Digestive Endoscopy 2019; **31**: 307–315 doi: 10.1111/den.13319

Original Article

Radical treatment for walled-off necrosis: Transmural nasocyst continuous irrigation

Takashi Tamura,[1] Masahiro Itonaga,[1] Kensuke Tanioka,[2] Yuki Kawaji,[1] Junya Nuta,[1] Keiichi Hatamaru,[1] Yasunobu Yamashita,[1] Takeichi Yoshida,[1] Yoshiyuki Ida,[1] Takao Maekita,[1] Mikitaka Iguchi[1] and Masayuki Kitano[1]

[1]*Second Department of Internal Medicine, Wakayama Medical University, and* [2]*Clinical Study Support Center, Wakayama Medical University Hospital, Wakayama, Japan*

Background and Aim: Treatment efficiency of walled-off necrosis (WON) using endoscopic ultrasound-guided drainage (EUS-D) with a double pigtail stent (DPS) is limited. Endoscopic necrosectomy is often carried out if EUS-D fails. However, endoscopic necrosectomy is associated with significant morbidity and mortality. Thus, we developed transmural nasocyst continuous irrigation (TNCCI) as an alternative therapeutic option for WON. This study aimed to evaluate the usefulness of TNCCI therapy for WON.

Methods: Between April 2009 and March 2018, 19 of 39 patients admitted with WON underwent EUS-D. Ten consecutive patients also received TNCCI therapy (TNCCI group) between May 2015 and March 2018. TNCCI was carried out by inserting an external tube from the gastroduodenal lumen into the WON under endoscopic ultrasonography guidance and then continuously irrigating the WON with saline at a rate of 40 ml/h. Nine consecutive patients who underwent EUS-D without TNCCI therapy between April 2009 and April 2015 were used for comparison (control group). Various parameters were compared between the TNCCI and control groups.

Results: Time taken to reduce WON (6 *vs* 32 days, $P = 0.001$), implementation rate of endoscopic necrosectomy (0% *vs* 55.6%, $P = 0.01$), and number of endoscopic necrosectomy sessions per patient (0 *vs* 0.8 ± 1.0, $P = 0.008$) were significantly lower in the TNCCI group than in the control group.

Conclusions: Walled-off necrosis can be effectively and safely treated by endoscopic drainage with a DPS and TNCCI. This technique can be an alternative therapeutic option before carrying out endoscopic necrosectomy.

Key words: endoscopic necrosectomy, endoscopic ultrasound-guided drainage, irrigation, plastic stent, walled-off necrosis

INTRODUCTION

ACCORDING TO THE 2012 revision of the Atlanta classification of acute pancreatitis, walled-off necrosis (WON) is defined as a local adverse event that occurs more than 4 weeks after the onset of necrotic pancreatitis.[1] WON is a mature, encapsulated collection of pancreatic and/or peripancreatic necrosis and has a well-defined inflammatory wall.[1] Most cases of WON are asymptomatic, and up to 60% resolve spontaneously.[2] However, WON sometimes becomes symptomatic following infection or an increase in size, leading to symptoms such as abdominal pain, early satiety, gastric outlet obstruction, biliary obstruction, and sepsis.[2] Management of symptomatic WON currently includes endoscopic, surgical, and percutaneous debridement.[3] A step-up approach was recently recommended for prevention of multiple organ failure related to severe acute pancreatitis.[4,5] In a step-up approach, endoscopic ultrasound-guided transmural drainage (EUS-D) and percutaneous drainage, endoscopic necrosectomy, and surgical necrosectomy are often carried out as the first-, second-, and third-line interventions in the treatment of WON, respectively.[5] The rate of a composite of major adverse events was reported to be lower among patients managed with a minimally invasive step-up approach than among those who underwent open necrosectomy (40% *vs* 69%, $P = 0.006$).[4] Consequently, fewer invasive techniques, endoscopic drainage, and minimally invasive retroperitoneal necrosectomies are increasingly being carried out before considering early open necrosectomy.[4]

Walled-off necrosis contains necrotic substances and, consequently, this condition is not necessarily improved by EUS-D.[3] Catheter drainage as the first intervention in a step-up approach improved WON in 35% of cases only.[4,6]

Corresponding: Masayuki Kitano, Second Department of Internal Medicine, Wakayama Medical University, 811-1, Kimiidera, Wakayama city, Wakayama 641-8509, Japan. Email: kitano@wakayama-med.ac.jp

Received 25 July 2018; accepted 13 December 2018.

Although many centers currently use a step-up approach in which endoscopic necrosectomy is carried out after failure of EUS-D,[5,7–9] endoscopic necrosectomy is associated with a high rate of adverse events and serious adverse events such as bleeding.[10]

Therefore, we developed transmural nasocyst continuous irrigation (TNCCI) therapy as an alternative to surgical and endoscopic necrosectomy. TNCCI involves placement of internal and external drainage tubes during EUS-D for WON and continuous irrigation of the internal contents through the external drainage tube. The present study aimed to evaluate the efficacy and safety of TNCCI therapy for WON.

