

New Technology, New Complications: Pancreatitis Complicating Double-Balloon Enteroscopy

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Double-balloon enteroscopy (DBE) is a novel endoscopic technique that allows for visualization of the entire small bowel and has the utility to perform biopsies and treat suitable lesions. Complications common to any endoscopic procedure such as bleeding or perforation can occur with this technique and should be discussed with the patient. We report a case of acute pancreatitis following DBE and review the literature regarding this rare complication.

Case Report

A 59-year-old woman with a suspected small-bowel polyp was referred to our institution for DBE. She had initially presented with an episode of melena without hemodynamic instability and without a drop in her hemoglobin level. Her work-up included esophagogastroduodenoscopy (EGD), which was unremarkable except for hiatal hernia, and colonoscopy, which revealed only sigmoid diverticula. Video capsule endoscopy (CE) from the referring medical center reportedly showed an ulcerated polyp somewhere between the jejunum and ileum. Our review of the CE confirmed the presence of an ulcerated small-bowel polyp; however, a computed tomographic (CT) enterography of the small bowel did not demonstrate the presence of a polyp or any other cause for her melena. An antegrade DBE (Fujinon) was performed under general anesthesia. A total of 100 push-pull cycles were completed, and the depth of insertion was estimated to be approximately 600 cm. India ink was injected into the submucosa to mark the distal limit of insertion, so that this point could be identified during a future retrograde DBE. The polyp was not identified, and the enteroscope

was carefully withdrawn, with continuous visualization of the mucosa. Mucosal erythema secondary to scope trauma was noted on the medial wall of the second portion of the duodenum. The entire procedure lasted 200 minutes. The patient made an uneventful recovery from anesthesia.

One hour after the procedure, the patient complained of epigastric pain and nausea. Upon examination, her abdomen was distended but without signs of peritoneal distress. A flat and upright radiograph of the abdomen demonstrated distended gas-filled loops of bowel without any free air suggestive of a perforated bowel. The patient was admitted for pain control and observation. The next morning, her pain had not improved, and a CT scan of the abdomen demonstrated thickening of the tail of the pancreas, with moderate surrounding edema and minimal fluid extending along the left pararenal space into the left paracolic gutter. Laboratory evaluations confirmed biochemical evidence of pancreatitis with a serum amylase of 851 U/L (ref., 26–102) and lipase of 828 U/L (ref., 7–160). The patient had no previous history of pancreatitis or any risk factors for the development of acute pancreatitis. Over the next 7 days, she made a slow recovery, with the return of her serum amylase to normal levels. After careful review of her history and the risk factors involved, it was decided that her pancreatitis was likely the result of the DBE.

Discussion

DBE, as first described by Yamamoto and colleagues in 2001,¹ allows direct visualization for diagnosis and therapeutic intervention at any site throughout the entire small bowel. The technique for advancement uses a push-and-pull method, with inflation and deflation of the balloons and telescoping of the intestine onto the overtube. This plication of the small bowel over the overtube allows the enteroscope to be inserted much further than the

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length of the enteroscope itself. DBE can be performed in an antegrade or retrograde fashion. The technical details of the technique have been previously published.² Yamamoto and associates reported visualization of the entire small bowel in 86% of cases,³ either by antegrade approach alone or by a combination of antegrade and retrograde approaches.

The success rate of DBE in diagnosing and treating small-bowel disease is promising, especially in cases of obscure gastrointestinal bleeding. Early studies have reported the diagnostic yield of DBE for obscure gastrointestinal bleeding to be in the range of 60–75%.^{4,7} Hadithi and colleagues compared DBE with CE prospectively in patients with obscure gastrointestinal bleeding.⁷ In 60% of patients, the bleeding source was found by DBE compared with 80% by CE ($P=.01$). Therapeutic intervention during DBE was possible in 51% of cases. Manner and colleagues reported three cases of Meckel diverticula diagnosed by DBE.⁸

DBE also has an expanding role beyond the evaluation of gastrointestinal bleeding. Oshitani and colleagues reported the diagnosis of deep small-bowel Crohn's disease by DBE, in which DBE was superior to radiologic studies in detecting aphthous ulcers and erosions.⁹ In some reports, DBE was able to detect small-bowel pathology missed on CE, including cases of small-bowel stromal tumors and adenocarcinoma.¹⁰ Small-bowel diaphragm disease secondary to nonsteroidal anti-inflammatory drug use has also been diagnosed and treated by DBE.¹¹

