Outcomes of Endoscopic Management of Sterile Walled-Off Pancreatic Necrosis

A Systematic Review

Francisco Valverde-López, MD, PhD, Samuel Han, MD, MS,† Sarah Coughlin, MD,‡ Nikhil Thiruvengadam, MD,‡ Christopher Moreau, BS,§ Venkata S. Akshintala, MD, PhD,‖ and Peter J. Lee, MBChB,‡ on behalf of the Collaborative Alliance for Pancreatic Education and Research*

Objectives: The aim of this study is to systematically review outcomes related to treatment success, mortality, and adverse events of endoscopic management in patients with sterile walled-off pancreatic necrosis.

Methods: We reviewed studies published from 2008 to 2018 from Medline and Embase that evaluated the endoscopic treatment of necrotizing pancreatitis. The primary outcome was success of treatment in resolving the collection. Secondary outcomes included length of hospitalization, mortality rate, and adverse events.

Results: Five studies were included, which entailed a total of 280 patients with a mean age of 51.8 years. The primary indication for endoscopic treatment was symptomatic walled-off pancreatic necrosis. Four studies used endoscopic transmural drainage, one of them combining percutaneous drainage and 1 study performed transpapillary drainage. The pooled treatment success was 94.3% with a mean time to resolution of 77.8 days. The mean length of stay was 16.3 days, and mortality rate was 1.3%. The overall adverse event rate was 24.6%, with bleeding the most common adverse event (11%), followed by pancreatic fistula formation (3.4%) and perforation (2.7%).

Conclusions: Although endoscopic management of sterile pancreatic necrosis has a high rate of treatment success, there is a relatively high rate of adverse events, bleeding being the most common.

Key Words: acute necrotizing pancreatitis, walled off pancreatic necrosis, acute pancreatitis, sterile necrosis

(*Pancreas* 2021;50: 1357–1362)

Acute pancreatitis (AP) is the third leading cause of gastrointestinal-related hospitalizations in the United States and its admission rate continues to rise over time.[1,2] In 20% of cases, acute necrotizing pancreatitis (ANP) may develop with higher rates of early organ failure, need for intervention, and mortality during the hospitalization.[3,4] Even among patients who recover from ANP, there is a high rate of morbidity including frequent admissions and poor quality of life.[5,6]

From the *Division of Gastroenterology and Hepatology, Hospital Universitario Virgen de las Nieves, Granada, Spain; †Division of Gastroenterology and Hepatology, University of Colorado Anschutz Medical Campus, Aurora, CO; ‡Division of Gastroenterology, Hospitals of the University of Pennsylvania, Philadelphia, PA; §Division of Gastroenterology, University of Texas Health San Antonio, San Antonio, TX; and ‖Division of Gastroenterology and Hepatology, Johns Hopkins Hospital, Baltimore, MD.

Received for publication April 19, 2021; accepted October 25, 2021.

Address correspondence to: Francisco Valverde-López, MD, PhD, Gastroenterology and Hepatology Department, Virgen de las Nieves University Hospital, Avenida de las Fuerzas Armadas 2, 18014-Granada, Spain (e-mail: fcovalverde89@gmail.com).

F.V.-L. and S.H. are cofirst authors.

The authors declare no conflict of interest.

DOI: 10.1097/MPA.0000000000001929

The greatest progress has been made in the management of infected walled-off pancreatic necrosis (WOPN) as demonstrated in several landmark randomized clinical trials.[7–9] These trials demonstrated the superiority of "step-up" endoscopic intervention via endoscopic ultrasound (EUS)-guided transmural drainage followed by direct endoscopic necrosectomy as needed, which has now become the standard of care.[10] However, limited data exist regarding the optimal management of sterile (noninfected) WOPN. According to the International Association of Pancreatology-American Pancreatic Association joint guidelines for the management of AP, there is grade 2C level evidence for intervening on symptomatic, sterile WOPN.[11] Whereas some suggest less than 1% of patients with sterile WOPN need an intervention, many others recommend an intervention if symptoms occur from WOPN.[12,13] We, therefore, performed a systematic review of studies involving management of sterile WOPN with the primary aim of describing outcomes related to treatment success, mortality, and adverse events in this population.