METHODS

THIS RETROSPECTIVE COHORT study was approved by the Institutional Review Boards of the Wakayama Medical University Hospitals (registry number: 2227)

Patients

All consecutive patients who underwent EUS-D for WON between April 2009 and March 2018 at Wakayama Medical University were identified by searching the medical database of the centers. WON was defined according to the contrast-enhanced computed tomography (CECT) criteria of the 2012 revision of the Atlanta classification[1] as a mature, encapsulated collection of pancreatic and/or peripancreatic necrosis with a well-defined inflammatory wall in CECT imaging. Indications for drainage of WON are: (i) refractory abdominal pain; and/or (ii) infected WON.

Transmural nasocyst continuous irrigation therapy was started in May 2015. All patients admitted between April 2009 and April 2015 underwent EUS-D without TNCCI, whereas all those admitted between May 2015 and March 2018 underwent EUS-D with TNCCI. Patients were included in the study if they had: (i) WON diagnosed according to the Atlanta Classification; and (ii) undergone EUS-D. Patients were excluded from the study if: (i) EUS-D was unsuccessful; and (ii) they were not followed up for 3 months or longer.

Procedure

Endoscopic ultrasound-guided transmural drainage of the TNCCI group

All patients underwent endoscopy with a linear array echoendoscope (UCT240, 260; Olympus Ltd, Tokyo, Japan) carried out by four endosonographers, all of whom were endoscopists certified by the Japan Gastroenterological Endoscopy Society and had at least 5 years of experience in carrying out EUS prior to this study. The WON cavity was punctured with a 19-gauge needle (SonoTip Pro Control Tip; Medi-Globe, Achenmühle, Germany) under EUS guidance with Doppler flow scanning (Fig. 1a,b). A 0.025-inch guidewire (VisiGlide; Olympus Corporation, Tokyo, Japan) was inserted through the needle and coiled into the WON. The needle was then withdrawn, and the guidewire was left in the WON (Fig. 1c).

Thereafter, the tract was dilated using a controlled radial expansion wire-guided balloon with a diameter of 8 mm (Ren; Kaneka, Osaka, Japan) (Maxforce; Cook Medical, Winston-Salem, NC, USA) (Fig. 1d). The diameter of the needle tract was sufficient to place a double pigtail stent (DPS) and an endoscopic nasobiliary drainage (ENBD) tube at first intervention. Using a double-lumen catheter (uneven double-lumen cannula; Piolax, Yokohama, Japan), guidewires with a diameter of 0.025 and 0.035 inch (Jagwire; Boston Scientific, Natick, MA, USA) were inserted into the WON (Fig. 1e). A DPS (7 Fr 4–12 cm) (Zimmon Biliary Stent; Cook Medical) was inserted into the WON as an internal drainage tube using the 0.025-inch guidewire. Meanwhile, a 7-Fr ENBD tube (Flexima ENBD Catheter; Boston Scientific) was inserted into the WON as an external drainage tube using the 0.035-inch guidewire. This tube was positioned far from the puncture site when possible (Fig. 1f).

Transmural nasocyst continuous irrigation treatment

Patients admitted between May 2015 and March 2018 underwent EUS-D followed by TNCCI. After carrying out EUS-D, WON was irrigated with natural instillation of saline only (40 mL/h) from the external drainage tube. Irrigation volume was selected based on the volumes reported in the previous report and the patient's body-weight.[5,10] Additional drainage stents (7 Fr, 4–12 cm) (Zimmon Biliary Stent) were inserted into the WON through an endoscope if, after 72 h, infection and symptoms had not adequately improved, position of the drain was inadequate, other remaining fluid collections were visible on CECT, or cessation of natural instillation. Natural instillation ceased in cases of obstruction of the drainage stent. TNCCI was continued after inserting an additional drainage stent (Fig. 2a). Duration of TNCCI depended on whether WON was resolved. When WON was not improved by TNCCI therapy, we replaced the DPS with a fully covered self-expandable metal stent (FCSEMS) (10 mm, 68 cm) (Wall-Flex stent; Boston Scientific), and continued TNCCI for WON (Fig. 2b). When WON was not improved by insertion