Although complications may become apparent only after substantial clinical experience, as with any new drug or therapeutic procedure, DBE appears to be a remarkably safe procedure. In 178 cases, Yamamoto and coworkers reported only two complications: multiple perforations in a patient with intestinal lymphoma and fever, and abdominal pain in a patient with Crohn's disease.³ Although no major complications of DBE were reported in a European multicenter study of 100 patients, minor complications were reported in 12% of patients, including abdominal pain in 9% of patients, sore throat in 1% of patients, brief fever in 1% of patients, and vomiting in 1% of patients.¹² In 275 cases, Heine and colleagues reported self-limited abdominal pain (less than 24 hours) in 20% of cases after DBE.⁴

Honda and colleagues reported the first case of acute pancreatitis following antegrade DBE for obscure gastrointestinal bleeding.¹³ The patient complained of abdominal pain immediately following the procedure and was found to have a serum amylase level of 702 U/L (ref., 50–159 U/L). A CT scan confirmed pancreatic and peripancreatic inflammation. The pancreatitis was managed medically, and the patient completely recovered. Groenen and colleagues reported two cases of acute pancreatitis following

DBE, both confirmed biochemically (via elevated amylase) and by CT scan.¹⁴ One patient had mild pancreatitis, but the other patient had severe pancreatitis with necrosis in the tail of the pancreas. Both cases were managed with supportive care, and both patients made a full recovery. Heine and associates also reported three cases of pancreatitis after antegrade DBE.⁴

In another study, Honda and colleagues measured serum amylase prior to and 3 hours after DBE and demonstrated hyperamylasemia in 6 of 13 patients (46.2%).¹⁵ Only 1 patient had symptoms suggestive of acute pancreatitis and was confirmed to have pancreatic inflammation on CT scan. The average procedure time in patients with elevated pancreatic amylase was not significantly longer than in patients without hyperamylasemia. Abdominal CT scans were not performed in patients with hyperamylasemia without abdominal pain.

Although pancreatitis is a well-known complication of endoscopic retrograde cholangiopancreatography (ERCP), there have also been case reports of pancreatitis following routine EGD,^{16,17} and even after colonoscopy.¹⁸ Blackwood and colleagues detected asymptomatic hyperamylasuria in 6.6% of patients undergoing gastrointestinal endoscopy.¹⁹

Case reports of pancreatitis following routine endoscopy as well as DBE suggest that ampullary cannulation is not required to develop acute pancreatitis. All reported cases have occurred with antegrade DBE, but case reports of pancreatitis following colonoscopy suggest that it could also result from the retrograde approach.

The pathogenesis of pancreatitis following DBE has been considered. There is certainly potential for pancreatic trauma during the procedure. The repetitive push-pull motion of the overtube may irritate the ampulla. Alternatively, during the foreshortening or plication of the small bowel over the overtube, the pancreas may be traumatized, as it is attached to the fixed duodenum. During retrograde approach, there could be direct pressure on the pancreas in the area of the transverse colon either from the endoscope or from hyperinflation.¹³ Groenen and associates questioned whether the pathogenesis may be pancreatic ductal hypertension¹⁴; during antegrade DBE, the situation may arise in which one balloon is inflated beyond the ampulla and the other in the duodenal bulb. A closed segment of duodenal hypertension may exert direct pressure on the pancreas or in the pancreatic duct. A long-standing theory of the pathogenesis of acute pancreatitis is that an increase in duodenal pressure may cause duodenal reflux into the pancreatic duct.²⁰

Our patient had a prolonged procedure, possibly contributing to the risk of pancreatitis; however, procedural length has not been recognized as a risk factor in other reported cases.¹³⁻¹⁵ We did notice mucosal trauma

on the medial wall of the duodenum upon withdrawing the enteroscope, suggesting that there may have been direct trauma to the ampulla or pancreas.

Conclusion

DBE may cause clinically significant pancreatitis in 1% of patients.⁴ The finding of asymptomatic serum amylase elevations in 38% of cases following antegrade DBE is of note and may suggest that the procedure frequently causes subclinical pancreatitis.¹⁵

This case highlights the risk of acute pancreatitis following DBE. Patients should be informed of this risk prior to the procedure. When the goal of DBE is to reach a mid–small-bowel lesion, the case could be made for performing retrograde DBE first, as no cases of pancreatitis have been reported with this approach. The greater complexity of the retrograde approach probably outweighs the theoretical benefits, but this strategy may be considered in a patient with a history of pancreatitis, as we know from ERCP data that this predicts future postprocedural attacks.²¹ We do not recommend the routine measurement of serum amylase or lipase in patients with mild abdominal pain following DBE, as mild abdominal pain is reported in up to 20% of cases,⁴ and 38% of patients may have asymptomatic amylase elevation.¹⁵ In patients who develop severe or persistent abdominal pain following DBE, the endoscopist should consider the complication of pancreatitis and evaluate the patient accordingly.

