

# ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: John Baillie, MB ChB, FRCP

## Use of Prophylactic Pancreatic Stents for the Prevention of Post-ERCP Pancreatitis



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### **G&H** What are the risk factors for developing post-endoscopic retrograde cholangiopancreatography pancreatitis?

**MF** Both patient-related and procedure-related factors are strong influences on the potential for post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis and are probably additive or even synergistic. Independent patient-related risk factors include suspected sphincter of Oddi dysfunction, young age, and a history of post-ERCP pancreatitis. In these high-risk patients, especially those who have multiple risk factors, the likelihood of developing post-ERCP pancreatitis was as high as 20% before the widespread adoption of prophylactic pancreatic stents. In contrast, the reported rates of post-ERCP pancreatitis in mixed-risk patients have typically been approximately 5%. This observation clearly demonstrates that ERCP should not be performed in patients with a marginal indication or benefit, particularly if performed by a provider with limited expertise.

Procedural factors for developing post-ERCP pancreatitis include any pancreatic manipulation, intentional or inadvertent. Pancreatic duct (PD) instrumentation, PD injection, PD sphincterotomy, difficult biliary cannulation, precut sphincterotomy, balloon dilation of the intact sphincter, and, recently, placement of metal biliary stents have all been shown to increase the risk of post-ERCP pancreatitis. Several studies have recently shown that deep pancreatic guidewire passage alone (independent of contrast medium injection), especially if repeated, is in fact a major risk for post-ERCP pancreatitis unless it is followed by a pancreatic stent. Although the mere avoidance of PD manipulation or injection might seem appealing, it is often

not possible and, even if such avoidance is possible, it is not sufficient in high-risk patients. Therefore, good technique in biliary cannulation alone is not the answer, and clearly guidewire cannulation without contrast injection will not prevent post-ERCP pancreatitis if the PD is instrumented with the wire in high-risk patients, or repeatedly in any patient. My center and another major center have now seen at least 6 severe PD perforations from attempted biliary wire cannulations with inadvertent PD wire passage performed at outside facilities.

### **G&H** How do PD stents prevent the risk and severity of post-ERCP pancreatitis?

**MF** We do not know exactly how PD stents prevent post-ERCP pancreatitis, although the mechanism probably involves preserving drainage of the gland and emptying it from reactive pancreatic enzymes. Regardless of the actual mechanism, the important point is that the stents do reduce the risk of post-ERCP pancreatitis. Pancreatic stent placement is the most rigorously studied prophylactic measure for the prevention of post-ERCP pancreatitis (Figures 1 and 2). This measure has been shown to decrease the risk of post-ERCP pancreatitis by 60% to 80% in patients both with high risk (in 12 studies) and those with low to mixed risk (in 2 studies). In the most recent meta-analysis, which was the first to include studies of lower-risk patients, PD stents were shown to reduce the risk of mild and moderate, as well as severe, post-ERCP pancreatitis.

PD stent placement is currently considered the standard of care in high-risk cases—as is the use of rectal non-steroidal anti-inflammatory drugs (NSAIDs)—and is also



**Figure 1.** A pancreatic stent placed prior to a fully covered self-expanding metallic biliary stent for management of benign papillary stenosis that was treated with a deep sphincterotomy.

increasingly being performed even in routine low-risk to medium-risk ERCP.

**G&H** Are rectal NSAIDs given at the end of the procedure equally effective?

**MF** Rectal NSAIDs have been shown to reduce the risk of post-ERCP pancreatitis by approximately 50% to 60% in at least 6 randomized controlled trials, and the efficacy of these agents has been confirmed by numerous meta-analyses. Direct comparison of NSAIDs and PD stents is difficult and thus far has only consisted of neural network studies, which is somewhat like comparing apples to oranges and concluding that one is better than the other.

It is important to keep in mind that NSAIDs are not a panacea and will not likely replace PD stents in most circumstances. Further study is underway at a number of centers.

**G&H** Should NSAIDs be used in combination with prophylactic PD stents?

**MF** For now, high-risk patients should undergo both PD stenting (if possible) and rectal NSAID administration (if not contraindicated). Even with this combined approach, the largest study conducted thus far still showed a 9% rate of post-ERCP pancreatitis, which is not ideal. Therefore, there is still room for improvement.

Even though an intervention may work, unless it is perfect, a multifaceted approach is needed. To obtain a satisfactory outcome, it is necessary to pay attention to the “4 Ps” of post-ERCP pancreatitis prevention: patient-



**Figure 2.** A pancreatic stent placed during difficult access to the bile duct due to a malignant hilar biliary obstruction.

related risk factors, procedure-related risk factors, pancreatic stents, and pharmacoprophylaxis.