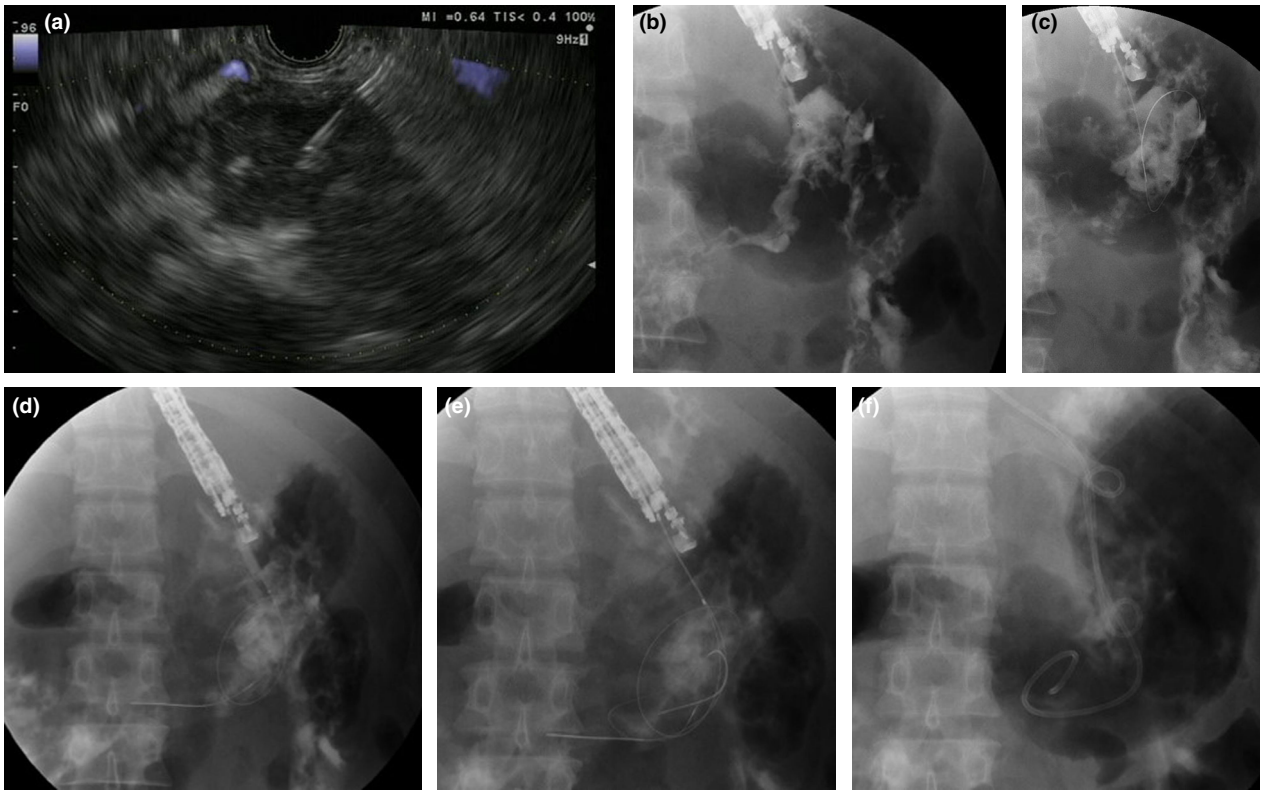

Figure 1 Deployment of a double pigtail stent (DPS) and a nasocyst drainage tube prior to transmural nasocystic continuous irrigation. Endoscopic ultrasound images showing (a) puncture of the walled-off necrosis using a 19-gauge needle. Fluoroscopy images showing (b) puncture of walled-off necrosis (WON) and injection of contrast agent into the WON cavity, (c) insertion of a guidewire through a fine needle into the WON, (d) dilation of the tract using a controlled radial expansion wire-guided balloon with a diameter of 8 mm, (e) insertion of two guidewires into the WON cavity and (f) placement of an endoscopic nasobiliary drainage tube and a DPS into the WON cavity.

of a FCSEMS and TNCCI therapy, endoscopic necrosectomy was considered (Fig. 3).

Minimally invasive step-up treatment (control group)

Patients admitted between April 2009 and April 2015 underwent EUS-D with a minimally invasive conventional step-up approach without TNCCI. The first step was EUS-D. Drainage was achieved by placement of one or more plastic stents. The placement plastic stent was a DPS (7 Fr, 4–12 cm) (Zimmon Biliary Stent) or a 7-Fr ENBD tube (Flexima ENBD Catheter). When there was no clinical improvement after 72 h, position of the drain was inadequate, or drainage of other fluid collections was required, an additional drainage stent (7 Fr, 4–12 cm) (Zimmon Biliary Stent) was inserted into the WON through an endoscope. Thereafter, when there was no clinical improvement, endoscopic necrosectomy was done (Fig. 4).

Endoscopic necrosectomy

Endoscopic necrosectomy and lavage were carried out 1–2 times per week until all necrotic and purulent material was evacuated. The tract was dilated using a large balloon (12–15 mm) (CRE PRO Wireguided Biliary Dilatation Balloon Catheter; Boston Scientific), and the endoscope was advanced into the cavity. Endoscopic necrosectomy was carried out by introducing a Dormia basket (FG-22Q-1; Olympus) using a gastroscope (GIF 260; Olympus).

Post-procedural care and follow up

Walled-off necrosis was assessed by CT within 3 days after treatment and at least once per week thereafter until

