ETD of WON with more than 40% solid debris is associated with increased complications as well as frequent requirement of direct endoscopic necrosectomy. (4) We have previously reported that ANC in early phase of illness can be safely and effectively treated with initial PCD followed by ETD when it gets walled off. (5)

ETD upfront in early phase of illness when the ANC is not walled off is associated with significant concerns. In absence of walled off collection ETD is associated with risk of pneumoperitoneum or pneumoretroperitoneum and consequent infective complications. It would be interesting to know the frequency of this complication in current study especially as 45% patients had ascites and 35% had no or partial wall formation. Also, majority of patients in early phase of illness have an associated organ failure with respiratory failure being commonest, as was in the current study also. ETD in patients with acute lung injury is difficult and usually requires anaesthesia support. It would also be interesting to know the sedation/anaesthesia used for ETD in both groups.

The stents used by authors ranged from multiple plastic stents to fully covered oesophageal/biliary metallic stents to lumen apposing metal stents. (1) As metal stents have a wider lumen leading on to better drainage compared to plastic stents, it would be interesting to know the differences in outcome, especially in early phase, between various stents. ANC are heterogeneous group of collections varying in their solid necrotic content and this impacts outcome of drainage. Therefore, it would also be interesting to know proportion of solid necrotic content as well as baseline extent of pancreatic necrosis/computed tomography severity index (CTSI) in both groups. For these reasons, additional prospective large sample size studies comparing ETD upfront with current standard of care of initial PCD followed by on demand necrosectomy in early phase are needed.

CONFLICTS OF INTEREST

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Response to Singh et al. and Rana et al.

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We would like thank Singh and Mian (1) for their comments. We agree that addressing the assessment of baseline severity of illness and comorbidity variables is extremely important. As shown in Table 3 (2), 171 of 193 (89%) patients were referred from other facilities. Our referral-based practice makes determining initial severity of illness very difficult to reliably determine, even using simple severity measures such as BISAP and Ranson, because we often cannot access sufficient records and data. Although we have these data readily available for patients within our healthcare system, the lack of information on many referred patients led us to not report initial severity. We agree with the authors that a detailed assessment of predictors of mortality will be extremely valuable, and is a focus of our ongoing analysis of the cases. In our database, there were only 15 cases of mortality, which are too few adverse outcomes to allow performance of meaningful multivariate regression analysis. Such an analysis would require a significantly larger dataset, which should be the focus of future multicenter collaborative studies.

We agree with Rana and Gupta (3) that the concern regarding the risk of pneumoperitoneum and retroperitoneal leakage has been one of the major factors arguing against early endoscopic transmural drainage; however, our data did not demonstrate a higher risk. As we reported, only 7 cases of perforation occurred in the entire population of 193 patients who required intervention. Interestingly, all 7 of these were in the delayed intervention group, with no cases of peritoneal or retroperitoneal perforation in the early intervention cohort. It is our institutional practice that all cases of endoscopic drainage of necrosis or pseudocysts are performed under general anesthesia to reduce the risk of pulmonary aspiration. As such, there was no increased utilization of anesthesia support in the early intervention group. We did not report data on percent solid necrosis because this variable is often markedly underestimated by computed tomography (CT) imaging, and only a minority of our cases had previous MRI or preintervention ultrasound. We chose to report CT findings using the CT scoring system used by the Dutch Pancreatitis Study Group because we felt that the studies performed *via* that group would be the most useful comparison with our current data (4).

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Screening for Gastric Cancer

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The study by Kaji et al. (1) reports that in Japan, endoscopy and histological examination of gastric biopsies can alone predict the risk of gastric cancer. These procedures are both invasive and costly, albeit necessary to prevent this deadly tumor. It is not known whether the same strategy would be cost effective in countries with far lower prevalence of this malignancy, as it is the case in the United States, where it ranks 14th as the cause of death for cancer and 8th in the United Kingdom and France (2). This difference might stem from highly different circulation in different regions of *Helicobacter pylori* strains harboring the pathogenicity island. This is a chromosomal segment that encompasses genes involved in virulence, including cytotoxin-associated gene A (*cagA*) that codes for the CagA protein, which is a proven carcinogen (3). The C-terminal variable region of *cagA* is polymorphic in the sequence of nucleotides flanking the regions encoding the EPIYA repeats. In Asian countries, *cagA* mostly encodes CagA proteins that can be defined as hypercarcinogenic because they are the most efficient in binding SHP-2 with consequent disturbance of various cell functions, which eventually can lead to cancer. These strains are infrequent in Europe. Here, type III (or incomplete) intestinal metaplasia poses a 4.58 times increased risk of stomach cancer compared with type I (4); however, the staining for type III metaplasia is potentially carcinogenic for the personnel. Local epidemiology might determine which test has to be implemented to prevent gastric neoplasia. In Turin, Italy, 18% of the general population was found to be infected by CagA-positive strains of *H. pylori*. Because in the same area 2.3% of men died of gastric cancer before age 74 years (5), we estimate that 1 in 8 men and 1 in 25 women infected by a CagA-positive strain of *H. pylori* will die of this malignancy before that age (5). In our setting, therefore, it would be more cost effective to test for antibodies against CagA and to treat the individuals who test positive.

CONFLICTS OF INTEREST

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Ideal Screening for Gastric Cancer Might Vary Across Different Regions Worldwide

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As stated by Professor Ponzetto, the incidence rate of gastric cancer markedly varies across different countries. Approximately half of the incidence of gastric cancer has been reported in East Asian countries, including Japan, and the mortality rate associated with this cancer is higher in the East Asian region than in other regions of the world. This is attributable to the East Asian cytotoxin-associated gene A (CagA) exhibited by *Helicobacter pylori* (HP) in East Asia; this gene is more pro-oncogenic than the Western CagA (1). The annual number of deaths from gastric cancer in Japan is more than 40,000, with this cancer being the second and fourth leading cause of death among all cancers in men and women, respectively (2). Early diagnosis and treatment are crucial in reducing mortality; therefore, population-based gastric cancer screening has been conducted throughout Japan since the 1960s; it was primarily performed through radiographic screening in the beginning. This screening program has played a vital role in reducing mortality. Recently, endoscopic screening has also been introduced in some municipalities, including Kanazawa city. In 2017, the Japanese Society of Gastrointestinal Cancer Screening approved endoscopic examination for population-based gastric cancer screening and recommended that the screening should be performed every 2 years in all individuals (3). In the abovementioned background, we showed that risk stratification is possible through endoscopic examination itself; therefore, the next examination should be individually set according to the risk of each case, which can be determined