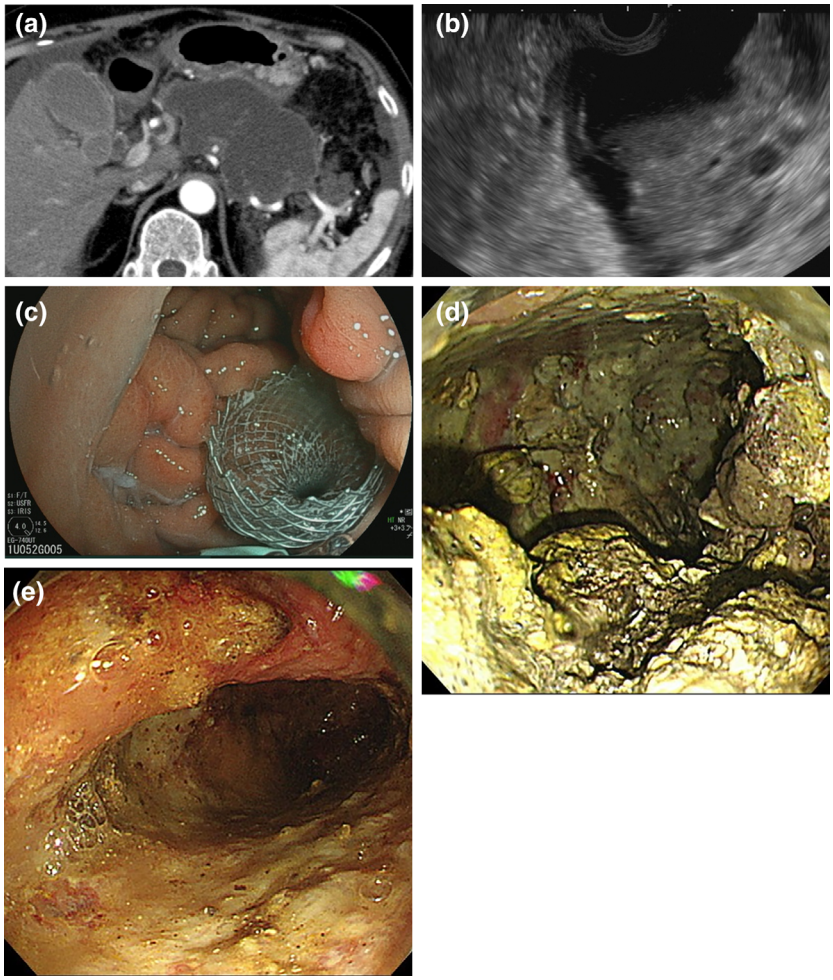

Figure 3 Endoscopic treatment of walled-off necrosis (WON). (a) Computed tomography image of WON. (b) Endoscopic ultrasonography image of WON with fluid component and necrotic tissues. (c) A lumen-apposing metal stent (LAMS) placed for WON. (d) Direct endoscopic necrosectomy (DEN) through the LAMS, showing a large amount of necrosis. (e) Endoscopic images of WON after successful DEN.

(0% vs. 6%) or adverse event (32% vs. 48%). A Japanese multicenter study, WONDER-01,[47] comparing immediate DEN and the step-up approach is ongoing as well. In addition to the initial necrosectomy, protocolized management, which required repeat cross-sectional imaging within 14 days, with regularly scheduled DEN if WON reduction was <50%, resulted in faster WON resolution with fewer adverse events and a similar number of interventions.[48] In addition to the timing of DEN, devices for DEN are not standardized either. Currently, multiple devices are used for debridement of necrotic tissues during DEN, such as a snare, a basket, and forceps at the discretion of each endoscopist.