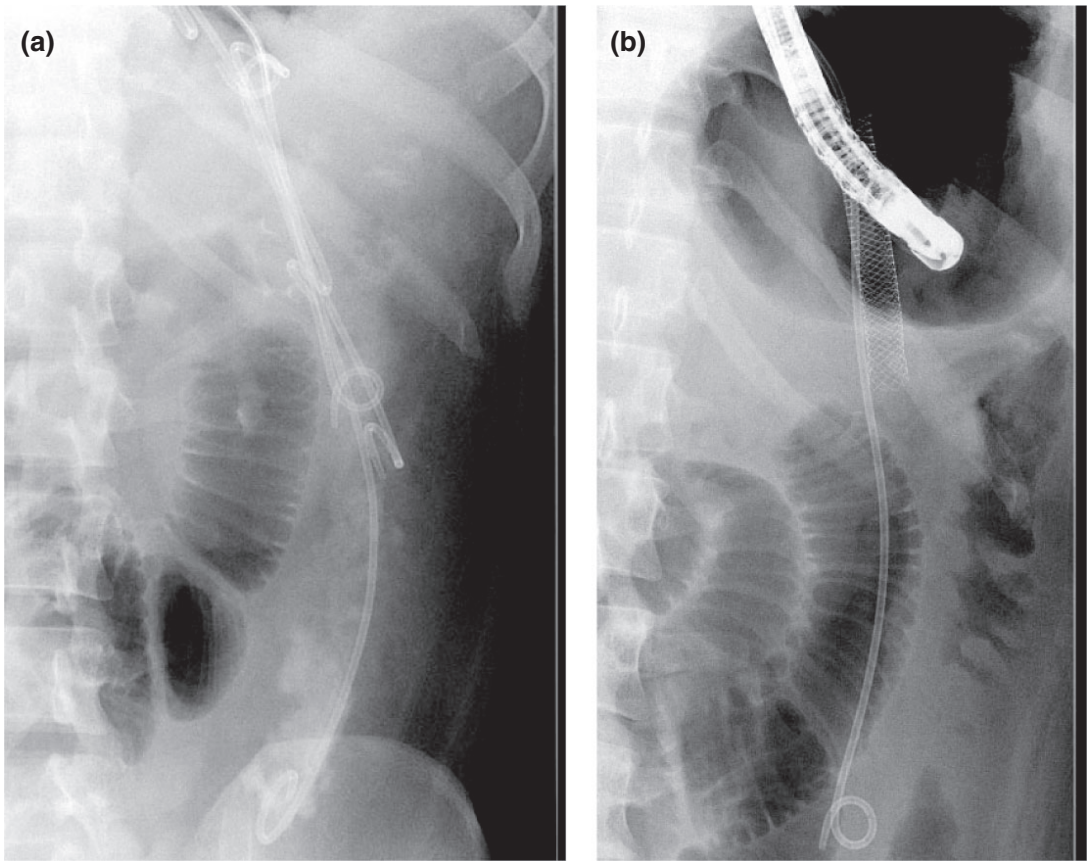

Figure 2 Fluoroscopy images showing (a) placement of an endoscopic nasobiliary drainage (ENBD) tube far from the puncture site and three double pigtail stents (DPS) into the walled-off necrosis (WON) cavity, (b) placement of an ENBD tube far from the puncture site and a fully covered self-expanding metal stent into the WON cavity.

WON was resolved. All patients were admitted to our center for observation after the procedure. Resolution of WON and pancreatic duct leakage was assessed by CECT at 8–12 weeks after initial transmural drainage. When complete resolution was achieved, all stents were removed. However, when WON was not resolved, stent

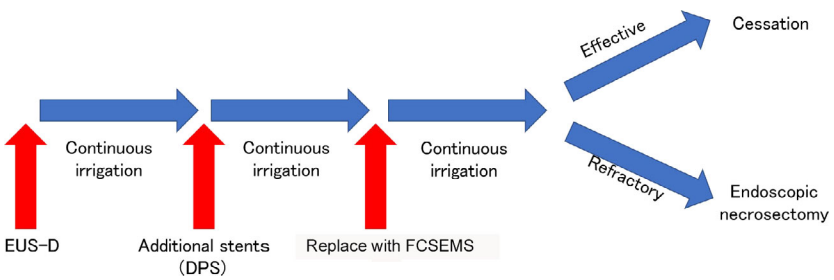

Figure 3 Flow chart of treatment in the transmural nasocyst continuous irrigation (TNCCI) group. After carrying out endoscopic ultrasound-guided drainage (EUS-D), walled-off necrosis (WON) was irrigated. Additional drainage stents were inserted into the WON when there was no clinical improvement, the position of the drain was inadequate or other fluid collections could be drained, or the spontaneous release of saline ceased. TNCCI was continued after inserting the additional stents. Duration of TNCCI depended on whether WON was resolved. When WON was not improved by TNCCI therapy, we considered replacing the double pigtail stent (DPS) with a fully covered self-expanding metal stent (FCSEMS) and continuing TNCCI. When WON was not improved by insertion of a FCSEMS and TNCCI therapy, endoscopic necrosectomy was considered.