**G&H** Which of the many PD stent sizes and designs are most effective for prophylaxis of post-ERCP pancreatitis?

**MF** Data and opinions regarding PD stent choices vary widely. In my opinion, soft material (4- or 5-French [Fr]) stents are the best and safest. My colleagues and I principally use 2 types of prophylactic stents depending on the circumstances: a 4-Fr, 11-cm, soft, unflanged, single-pigtail stent (Freeman stent, Hobbs Medical) if a guide-wire can easily be passed all the way to the tail; or a 5-Fr, double-inner and double-outer flanged, ultrasoft material stent (Geenen Sof-Flex stent, Cook Endoscopy) if the wire does not pass beyond the genu. For very high-risk patients, such as those who have undergone an ampullectomy, we often place dual side-by-side stents, one of each of the aforementioned types, as long as there is an adequate PD diameter to accommodate both stents.

**G&H** How significant of an issue is early migration of a stent into the bowel, and can this problem be reduced?

**MF** Early outward migration is a significant problem, particularly as it can lead to delayed-onset post-ERCP pancreatitis. A randomized trial conducted years ago, but published only recently, in *Gastrointestinal Endoscopy* showed that immediate removal of a PD stent afforded no protection compared with no PD stent placement at all in patients undergoing precut sphincterotomy. In our recent salvage PD

stent study, my colleagues and I showed that delayed-onset post-ERCP pancreatitis occurred frequently in patients with PD stents that migrated out in the first day or so.

One way to reduce this problem is to use the aforementioned stents—either very long and unflanged small-caliber 3- or 4-Fr (9-11 cm) stents, or short, soft, double- or single-inner flanged, straight 4- or 5-Fr stents. We have found virtually no premature outward migration of the latter type of stents, but approximately 90% spontaneous passage at 3 weeks.

### G&H Are there any other significant limitations or disadvantages of using prophylactic PD stents?

**MF** Limitations and disadvantages of PD stent placement include unsuccessful stent placement (eg, the inability to advance a wire into the PD or the inability to place a stent after wire placement, resulting in an increased risk of post-ERCP pancreatitis), inadvertent duct injury during stent placement, long-term stent-related duct/gland injury, and the need for follow-up after stent placement. A significant problem with pancreatic stents is variable expertise and familiarity with their placement. Therefore, PD stent placement alone may not be the sole solution to preventing post-ERCP pancreatitis, especially in less experienced hands.

### G&H Could you describe the design and principal findings of your recent study on salvage PD stenting?

**MF** In this study of approximately 3000 ERCPs performed over a several year interval, 14 patients in whom severe post-ERCP pancreatitis was predicted (systemic inflammatory response syndrome [SIRS] and Bedside Index for Severity of Pancreatitis score of  $\geq 3$ ) underwent immediate repeat ERCP to place a PD stent if none had been placed or to replace a PD stent that had outwardly migrated prematurely. There was prompt and dramatic resolution of post-ERCP pancreatitis by pain score, amylase/lipase levels, and resolution of SIRS.

### G&H What are your recommendations to ERCP endoscopists based on this study?

**MF** This was a hypothesis-generating study, more for proof of principle than for determining recommendations for routine practice. However, experts at placing PD stents may consider doing early salvage PD stenting in special circumstances, such as after early onset of predicted severe post-ERCP pancreatitis when no PD stent has been placed or when the stent has migrated outward within the first day or two. An internationally renowned expert recently told me of helplessly watching a patient develop severe post-ERCP pancreatitis over 2 weeks following an ampullectomy, in which the PD stent fell out by the morning after the procedure. I

think that it would have been reasonable to have gone back immediately and replaced the stent. The expert endoscopist told me that had he seen the preliminary data from our salvage study that he would have considered urgently replacing the PD stent, and he would consider doing that maneuver next time he encountered such a scenario. However, caution should be exercised by less experienced endoscopists, who might do more damage than good by trying and failing to place a PD stent, or in the setting of mild to moderate post-ERCP pancreatitis, in which case no action is necessary.

In addition, it is important to keep in mind that PD stents are not an extension of biliary stents, which are often inserted after fairly forceful jamming of an 035 wire into the bile duct; such maneuvers in the PD can lead to serious injury, as previously outlined. In order to reliably and safely place pancreatic stents, endoscopists need to learn to use small guidewires and avoid side branches, as well as learn to reliably negotiate small and tortuous ducts. Endoscopists also need to have access to a variety of PD stents for different circumstances. There are a number of videos available to study techniques of PD stent placement that may be helpful.

### G&H What are the next steps in research?

**MF** Three letters to the editor were sent to *Endoscopy* about our salvage study, all asking for a randomized controlled trial. My coauthors and I agree in principle, although it would be difficult to find enough patients with predicted severe post-ERCP pancreatitis at advanced centers (as this severity of complication is now very rare) as well as an adequate sample size and funding.

The other major study that is needed, and currently underway, is a comparison of NSAIDs alone vs NSAIDs plus pancreatic stents. Results of this study will be very interesting but highly dependent on the participants' expertise at placing PD stents in difficult circumstances.

*Dr Freeman has consulted for Boston Scientific, Xlumena Corporation, and Cook Endoscopy, and he has been an unpaid consultant for Hobbs Medical regarding the Freeman pancreatic stent.*

### Suggested Reading

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