MATERIALS AND METHODS

Search Strategy and Study Selection

All studies of endoscopic, percutaneous, and surgical treatment of necrotizing pancreatitis were sought in Medline (PubMed) and Embase between January 2008 and December 2018. The following search terms were used: "acute necrotizing pancreatitis" OR "sterile necrosis acute pancreatitis" OR "infected pancreatic necrosis" OR "walled off pancreatic necrosis" OR "endoscopic management acute pancreatitis" OR "endoscopic necrosectomy" OR "endoscopic necrotizing pancreatitis" OR "mortality necrotizing pancreatitis" OR "endoscopic management pancreatic necrosis." In addition, the references of all included articles and review articles were searched to identify any potentially missing studies.

Definitions of key search terms were derived from the revised Atlanta classification.[14] Specifically, diagnosis of AP required 2 of the following 3 features: (1) abdominal pain consistent with the disease (acute onset of a persistent, severe, epigastric pain often radiating to the back); (2) serum lipase activity (or amylase activity) at least 3 times greater than the upper limit of normal; and (3) characteristic findings of AP on computed tomography (CT) or magnetic resonance imaging or transabdominal ultrasonography. Necrotizing pancreatitis was defined as the development of necrosis in the pancreatic parenchyma, peripancreatic tissue, or both confirmed on imaging. Infected pancreatic necrosis (IPN) was defined as extraluminal gas in the pancreatic or peripancreatic tissue on imaging, a positive bacterial or fungal culture on aspiration of necrotic tissue, or signs of persistent sepsis (fever, elevated white blood cell count, organ failure). Conversely, sterile necrosis was defined as the absence of such features in necrotizing

pancreatitis. Endoscopic management referred to the use of transmural drainage or necrosectomy and/or transpapillary drainage of the collections. Treatment success was defined as improvement of clinical symptoms and decrease in the size of the walled-off necrosis collection to less than 3 cm in diameter.

Studies were required to be in English peer-reviewed journals and could be either retrospective or prospective. Studies were required to include demographic data of ANP and data referring to the endoscopic management of specifically sterile necrosis. Specific endoscopic procedures required detailed description. We excluded studies that were case series or case reports detailing less than 5 patients, nonhuman studies, abstracts, or letters to the editor and studies involving a pediatric (<18 years) population.

The Preferred Reporting Items for Systematic Reviews and Meta-analyses criteria were adhered to.[15] To assess the quality of the included studies, we (S.C., F.V.L.) used the Methodological Index for Nonrandomized Studies (MINORS) as they were all nonrandomized, interventional studies.[16] The MINORS is comprised of 12 items that assess study validity, methodology, and completeness of reporting. Each item is assigned a score of 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate). The first 8 items apply to both noncomparative and comparative studies, whereas the remaining 4 relate only to studies with 2 or more groups. The global ideal score is thus 16 for noncomparative studies and 24 for comparative studies, with higher scores indicating greater quality.

Data Extraction

Two reviewers (F.V.L., S.H.) performed data extraction independently using a standardized data collection form. The information collected included study design, year of publication, country of origin, number of patients, baseline patient demographics and characteristics, endoscopic treatment details, treatment results, time to treatment success, mortality, and adverse events. Discrepancies were discussed between the 2 reviewers, and if no consensus could be reached, a third reviewer (P.L.) made a final decision.

Outcomes of Interest

The primary outcome was treatment success, which was defined as reduction in the size of the necrotic collection to less than