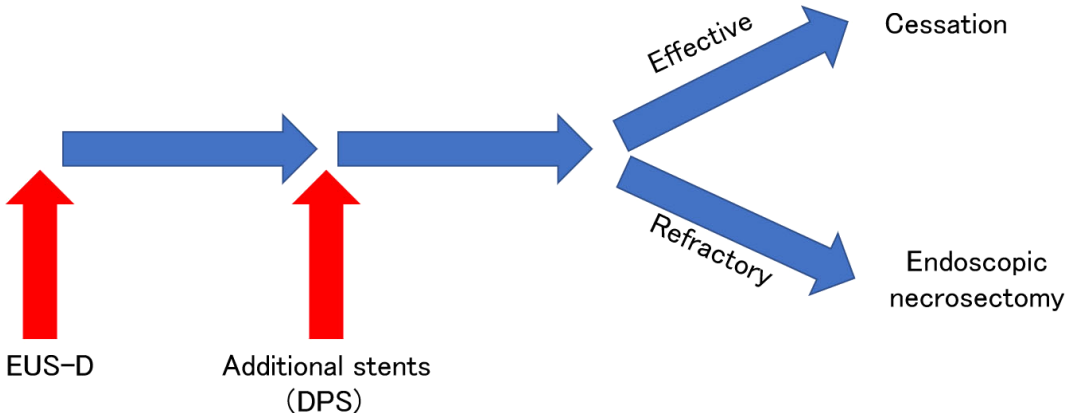

Figure 4 Flow chart of treatment in the control group. The first step was endoscopic ultrasound-guided drainage (EUS-D). When there was no clinical improvement, the position of the drain was inadequate, or other fluid collections could be drained, an additional stent was inserted into the walled-off necrosis using an endoscope. Thereafter, when there was no clinical improvement, endoscopic necrosectomy was carried out. DPS, double pigtail stent.

removal was deferred and imaging was repeated after a further 2–4 weeks.

Outcome measurements

Primary outcome was the amount of time taken to reduce WON by 50% or more based on CECT imaging. Secondary outcomes were incidence of adverse events, number of endoscopic reintervention sessions per patient, number of endoscopic necrosectomy sessions per patient, implementation rate of endoscopic necrosectomy, periods of fasting and hospitalization after the first EUS-D, new-onset organ failure after the first EUS-D and clinical success rate. We defined organ failures as follows: central nervous system failure, Glasgow coma score <13; respiratory failure, PaO_2/FiO_2 ratio <200; coagulopathy, platelet count $\leq 8.0 \times 10^{10}$/L; renal failure, serum creatinine >1.9 mg/dL; and cardiovascular failure, systolic blood pressure ≤90 mmHg. We defined new-onset organ failure as organ failure persisting for at least 48 h after the first EUS-D.[11]

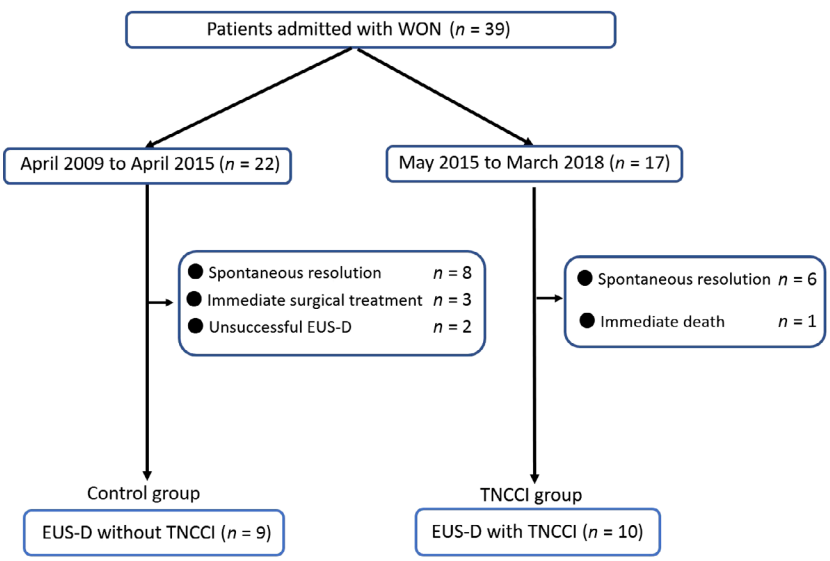

Figure 5 Flow chart showing the inclusion and exclusion of patients. EUS-D, endoscopic ultrasound-guided drainage; TNCCI, transmural nasocyst continuous irrigation; WON, walled-off necrosis.

Table 1 Baseline characteristics of patients admitted with WON who underwent EUS-D

	TNCCI group (n = 10)	Control group (n = 9)	P-value
Male/female	9/1	7/2	0.59
Age (years)	57.4 ± 19.6	56.9 ± 6.0	0.74
Cause of pancreatitis			
Alcohol	50% (5/10)	44.4% (4/9)	1.00
Iatrogenic	20% (2/10)	22.2% (2/9)	1.00
Unknown	30% (3/10)	33.3% (3/9)	1.00
Long axis of WON (mm)	120.5 ± 37.2	103.7 ± 23.8	0.36
APACHE II score	10.1 ± 5.8	6.7 ± 4.0	0.10
Organ failure	20% (2/10) (renal failure, respiratory failure)	11.1% (1/9) (renal failure)	1.00
Infiltration of WON into pelvic cavity	20% (2/10)	11.1% (1/9)	1.00
Pancreatic duct leakage[†]	70% (7/10)	66.6% (6/9)	1.00
Duodenal stricture	10% (1/10)	0% (0/9)	1.00

Data are reported as mean ± standard error or n (%).
[†]Pancreatic duct leakage was diagnosed by enhanced computed tomography or endoscopic retrograde pancreatography.
APACHE, Acute Physiology and Chronic Health Evaluation; EUS-D, endoscopic ultrasound-guided transmural drainage; TNCCI, transmural nasocyst continuous irrigation; WON, walled-off necrosis.

