Can we now recommend hydrogen peroxide for pancreatic necrosectomy? Time for controlled data

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Endoscopic ultrasound (EUS)-based transmural drainage has emerged as a first-line intervention for pancreatic walled-off necrosis (WON), either as solo therapy or as part of a minimally invasive step-up approach including percutaneous drainage and video assisted retroperitoneal debridement. In contrast to pancreatic pseudocysts, for which resolution is expected following transmural drainage and stent placement, WON represents a distinct clinical entity often requiring additional method(s) of endoscopic intervention including endoscopic transmural retroperitoneal necrosectomy.

Technical aspects of EUS-guided intervention have evolved from off-label use of endoscopic retrograde cholangiopancreatography accessories to dedicated drainage devices, specifically lumen apposing metal stents (LAMS). Some of these devices allow access to WON using an electrocautery-enhanced delivery catheter, followed by deployment of a LAMS with a luminal diameter sufficient to both provide robust drainage and serve as an entry port for endoscopic necrosectomy. Multicenter retrospective data have demonstrated high rates of both technical and clinical success following endoscopic therapy of WON with LAMS, with an acceptable adverse event rate and a low requirement for additional non-endoscopic interventions [1].

Yet even LAMS are not a panacea, as they can be subject to luminal occlusion and requirement for endoscopic re-intervention, and numerous questions still abound regarding optimal technical aspects of endoscopic management of WON. Should endoscopic necrosectomy be performed during the index procedure or deferred to a second-stage procedure following stent placement and tract maturation? Is a single transmural drainage site sufficient or should multiport drainage be considered? When should a nasocystic tube be placed to allow for irrigation of the necrotic cavity? What is the role of either endogenous (gastric acid) or exogenous chemical debridement of the cavity?

The last question is the subject of the study presented in this issue of *Endoscopy International Open* by Bansal et al, who report the results of a prospective open-label study. Study subjects underwent EUS-guided drainage of WON with placement of a fully covered self-expanding metal stent, followed by step-up therapy including endoscopic necrosectomy using hydrogen peroxide [2].

Use of hydrogen peroxide as an adjunct to endoscopic necrosectomy has been previously described. Siddiqui et al reported a case series of 14 patients who underwent EUS-guided drainage and necrosectomy, several of whom required no further debridement following lavage with 100 cc to 500 cc of 3 % hydrogen peroxide at 1:5 – 1:10 dilution [3]. And in the previously referenced multicenter retrospective study of endoscopic therapy of WON using LAMS, 31 % (38/124) of patients were treated with hydrogen peroxide [1].

In the current study by Bansal et al, luminal stent occlusion by necrotic debris was relieved using a snare or forceps—otherwise by protocol all further necrosectomy was performed via hydrogen peroxide lavage, and no intracavitary mechanical debridement was permitted. Among 64 patients included in the analysis, technical success was reported in 100 % and clinical success was reported in 90.6 %. Mean number of necrosectomy sessions was 3.2 (range 1 – 5). Five patients required per-

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cutaneous catheter drainage and 1 patient required surgical intervention.

Endoscopists who perform endoscopic necrosectomy will attest that mechanical debridement of a necrotic collection can be a laborious endeavor employing a range of endoscopic accessories not designed or optimally suited for this purpose. A chemical lavage technique that facilitates (or eliminates) mechanical debridement might offer a welcome alternative. But are the data presented by Bansal et al sufficient to justify widespread adoption of hydrogen peroxide for this purpose?

One of the limitations of open-label studies, without blinding or randomization, is that at some level study entry and study interventions are subjective and at the discretion of the clinician-investigator. This study included patients "who were amenable to endoscopic drainage." How many patients were screened and felt not amenable to endoscopic drainage, either due to anatomic or other considerations, and are the data failing to capture the number of patients who require percutaneous or surgical therapy and hence overestimating the true clinical success rate of endoscopic intervention? The criteria which prompted endoscopic reintervention at 48 hours are not rigorously detailed, and conceivably may have been based on clinical gestalt rather than clearly defined objective measures. And importantly, no multiple variable analysis is reported to offer insight into potential confounding variables associated with clinical outcomes.

It is worth noting that nearly one-third (28%) of patients achieved the primary study endpoint with stent placement alone, without requirement for further necrosectomy. The authors report that patients with more than 40% solid debris on EUS exam were more likely to require necrosectomy. At least 1 prior prospective study of LAMS for pancreatic fluid collection drainage utilized a cut-off of greater than 30% solid content as grounds for study exclusion [4]. Whether the proportion of solid necrotic debris may help triage patients to drainage/stent alone vs drainage/stent plus necrosectomy early in the endoscopic management of WON will require future investigation.

A full understanding of the safety considerations of hydrogen peroxide necrosectomy will require more extensive published experience. Three patients in the current study experienced life-threatening bleeding events, none of which were directly attributed to hydrogen peroxide lavage. While not specifically described to date following use of hydrogen peroxide for pancreatic necrosectomy, numerous reports exist regarding embolic events following hydrogen peroxide use in neurosurgical procedures [5 – 7], fistula interrogation [8, 9], and soft tissue wound debridement [10, 11].

The authors are correct to conclude that prospective randomized studies are needed to validate this technique employing step-up therapy with hydrogen peroxide irrigation. Endoscopic intervention for pancreatic necrosis is a rapidly-evolving, exciting area for interventional endoscopists. Most of the supporting data originate from uncontrolled retrospective or prospective studies – with, a skeptic might argue, "cherry-picked" patients and no comparative arms. Expert opinion abounds, and some inherent variability in technique may be justifiable on this basis or as mandated by specific patient characteristics on a case-by-case basis. But it is high time for rigorous controlled data which will enable us to take the step from stating this is how *we* perform necrosectomy, to this is how *we all should* perform necrosectomy.

Competing interests

Dr. Yachimski is a consultant for Boston Scientific.

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