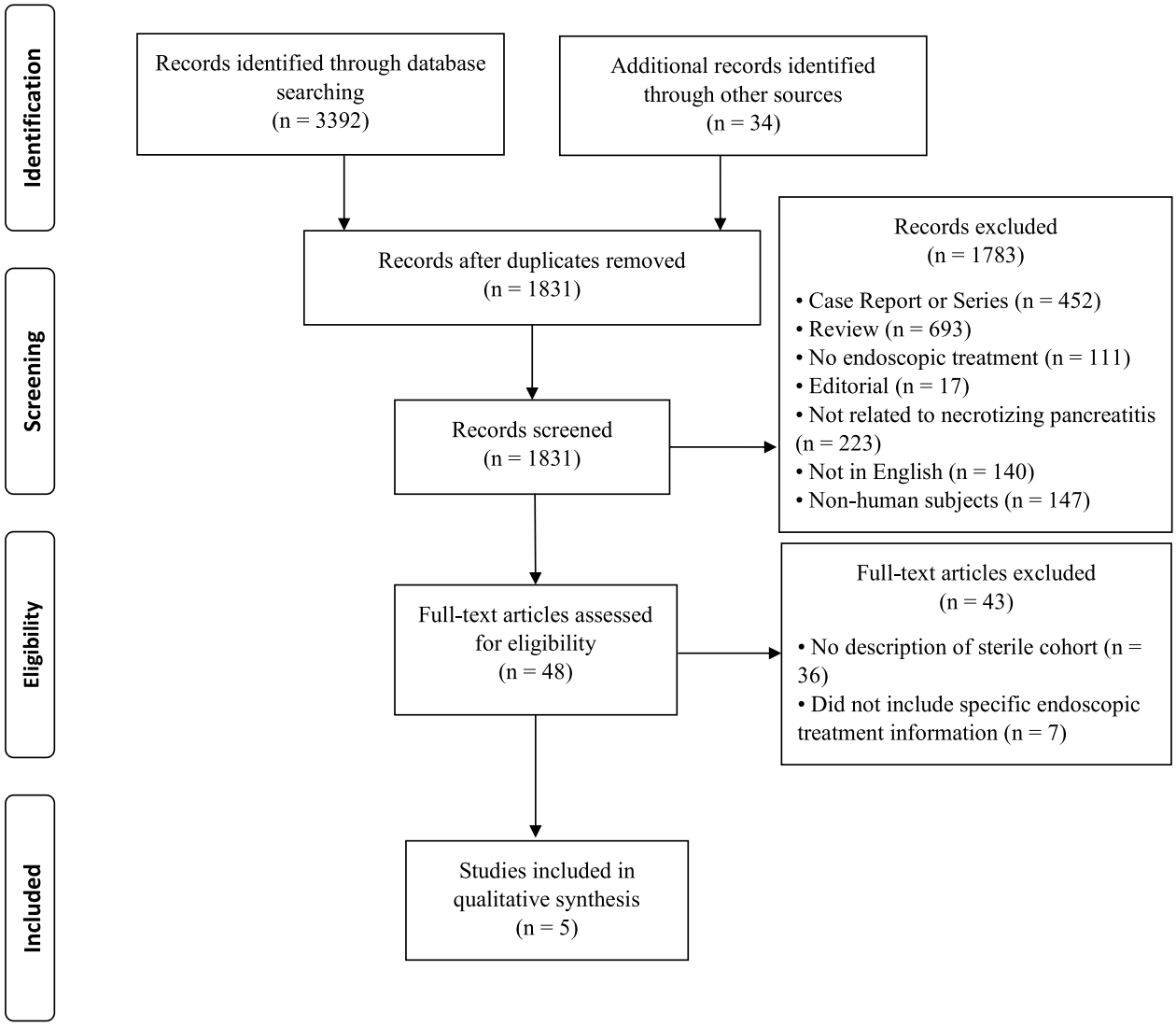

FIGURE 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flowchart of study selection process.

TABLE 1. Design of Included Studies

Study, Year	Country	Study Period	Single or Multicenter	Type	No. Subjects	Endoscopic Treatment
Smoczyński et al, 2014[17]	Poland	2001–2011	Single center	Retrospective	112	Transmural or transpapillary drainage
Khreiss et al, 2015[18]	US	2008–2013	Single center	Retrospective	20	Transmural drainage and necrosectomy
Watanabe et al, 2017[19]	Japan	1999–2015	Single center	Retrospective	13	Transmural drainage
Smoczyński et al, 2016[20]	Poland	2001–2013	Single center	Retrospective	22	Transmural drainage
Hyun et al, 2019[13]	US	2007–2017	Single center	Retrospective	113	Dual modality drainage (percutaneous and endoscopic transmural drainage)

3 cm in addition to improvement of symptoms. Secondary outcomes included time to resolution, mortality, and adverse events.

Statistical Analysis

Descriptive statistics were used to depict outcomes in terms of mean (standard deviation [SD]) or proportion and frequency, n (%).