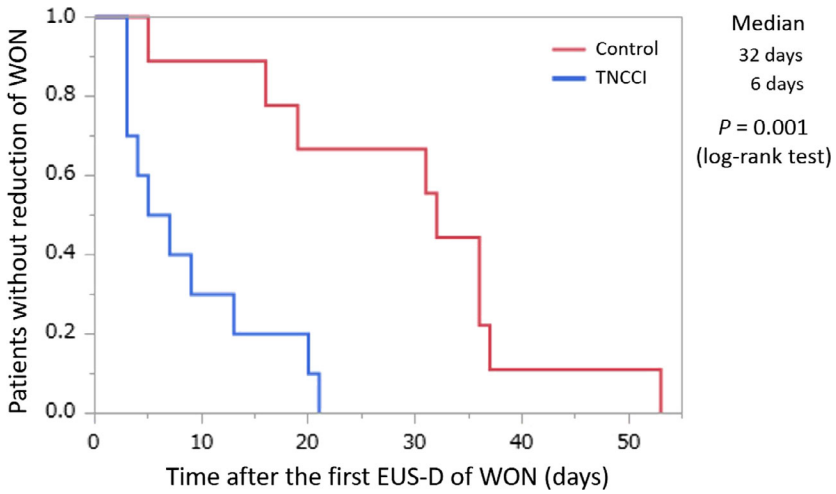

Figure 6 Kaplan–Meier curves showing the cumulative period until walled-off necrosis (WON) was reduced (intention-to-treat analysis). The cumulative amount of time taken to reduce WON was significantly shorter in the transmural nasocyst continuous irrigation (TNCCI) group than in the control group (P = 0.001, log-rank test). EUS-D, endoscopic ultrasound-guided drainage.

Clinical success was defined as a decrease in the size of WON by ≥50% detected by follow-up imaging after 4–6 weeks, together with resolution of symptoms.

Statistical analysis

Data are reported as mean ± standard error or n (%). In each group, the amount of time taken to reduce WON was estimated using the Kaplan–Meier method. Patients in whom WON was not reduced were censored at the date of the last follow up or at death. Amount of time taken to reduce WON was compared between the two groups using the log-rank test. Wilcoxon rank sum test was used to compare means, and Fisher's exact test was used to compare proportions. P values ≤0.05 were considered significant. Statistical analyses were done using Statistical Analysis JMP (Version Pro 13).

RESULTS

Study population

THIRTY -nine patients with WON were admitted to our institution. Twenty of these patients were ineligible.

Table 2 Results of EUS-guided drainage/debridement of WON

	TNCCI group (n = 10)	Control group (n = 9)	P-value
No. of sessions of endoscopic reintervention per patient	1.0 ± 1.2	1.4 ± 1.5	0.43
Type of stent used for the first EUS-D			
ENCD alone	0% (0/10)	66.6% (6/9)	**0.003**
DPS alone	0% (0/10)	22.2% (2/9)	0.21
ENCD + DPS	100% (10/10)	11.1% (1/9)	**<0.001**
Additional stent used			
DPS	70% (7/10)	100% (9/9)	0.21
DPS + FCSEMS	20% (2/10)	0% (0/9)	0.47
Implementation rate of endoscopic necrosectomy	0% (0/10)	55.6% (5/9)	**0.01**
No. of sessions of endoscopic necrosectomy per patient	0	0.8 ± 1.0	**0.008**
Period of fasting (days)	18.6 ± 19.2	31.0 ± 18.6	0.10
Period of hospitalization (days)	45.7 ± 29.4	56.8 ± 24.7	0.40
New-onset organ failure after intervention	0% (0/10)	11.1% (1/9) (respiratory failure)	0.47
Incidence of adverse events	0% (0/10)	22.2% (2/9) (bleeding and perforation)	0.21
Rate of clinical resolution	100% (10/10)	100% (9/9)	1.00

Data are reported as mean ± standard error or n (%).
P values ≤0.05 (shown in bold font) are considered significant.
DPS, double pigtail stent; ENCD, endoscopic nasocyst drainage; EUS-D, endoscopic ultrasound-guided drainage; FCSEMS, fully covered self-expanding metal stent; TNCCI, transmural nasocyst continuous irrigation; WON, walled-off necrosis.

Among the 13 ineligible patients admitted between April 2009 and April 2015, eight patients were excluded because WON spontaneously resolved, two patients were excluded because EUS-D was unsuccessful and three patients were excluded because surgical treatment was immediately carried out without EUS-D. EUS-D failed when the distance between the tip of the endoscope and the WON was too long. Among the seven ineligible patients excluded between May 2015 and March 2018, six patients were excluded because WON spontaneously resolved and one patient was excluded because he died of respiratory failure before EUS-D could be carried out (Fig. 5). Clinical characteristics of the patients are summarized in Table 1. The clinical characteristics of the patients did not significantly differ between the two groups.