To overcome the limitations of the nonstandardized approach, the algorithm-based or structured approach has been reported to improve clinical outcomes in the management of WON.[49–51] Two studies proposed similar algorithms: EUS-guided drainage first, in combination with percutaneous drainage if deeply extended. Then the step-up endoscopic/percutaneous necrosectomy is performed if the response is suboptimal. And surgery is finally considered if necessary. After the application of this protocol, the treatment success rates increased from 60% to 91%, although the number of interventions were similar.[49] As for step-up approaches, there are multiple options, such as DEN, VARD, multiple transluminal gateway, single transluminal gateway transcystic multiple drainage,[52] dual modality drainage of transluminal and the percutaneous approach (Fig. 1).[53] These approaches are selected based on

the extension of WON, but depend much on the preferences of endoscopists or radiologists. The standardization of the treatment approach in complicated WONs needs further investigation to improve the safety and effectiveness of endoscopy-oriented management of WON. Finally, surgical necrosectomy is sometimes necessary, although a less invasive endoscopic or percutaneous approach is the current standard of care for WON. In a Japanese multicenter cohort study of pancreatic necrosis,[54] 27% (33/122) of interventions were open surgical necrosectomy. In the multivariable analysis, age and severity of pancreatitis, but not surgical necrosectomy, were associated with mortality. Thus, the appropriate timing and indication of conversion to this useful but invasive surgical necrosectomy needs to be clarified.

The structured approach including device selection was also reported[51]; DEN was performed using a cap-fitted therapeutic gastroscope attached with the irrigation pump. For debridement, hot snares are used for adherent debris, cold snares for nonadherent debris, rat-tooth forceps if extensive collateral vessels, and hemostatic forceps for hemostasis. For extraction of necrotic tissues, snares and rat-tooth forceps are used and retrieval nets in the late phase of extraction. For irrigation, normal saline mixed with gentamicin is used during the procedure and hydrogen peroxide for lavage at the end of the procedure. Although the treatment success rate was not significantly different, the structured approach reduced the number of necrosectomy sessions. According to these studies, the establishment of algorithm-based or structured approach is essential to increase the treatment efficacy of endoscopic management of WON. Other agents, such as anhydrous ethanol[55] and streptokinase,[56] were also investigated for irrigation. Device selection is also important for the safety and effectiveness of DEN. Conventionally, snares are often used for debridement. Recently, the usefulness of the EndoRotor (Interscope Medical, Worcester, MA, USA), a novel automated mechanical endoscopic tissue resection, was reported.[57] This device consists of a fixed outer cannula with a hollow inner cannula, and can suck, cut, and remove small necrotic pieces through the catheter, with a motorized cutting tool rotating and resecting tissues. To enhance the effectiveness, a larger (5 mm) device was developed and its feasibility was reported.[58] A future study is warranted to compare this dedicated device with conventional devices.

Although clinical outcomes of DEN are improving gradually, procedure standardization including its indication, timing, and devices is still necessary to further improve its safety and efficacy. To achieve this structured approach with multiple device selection, a centralized approach by experts might improve clinical outcomes of complicated WON, since the association of the hospital volume with mortality has already been reported.[59]

DISCONNECTED PANCREATIC DUCT SYNDROME

DISCONNECTED PANCREATIC DUCT syndrome is often encountered in necrotizing pancreatitis and can affect long-term outcomes of WON as well as its management (Fig. 2). In our systematic review and meta-analysis,[60] DPDS was diagnosed in 40–69%. Although DPDS did not affect treatment success, it was associated with a higher rate of recurrence after successful endoscopic treatment of PFCs, with a pooled OR of 6.72. Long-term transmural stent placement might be preferable to reduce recurrence, especially in cases with DPDS. In a subgroup analysis of our meta-analysis,[61] the rate of PFC recurrence was lower in cases with long-term transmural PS placement with a pooled OR of 0.14, at the cost of adverse events (OR of 14.77). However, in an RCT in cases with WON treated by large-bore, covered metal stents,[62] exchange to PS was technically unsuccessful in 11.5% and stent migration was observed in 19.2% at the median follow-up of 8 months. Recurrent PFC rates at 3 months were 5.8%, both in the stent and no-stent groups. While long-term transmural stent placement may reduce a risk of PFC recurrence, it has an inherent risk of intestinal perforation as well as migration. Three colon perforations (8.3%) were reported during the median follow-up period of 56.2 months, with one perforation managed surgically.[63] Thus, the benefit of long-term transmural stent placement needs to be balanced against the risk of stent-related adverse events, and further investigation is necessary to clarify patient selection who would benefit from long-term stent placement.

