pancreatitis (1). The article astutely detects the outcomes of early step-up interventions in the management of necrotizing pancreatitis.

We commend the authors for their study, which is likely the first study to assess the safety and impact of early interventions in acute necrotizing pancreatitis. Its robustness and reassuring results will pave the way for further large-scale studies evaluating the appropriate timings for interventions in patients with acute necrotizing pancreatitis, especially patients not responding to conservative management. We would like to bring forth some points, which if answered will increase the understanding of the study population and enable widespread reproducibility of the study.

Though patients undergoing early interventions ($n = 76$) had similar characteristics to patients undergoing late interventions ($n = 117$), were there differences in the baseline co-morbidities between the two groups? Also was any risk stratification done at the time of initial presentation on the basis of either presence of systemic inflammatory response syndrome (SIRS), Ranson score, or APACHE II? These parameters are strongly correlated with an increased risk of mortality (2, 3). This stratification may be of crucial importance in identifying subgroups that may require early interventions.

As most of the patients received early interventions due to infections (90.8%), source reduction was the most important reason for the dramatic clinical response seen. This is similar to studies supporting the role of early source control in intra-abdominal sepsis (4). However, the patients who had deteriorated despite the early interventions as witnessed by increased length of stay in the intensive care (median 2.5 days vs 0 days, $p < 0.001$), higher need for necrosectomy (7 vs 1%, $p = 0.04$) and higher mortality rates (13.2 vs 4.3%, $p = 0.02$) should have been further evaluated. The reasons for mortality are not reported by the authors. We suggest performing a multivariate regression analysis to compare the patients who had a poor outcome despite the intervention across both the groups. This will help elucidate the variables that portend a poorer outcome even with the interventions.

This is an observational study with retrospective analysis of results. To provide further credence to the findings, it is critical to describe any other management differences between the two groups. This should include the initial management of pancreatitis, type of antibiotics used, early management of sepsis, and the time difference between the failed interventions to repeat interventions.

Overall we strongly feel this study addresses a very important knowledge gap (5). With an enhanced understanding of the parameters highlighted above, its findings can be externally validated through prospective studies in the future. This will add to the present armamentarium of management options for patients with acute necrotizing pancreatitis who are not responding or are worsening with conservative management.

CONFLICTS OF INTEREST

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Specific author contributions: Both of the authors were involved in conceptualizing the article. Achintya Dinesh Singh, MBBS, MD wrote the first draft of the manuscript. Both the authors finalized the manuscript.

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Endoscopic Transluminal Drainage in the Early Phase of Acute Necrotising Pancreatitis

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We read with keen interest the study by Trikudanathan et al. in a recent issue of American Journal of Gastroenterology and congratulate the authors for an elegantly conducted study that has expanded the indications for endoscopic intervention in ANP. Patients with symptomatic acute necrotic collections (ANC) in 2nd to 4th week of illness are a therapeutic challenge. This difficulty arises because of following reasons:

a. The collections at this stage of illness are usually not walled off.
b. These collections usually have a predominantly solid necrotic component that is poorly demarcated from viable tissue.

Surgical debridement of ANC in early (<4 weeks) phase of illness is associated with increased complications. (2) Therefore, the current treatment approach is to delay necrosectomy by giving antibiotics and/or percutaneous drainage (PCD). This step up approach of PCD followed by on demand necrosectomy in later phase of illness when the ANC become organized and demarcated is the current standard of care. (3)

Endoscopic transluminal drainage (ETD) of walled off necrosis (WON) has been shown to be safe and effective and this is because the necrotic collection at delayed stage (>4 weeks after onset of illness) becomes walled off with predominance of liquid component. (4)

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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