RESULTS

Design of Included Studies

The Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram is shown in Figure 1. Our database search yielded 1804 studies, of which 1783 were excluded on initial screening of their title and abstract. A total of 48 full-text studies were assessed for eligibility with 5 studies meeting the inclusion criteria. Study designs of the included studies are displayed in Table 1. There were 2 studies from the United States, 2 from Poland (same study group), and 1 study from Japan. All were retrospective, single-center studies.

Baseline Characteristics of Patients

The 5 studies incorporated a total of 280 patients, of which the mean age was 51.8 years and 69.7% (n = 186) were men (Table 2). The most common etiologies of the necrotizing pancreatitis were alcohol (41.1%) and gallstones (37.1%). The mean diameter of the necrotic collection was 13.7 cm (SD, 5.5 cm).

Inclusion and Exclusion Criteria

In all 5 studies, WOPN was defined in accordance to the revised Atlanta classification.[14] Sterile WOPN was defined in all 5 studies as either the absence of positive culture results from aspiration or a lack of signs of sepsis. The primary indication for

TABLE 2. Pooled Baseline Characteristics

Study, Year (n)	Age, Mean (SD), y	Sex, n (%)	BMI, Mean (SD), kg/m^2	Etiology, n (%)	Size, Mean (SD), cm	Stent Details
Smoczyński et al, 2014[17] (n = 112)	—	Male, 83 (74.1) Female, 29 (25.9)	—	Alcoholic, 71 (63.4) Gallstone, 37 (33) Post-ERCP, 3 (2.7) Idiopathic, 1 (0.9)	Median, 11.6 (range, 4.5–26.7)	10 Fr DPS and 7 Fr/8.5 Fr nasocystic drain
Khreiss et al, 2015[18] (n = 20)	Median, 55	Male, 9 (45) Female, 11 (55)	29.8 (7.3)	Gallstones, 9 (45) Alcohol, 3 (15) Idiopathic, 2 (10)	11.2 (4.9)	Two 10-Fr DPS or 10 mm SEMS
Watanabe et al, 2017[19] (n = 13)	—	—	—	—	—	7 Fr DPS and a 7 Fr nasocystic drain
Smoczyński et al, 2016[20] (n = 22)	50.7	Male, 15 (68.2) Female, 7 (31.8)	—	Alcohol, 15 (68.2)	8	Transpapillary nasal drain (7 Fr or 8.5 Fr) and pancreatic stent (5–10 Fr)
Hyun et al, 2019[13] (n = 113)	51.4 (15.8)	Male, 79 (69.9) Female, 34 (29.3)	28.9 (6.9)	Gallstones, 58 (51.3) Alcohol, 26 (23) Idiopathic, 13 (11.5) Hypertriglyceridemia, 3 (2.7) Post-ERCP, 2 (1.8)	14.2 (4.5)	Two 7-Fr DPS or LAMS
Combined (n = 280)	51.8	Male, 186 (66.4) Female, 81 (28.9) Unknown, 13 (4.6)	29	Gallstones, 104 (37.1) Alcohol, 115 (41.1) Idiopathic, 16 (5.7) Post-ERCP, 5 (1.8) Hypertriglyceridemia, 3 (1.1) Unknown, 37 (13.2)	13.7 (5.5)	DPS (4 studies) SEMS (1 study) Pancreatic duct stent (1 study) LAMS (1 study)

BMI indicates body mass index; SEMS, self-expanding metal stent; LAMS, lumen-apposing metal stent; ERCP, endoscopic retrograde cholangiopancreatography.

endoscopic treatment was symptomatic WOPN, which was defined slightly differently for each study. Hyun et al[13] defined symptomatic WOPN as having gastric, duodenal, or biliary obstruction and/or failure to improve because of the inability to eat or failure to thrive. In their 2 studies, Smoczyński et al[17,20] defined symptomatic WOPN as having symptoms connected with the presence of the WOPN. Khreiss et al[18] and Watanabe et al[19] similarly defined these symptoms as having abdominal pain, gastric outlet obstruction, weight loss, or episodes similar to recurrent bouts of pancreatitis.