Pancreatic function can be affected by necrotizing pancreatitis and subsequent WON. In the follow-up studies of surgical necrosectomy, treatment of diabetes was necessary in 36–56% and pancreatic exocrine replacement treatment was administered in 16–42% after treatment of necrotizing pancreatitis.[64,65] This pancreatic insufficiency is considered the consequence of pancreas atrophy, as EUS revealed morphological changes of chronic pancreatitis in the upstream pancreas of the disconnected duct in about one-third of cases with DPDS.[66] The incidence of new-onset diabetes was reported in DPDS: 34.4% and 16.6%, respectively, in cases with and without DPDS. Furthermore, the incidence of diabetes was higher in DPDS at the head of the pancreas (39.2%) than at the body/tail (23.7%).[67] To resolve the long-term effects of DPDS, bridging of the disconnected ducts was attempted by various techniques,[68–

[70] but its long-term outcomes have not been revealed in terms of preservation of the pancreatic function.

In summary, DPDS is not uncommon after necrotizing pancreatitis and can increase the recurrence of PFC and the incidence of new-onset diabetes. While we need to recognize and diagnose DPDS in cases with necrotizing pancreatitis, its management such as long-term transmural stent placement and bridging the pancreatic duct needs to be established.

FUTURE PERSPECTIVES

AS WE DISCUSSED above, there are some topics to be established in the management of WON. Among them, the timing of interventions, both drainage and necrosectomy, is the most intensely investigated. Furthermore, long-term outcomes in terms of pancreatic function after necrotizing pancreatitis are increasingly discussed, too. Follow-up data of the POINTER trial,[26] which originally demonstrated nonsuperiority of immediate drainage for infected pancreatic necrosis, were recently reported[71]; while confirming the delayed drainage reduced the number of interventions, this follow-up study demonstrated there were no differences in the new development of pancreatic endocrine and exocrine insufficiency by the timing of drainage. These results suggest there are no disadvantages of delayed drainage in short- or long-term outcomes, but in clinical practice we still intervene early for infected necrosis and need to explore indications for early drainage by employing a biomarker- or encapsulation-oriented approach, rather than a one-size-fits-all approach. Another matter of debate in terms of timing is immediate or step-up necrosectomy after drainage. In the DESTIN trial,[46] the number of reinterventions was reduced by the immediate necrosectomy after EUS-guided drainage compared to the conventional step-up approach. While procedure-related adverse events did not increase by the immediate necrosectomy, this study was conducted in six expert centers. Thus, extrapolation of the study results needs caution, as an inverse association of the hospital volume with mortality was reported in the nationwide inpatient database.[59] It should be further investigated whether complex WON should be managed only in expert centers, or immediate necrosectomy can be safely applicable to the nonexpert centers.

In summary, while standardized protocol of WON management might increase safety and efficacy, a tailored approach is also necessary in the management of WON, as it varies in its size, distribution, and degree of necrosis and clinical outcomes can be affected by patients' conditions and can be operator- or hospital-dependent.

CONCLUSION

ENDOSCOPIC MANAGEMENT IS often utilized as a first-line treatment for WON, but clinical outcomes of WON are still suboptimal. The standard approach for WON in terms of indications and timing should be established to further improve the safety and efficacy of endoscopic drainage and necrosectomy when necessary. Given the rarity of this disease, an international, multicenter consortium would play an important role for the standardization of its management through clinical trials and guidelines.

CONFLICT OF INTEREST

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