Kaplan–Meier curves showing the amount of time taken to reduce WON are presented in Figure 6. Duration until reduction of WON was significantly shorter in the TNCCI group than in the control group (median 6 *vs* 32 days, P = 0.001, log-rank test). Secondary end points are listed in Table 2. Endoscopic necrosectomy was carried out more frequently in the control group than in the TNCCI group (55.6% *vs* 0%, P = 0.01). Number of endoscopic necrosectomy sessions per patient was significantly lower in the TNCCI group than in the control group (0 *vs* 0.8 ± 1.0, P = 0.008). WON was drained using a FCSEMS in one patient in the TNCCI group. Number of endoscopic reintervention sessions per patient, duration of fasting, and duration of hospitalization did not significantly differ between the TNCCI and control groups (P = 0.43, P = 0.10, and P = 0.40, respectively). One of the nine patients (11.1%) in the control group showed respiratory failure after the first EUS-D, whereas no patient showed new-onset organ failure in the TNCCI group. In addition, two of the nine patients (22%) in the control group suffered adverse events, namely, peritonitis and bleeding during endoscopic necrosectomy. There was no significant difference in adverse events between the two groups (P = 0.21). Additionally, no adverse events were observed in the TNCCI group. WON was finally improved in both groups without surgical necrosectomy and did not recur in either group.

DISCUSSION

THE PRESENT STUDY showed that WON was reduced more rapidly in the TNCCI group than in the control group, in which patients were managed using a conventional step-up treatment. Moreover, implementation rate of endoscopic necrosectomy was significantly lower in the TNCCI group than in the control group. Average APACHE II score was 10.1 in the TNCCI group, which is as high as in previous reports;[4,11] however, TNCCI did not cause multiple organ failure. These results suggest that

TNCCI improves the initial drainage of WON and prevents deterioration of the patient's general condition until the next treatment. Necrotic substances are less effectively washed out by TNCCI during the first catheter drainage than by debridement during endoscopic necrosectomy because the fistula created during TNCCI is smaller than that created during endoscopic necrosectomy.[5] However, TNCCI seems to prevent the deterioration of sepsis by removing purulent material from the abscess by continuous irrigation. In addition, WON had spread to the pelvic cavity in two patients in the TNCCI group, in which WON was resolved by placing an ENBD tube into the pelvic cavity and carrying out TNCCI. The incidence of adverse events was lower in the TNCCI group (0%) than in the control group (22.2%). These results suggest that TNCCI can resolve WON without endoscopic necrosectomy.

Kumar *et al.*[12] reported that direct endoscopic necrosectomy reduces new antibiotic use, pulmonary failure, endocrine insufficiency, and duration of hospitalization compared with the step-up approach ($P < 0.005$), suggesting that effective drainage at an early time point is important for WON treatment. In contrast, in a report of 639 consecutive patients with WON, the percentage of cases who suffered from adverse events was lower among those whose first intervention was catheter drainage than among those who underwent primary endoscopic necrosectomy (42% *vs* 64%; $P = 0.003$).[9] Yasuda *et al.*[5] reported that two-thirds of the adverse events associated with endoscopic necrosectomy occur during the procedure and one-third occur between the sessions. In the present study, two patients in the control group suffered bleeding and perforation during endoscopic necrosectomy, whereas no patients experienced adverse events in the TNCCI group. Our results suggest that TNCCI is superior to the conventional step-up approach because endoscopic necrosectomy, which causes more adverse events, was not required in the TNCCI group.

Necrotic substances in WON may not be sufficiently removed with DPS and ENBD. In this study, WON was not resolved in two patients who underwent EUS-D using DPS and TNCCI. In these patients, WON was resolved by replacing the DPS with a FCSEMS by endoscopy and continuing TNCCI. In addition, the use of a nasotube for TNCCI has some disadvantages such as risk of self-removal and pain. Overall efficacy of EUS-D of WON is better using a FCSEMS than using a DPS.[13–16] The novel saddle-shaped lumen-apposing fully covered self-expanding metal stent (LAMS) has been reported to have a high success rate for drainage debridement of WON.[3,17] In addition, it was recently reported that treatment of WON is improved by carrying out continuous irrigation in addition to EUS-D using a FCSEMS and a LAMS before endoscopic necrosectomy.[10,18] However, FCSEMS and LAMS are more expensive than DPS. Moreover, FCSEMS involves a risk of stent migration and abutment of the end of the stent against the luminal wall, which may cause bleeding and tissue injury.[16] In addition, the efficacy of intermittent irrigation by EUS-D with transduodenoscopy has been reported.[19] Continuous irrigation is problematic when an infusion pump is used for this; symptoms may appear by elevation of intracystic pressure when the internal drainage stent is obstructed. However, as we used natural instillation during continuous irrigation, instillation stopped when the internal drainage stent became obstructed. Intermittent irrigation is required to create a large diameter for the needle tract to control the infection and remove debris.[19] In contrast, continuous irrigation with natural instillation is not necessary for the creation of a large fistula at the first intervention, because continuous irrigation can control WON infection by avoiding debris stagnation. Taking our results into consideration, endoscopic drainage using a DPS together with TNCCI can be carried out as the first step in the treatment of WON. When this approach is ineffective, endoscopic drainage using a FCSEMS or a LAMS should be considered. Further studies comparing EUS-D followed by TNCCI and EUS-D using a FCSEMS or a LAMS are required to determine the most appropriate first intervention in the treatment of WON.