Treatment Methods

Four of the 5 procedures used endoscopic transmural drainage for primary treatment of the WOPN (Table 2).[13,17–19] The remaining study (Smoczyński et al[20]) examined the use of transpapillary pancreatic duct stenting as the primary treatment modality. Of the 4 studies incorporating transmural drainage, 3 used EUS for visualized access to the necrotic collection.[13,T8,19] Double pigtail stents (DPS) were used in all 4 studies involving transmural drainage with concomitant nasocystic drains placed in 2 studies.[17,19] Self-expanding metal stents (SEMS) were used in a single study (Khreiss et al[18]) and 1 study (Hyun et al[13]) used lumen-apposing metal stents (LAMS). Lastly, 1 study (Hyun et al[13]) used dual-modality drainage in the form of combined CT-guided percutaneous drainage with endoscopic transmural drainage.

Systematic Review Results

Treatment Success

The pooled treatment success was 94.3% (n = 264) with a mean time to resolution of 77.8 (55.4) days (Table 3). Watanabe et al[19] reported the lowest treatment success rate at 76.9%, whereas Hyun et al[13] reported a 99.1% treatment success rate.[13,19] The mean length of stay was 16.3 days, and the mortality rate was 1.3% (range, 0.8–1.8%).

Adverse Events

The overall adverse event rate was 24.6% (Table 3). Bleeding was the most common adverse event (11%), followed by pancreatic fistula formation (3.4%) and perforation (2.7%).

Quality of Included Studies

In regard to the quality of the included studies based on the MINORS criteria, Smoczyński et al[20] had a score of 11/16, Khreiss et al had a score of 19/24, Watanabe et al had a score of 12/16, Smoczyński et al had a score of 11/16, and Hyun et al had a score of 19/24.

DISCUSSION

The present systematic review assesses the epidemiological data, outcomes, and complications of patients who underwent endoscopic therapy for sterile ANP. We found a pooled treatment success of 94.3% with EUS-guided drainage using DPS representing the most common treatment method of the studies analyzed. Adverse event rates, however, were considerable, with a pooled rate of 24.3% and bleeding being the most common (11%) adverse event, followed by pancreatic fistula formation (3.4%) and perforation (2.7%).

Differentiating between IPN and sterile ANP is not always easy and a definitive diagnosis of sterile ANP is nearly impossible. Typically, clinical deterioration and presence of gas in the CT are suggestive data of IPN, and for the purpose of our review, we defined sterile ANP as the absence of these features, although some of these collections may have been subclinically infected.[21] Smoczyński et al[17] found infections in 36.9% of necrotic collections after drainage although the indications of the procedure were mainly adjacent organ compression, abdominal pain or weight loss. Although their initial treatment success rate was 92.9%, long term success was 83.9%, which is similar to other studies including patients with IPN.[22,23] This could be related to including patients with nonevident IPN. The study of Hyun et al[13] compared

TABLE 3. Pooled Primary and Secondary Outcomes

Study, Year (n)	Treatment Success, %	Time to Resolution, Mean (SD), d	Length of Stay, Mean (SD), d	Mortality, n (%)	Adverse Events, n (%)
Smoczyński et al, 2014[17] (n = 112)	92.9 (104/112)	—	29	2 (1.8)	Bleeding, 19 (17) Perforation, 6 (5.4) Stent migration, 3 (2.7) Sepsis, 1 (0.9)
Khreiss et al, 2015[18] (n = 20)	90 (18/20)	108 (99)	3	0 (0)	Infection, 2 (10) Bleeding, 1 (5) Perforation, 1 (5)
Watanabe et al, 2017[19] (n = 13)	76.9 (10/13)	—	—	—	—
Smoczyński et al, 2016[20] (n = 22)	90.9 (20/22)	—	—	—	—
Hyun et al, 2019[13] (n = 113)	99.1 (112/113)	72.4 (47.7)	17.1 (16.6)	1 (0.8)	Bleeding, 9 (3.8) Fistula, 9 (3.8) Gastric outlet obstruction, 6 (5.3) Biliary stricture, 4 (3.5) Acute kidney injury, 4 (3.5)
Combined (n = 280)	94.3 (264/280)	77.8 (55.4)	16.3	3 (1.3)	Total, 65 (24.6) Bleeding, 29 (11) Fistula, 9 (3.4) Perforation, 7 (2.7) Gastric outlet obstruction, 6 (2.3) Biliary stricture, 4 (1.5) Acute kidney injury, 4 (1.5) Stent migration, 3 (1.1) Sepsis, 3 (1.1)