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Review

Pancreatitis, a New Complication of Double-Balloon Enteroscopy

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Double-balloon enteroscopy (DBE) is a new endoscopic technique. With the advent of DBE, endoscopic diagnostic and treatment strategies for small intestinal diseases have changed dramatically. DBE enables visualization of the entire small bowel and allows interventional therapy in the small intestine. In combination with capsule endoscopy, DBE has the potential to become a standard of enteroscopy by replacing conventional push enteroscopy and intraoperative enteroscopy.¹⁻³

DBE was developed by Yamamoto and colleagues, and recently, a specialized system for the double-balloon method has been made commercially available (Fujinon).^{4,5} This system uses two types of endoscopes. The standard type for regular use is composed of a thin endoscope with an 8.5-mm diameter and a 200-cm working length (Fujinon EN-450 P5), a 145-cm soft overtube with an outer diameter of 12.2 mm, and a specially designed pump. A soft latex balloon attached at the tip of the endoscope can be inflated and deflated using the pump through an air channel in the endoscope. The soft overtube also has a latex balloon at its tip that can be inflated and deflated. The pressure in both balloons is monitored and regulated at 6 kPa. In addition to the standard endoscope, there is a therapeutic double-balloon endoscope (Fujinon EN-450 T5). This endoscope has a larger channel, which is 2.8 mm in diameter. The outer diameter of the endoscope is also larger (9.4 mm) to accommodate the larger channel.

In addition to direct observation and sampling, DBE allows for interventional therapy and can be performed either orally or anally. The use of push-pull cycles of an affected area with controlled movement of the endoscope

via an accessory channel enables interventions, including biopsies, hemostasis,⁶ balloon dilatation,⁷ stent placement,⁸ polypectomy,⁹ and endoscopic mucosal resections.¹⁰ Although both capsule endoscopy and DBE are remarkable innovations that enable access to the entire small bowel, a striking feature of DBE compared with capsule endoscopy is this capability of intervention.

As DBE is based on a new insertion technique using two balloons and a soft elastic overtube, endoscopists should pay attention to any data reported in the literature regarding unexpected complications. There have been several reports referring to complications associated with DBE, including abdominal pain, vomiting, fever, sore throat, and perforation. Specifically, reports in the literature have thus far noted the following complications associated with DBE: 1 case of perforation and 1 case of fever and abdominal pain in 178 procedures¹¹; fever, mucosal trauma, and neck pain in 248 procedures¹²; 20% of patients (N=275) experiencing abdominal pain and 3 cases of pancreatitis in 316 procedures¹³; cases of pneumonia, fever, nausea, abdominal pain, neck pain, trauma of the mucosa in 147 procedures¹⁴; 1 case of bleeding after polypectomy in 70 procedures¹⁵; 1 case of perforation in 50 procedures¹⁶; 1 case of perforation after diathermia in 75 procedures¹⁷; 3 cases of abdominal pain in 89 procedures¹⁸; 15% of patients (N=152) experiencing mucosal bleeding due to the balloon in 191 procedures¹⁹; and 3 cases of perforations, 2 cases of bleedings, and 1 case of enteritis in 635 procedures.²⁰

In the case reported by Decker and colleagues,²¹ a patient developed pancreatitis following DBE. The patient underwent antegrade DBE, and epigastric pain occurred 1 hour after the procedure. She was carefully observed, and abdominal computed tomography scan performed the next day exhibited thickening of the pancreatic tail along with surrounding edema and fluid extension. Biochemical data also confirmed elevated levels of serum amylase and lipase. The patient was treated conservatively and recovered uneventfully. There have been three previous reports of pancreatitis associated with antegrade DBE that include 6 patients, and all the patients were treated conservatively and recovered.^{13,22,23} Although pancreatic trauma is suggested during the procedure of DBE, the underlying mechanisms involved in the development of pancreatitis have not yet been clarified. Possible factors may include repeated stretching of the enteroscope, direct trauma to the ampulla by either balloon or overtube, or ischemic trauma during the long procedure; ductal hypertension following the increase in duodenal pressure could be another factor. There is no clear answer regarding the avoidance of pancreatitis after DBE. One possible tip would be to avoid forceful retraction during the withdrawal of the endoscope and overtube to minimize unnecessary force to the pancreas.

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