A limitation of the present study is that it included a small number of cases and was of a retrospective, single-center design, which introduced a certain bias. In addition, the TNCCI group used FCSEMS plus TNCCI as a salvage whereas the control group did not use FCSEMS and instead used the step-up approach which might have lengthened the time to recovery and introduced FCSEMS as a confounding factor. Nonetheless, TNCCI is a good novel method and this study proved its safety and efficacy. A prospective, randomized, controlled trial is necessary to confirm the superiority of EUS-D using a DPS and FCSEMS with TNCCI therapy.

In conclusion, EUS-D using a DPS with TNCCI is an effective and safe approach to treat WON. We recommend this method is done before considering endoscopic necrosectomy and suggest that most cases of WON can be resolved without endoscopic necrosectomy, which is highly invasive.

ACKNOWLEDGMENTS

WE THANK ALL members of the Second Department of Internal Medicine and the Clinical Study Support Center at Wakayama Medical University.

CONFLICTS OF INTEREST

AUTHORS DECLARE NO conflicts of interest for this article.

REFERENCES

1 Banks PA, Bollen TL, Dervenis C *et al.* Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013; **62**: 102–11.

2 Yeo CJ, Bastidas JA, Lynch-Nyhan A, Fishman EK, Zinner MJ, Cameron JL. The natural history of pancreatic pseudocysts documented by computed tomography. *Surg. Gynecol. Obstet.* 1990; **170**: 411–7.

3 Siddiqui AA, Kowalski TE, Loren DE *et al.* Fully covered self-expanding metal stents versus lumen-apposing fully covered self-expanding metal stent versus plastic stents for endoscopic drainage of pancreatic walled-off necrosis: clinical outcomes and success. *Gastrointest. Endosc.* 2017; **85**: 758–65.

4 van Santvoort HC, Besselink MG, Bakker OJ *et al.* A step-up approach or open necrosectomy for necrotizing pancreatitis. *N. Engl. J. Med.* 2010; **362**: 1491–502.

5 Yasuda I, Nakashima M, Iwai T *et al.* Japanese multicenter experience of endoscopic necrosectomy for infected walled-off pancreatic necrosis: the JENIPaN study. *Endoscopy* 2013; **45**: 627–34.

6 Nemoto Y, Attam R, Arain MA *et al.* Interventions for walled off necrosis using an algorithm based endoscopic step-up approach: outcomes in a large cohort of patients. *Pancreatology* 2017; **17**: 663–8.

7 Seifert H, Wehrmann T, Schmitt T, Zeuzen S, Caspary WF. Retroperitoneal endoscopic debridement for infected peripancreatic necrosis. *Lancet* 2000; **356**: 653–5.

8 Bakker OJ, van Santvoort HC, van Brunschot S *et al.* Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. *JAMA* 2012; **307**: 1053–61.

9 van Santvoort HC, Bakker OJ, Bollen TL *et al.* A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. *Gastroenterology* 2011; **141**: 1254–63.

10 Gornals JB, Consiglieri C, Busquest J *et al.* Endoscopic necrosectomy of a walled-off pancreatic necrosis using a lumen-apposing metal and irrigation tehnique. *Surg. Endoscopy* 2016; **30**: 2592–602.

11 Johnson CD, Abu-Hilal M. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. *Gut* 2004; **53**: 1340–4.

12 Kumar N, Conwell DL, Thompson CC. Direct endoscopic necrosectomy versus step-up approach for walled-off pancreatic necrosis: comparison of clinical outcome and health care utilization. *Pancreas* 2014; **43**: 1334–9.

13 Talreja JP, Shami VM, Ku J, Morris TD, Ellen K, Kahaleh M. Transenteric drainage of pancreatic-fluid collections with fully covered self-expanding metallic stents. *Gastrointest. Endosc.* 2008; **68**: 1199–203.

14 Fabbri C, Luigiano C, Cennamo V *et al.* Endoscopic ultrasound-guided transmural drainage of infected pancreatic fluid collections with placement of covered self-expanding metal stents: a case series. *Endoscopy* 2012; **44**: 429–33.

15 Penn DE, Draganov PV, Wagh MS, Forsmark CE, Gupte AR, Chauhan SS. Prospective evaluation of the use of fully covered self-expanding metal stents for EUS-guided transmural drainage of pancreatic pseudocysts. *Gastrointest. Endosc.* 2012; **76**: 679–84.

16 Bazerbachi F, Sawas T, Vargas EJ *et al.* Metal stents versus plastic stents for the management of pancreatic walled-off necrosis: a systematic review and meta-analysis. *Gastrointest. Endosc.* 2018; **87**: 30–42.

17 Lang GD, Fritz C, Bhat T *et al.* EUS-guided drainage of peripancreatic fluid collections with lumen-apposing metal stents and plastic double-pigtail stents: comparison of efficacy and adverse event rates. *Gastrointest. Endosc.* 2018; **87**: 150–7.

18 Lakhtakia S, Basha J, Talukdar R *et al.* Endoscopic "step-up approach" using a dedicated biflanged metal stent reduces the need for direct necrosectomy in walled-off necrosis (with videos). *Gastrointest. Endosc.* 2017; **85**: 1243–52.

19 Ren YC, Chen SM, Cai XB, Li BW, Wan XJ. Endoscopic ultrasonography-guided drainage combined with trans-duodenoscope cyclic irrigation technique for walled-off pancreatic necrosis. *Dig. Liver Dis.* 2017; **49**: 38–44.