the outcomes of patients with sterile ANP and IPN and defined IPN as having a positive culture of the aspirated fluid. Although fluid culture has considerable false-positive and negative rates, this is one of the largest studies comparing outcomes of sterile ANP and IPN.[21,24] The IPN group had a greater length of stay (29.8 days vs 17 days, $P < 0.01$), higher rates of spontaneous pancreatic fistula (23.5 vs 7.8%, $P < 0.01$) and slightly higher mortality than the symptomatic ANP group (4.1% vs 0.9%, $P = 0.19$), but no difference was found between both groups in terms of other adverse events such as bleeding, gastric outlet obstruction or biliary obstruction. It must be noted that, in this study, dual modality drainage (combining percutaneous and endoscopic) was performed, so these results may not be as generalizable. Khreiss et al[18] analyzed 20 patients with symptomatic WOPN using EUS-guided drainage or necrosectomy with DPS or SEMS and compared it with a similar cohort of patients who underwent cystgastrosotomy using a minimally invasive surgical procedure. The endotherapy group had a shorter length of stay, but also had a higher need for re-interventions. They also suggested that larger WOPN and a higher body mass index can be related to failure of endotherapy.

Treatment of suspected or well-known IPN is mandatory to improve outcomes in these patients and it is well established in guidelines to perform minimally invasive treatment in addition to antibiotic therapy.[8,9,25,26] Few studies however have included data about sterile ANP, and the need for intervention in these patients is much lower than in patients with IPN.[4] In fact, in a large prospective series of 639 patients, only 2 (0.3%) required intervention for sterile necrosis, whereas 208 (33%) of patients with suspected or confirmed IPN eventually required intervention.[4] Furthermore, mortality in patients with sterile necrosis is almost exclusively in the early phase of AP secondary to multiple organ failure, suggesting that intervention may not be indicated in this subgroup of patients.[27,28]

Our study has several limitations. First, despite using nonrestrictive criteria in the strategy search, and after review of more than 1500 publications, very few studies met the inclusion criteria because of a lack of information regarding outcomes in sterile ANP, so our results may not be accurately representative of this population, although we found similar results in terms of treatment success and adverse events with other studies focused on IPN.[22,23] Second, there was considerable heterogeneity between the studies in terms of sample size and endoscopic procedures which could have affected to the results. Lastly and importantly, all the studies included in the review were retrospective and single-center in nature.

Despite its limitations, our study is, to our knowledge, the first systematic review performed specifically examining patients with sterile ANP. We found a relatively high rate of treatment success of endoscopic management in sterile ANP but with a considerable risk of adverse events that must be taken into account. Because the risk of mortality is much lower in patients with sterile WOPN compared with IPN, prospective and multicenter studies should be done to assess the potential benefits and risks of treatment of sterile ANP, ideally in comparison with conservative management.[5,6] Our review also shows that there are a lack of studies focused on sterile ANP, despite its importance and prevalence as a condition that often poses a dilemma for the clinician in choosing between an interventional or a conservative approach, emphasizing the continued need for further investigation.

REFERENCES

1. Peery AF, Crockett SD, Murphy CC, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update 2018. *Gastroenterology*. 2019;156:254–272.e11.
2. Gapp J, Hall AG, Walters RW, et al. Trends and outcomes of hospitalizations related to acute pancreatitis: epidemiology from 2001 to 2014 in the United States. *Pancreas*. 2019;48:548–554.
3. Singh VK, Bollen TL, Wu BU, et al. An assessment of the severity of interstitial pancreatitis. *Clin Gastroenterol Hepatol*. 2011;9:1098–1103.
4. van Santvoort HC, Bakker OJ, Bollen TL, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. *Gastroenterology*. 2011;141:1254–1263.
5. Garg PK, Madan K, Pande GK, et al. Association of extent and infection of pancreatic necrosis with organ failure and death in acute necrotizing pancreatitis. *Clin Gastroenterol Hepatol*. 2005;3:159–166.
6. Sternby H, Bolado F, Canaval-Zuleta HJ, et al. Determinants of severity in acute pancreatitis: a nation-wide multicenter prospective cohort study. *Ann Surg*. 2019;270:348–355.
7. van Brunschot S, van Grinsven J, van Santvoort HC, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. *Lancet*. 2018;391:51–58.
8. van Santvoort HC, Besselink MG, Bakker OJ, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. *N Engl J Med*. 2010; 362:1491–1502.
9. Bang JY, Arnoletti JP, Holt BA, et al. An endoscopic transluminal approach, compared with minimally invasive surgery, reduces complications and costs for patients with necrotizing pancreatitis. *Gastroenterology*. 2019;156:1027–1040.e3.
10. Baron TH, DiMaio CJ, Wang AY, et al. American Gastroenterological Association clinical practice update: management of pancreatic necrosis. *Gastroenterology*. 2020;158:67–75.e1.
11. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. *Pancreatology*. 2013;13(4 suppl 2):e1–e15.
12. Hollemans RA, Bakker OJ, Boermeester MA, et al. Superiority of step-up approach vs open necrosectomy in long-term follow-up of patients with necrotizing pancreatitis. *Gastroenterology*. 2019; 156:1016–1026.
13. Hyun JJ, Sahar N, Singla A, et al. Outcomes of infected versus symptomatic sterile walled-off pancreatic necrosis treated with a minimally invasive therapy. *Gut Liver*. 2019;13:215–222.
14. 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;62:102–111.
15. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med*. 2009;151:264–269, W64.
16. Slim K, Nini E, Forestier D, et al. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. *ANZ J Surg*. 2003;73:712–716.
17. Smoczyński M, Marek I, Dubowik M, et al. Endoscopic drainage/ debridement of walled-off pancreatic necrosis—single center experience of 112 cases. *Pancreatology*. 2014;14:137–142.
18. Khreiss M, Zenati M, Clifford A, et al. Cyst gastrostomy and necrosectomy for the management of sterile walled-off pancreatic necrosis: a comparison of minimally invasive surgical and endoscopic outcomes at a high-volume pancreatic center. *J Gastrointest Surg*. 2015; 19:1441–1448.
19. Watanabe Y, Mikata R, Yasui S, et al. Short- and long-term results of endoscopic ultrasound-guided transmural drainage for pancreatic pseudocysts and walled-off necrosis. *World J Gastroenterol*. 2017; 23:7110–7118.
20. Smoczyński M, Jagielski M, Jabłońska A, et al. Transpapillary drainage of walled-off pancreatic necrosis—a single center experience. *Wideochir Inne Tech Maloinwazyjne*. 2016;10:527–533.

21. van Baal MC, Bollen TL, Bakker OJ, et al. The role of routine fine-needle aspiration in the diagnosis of infected necrotizing pancreatitis. *Surgery*. 2014;155:442–448.

22. Papachristou GI, Takahashi N, Chahal P, et al. Peroral endoscopic drainage/debridement of walled-off pancreatic necrosis. *Ann Surg*. 2007; 245:943–951.

23. Seifert H, Biermer M, Schmitt W, et al. Transluminal endoscopic necrosectomy after acute pancreatitis: a multicentre study with long-term follow-up (the GEPARD study). *Gut*. 2009;58:1260–1266.

24. Rodriguez JR, Razo AO, Targarona J, et al. Debridement and closed packing for sterile or infected necrotizing pancreatitis: insights into indications and outcomes in 167 patients. *Ann Surg*. 2008; 247:294–299.

25. van Brunschot S, Hollemans RA, Bakker OJ, et al. Minimally invasive and endoscopic versus open necrosectomy for necrotising pancreatitis: a pooled analysis of individual data for 1980 patients. *Gut*. 2018;67:697–706.

26. Arvanitakis M, Dumonceau JM, Albert J, et al. Endoscopic management of acute necrotizing pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines. *Endoscopy*. 2018;50:524–546.

27. Johnson CD, Abu-Hilal M. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. *Gut*. 2004;53: 1340–1344.

28. Blum T, Maisonneuve P, Lowenfels AB, et al. Fatal outcome in acute pancreatitis: its occurrence and early prediction. *Pancreatology*. 2001; 1:237–241.