Why do pancreatic stents become occluded?

Endoscopic drainage procedures of the main pancreatic duct (MPD) are increasingly performed for management of pain in severe chronic pancreatitis. This treatment is widely accepted as a first-line management that may avoid the need for surgery in the majority of the cases. However, when a stricture of the MPD is present, long-term management is associated with the need for stent exchanges, because pancreatic stents always become occluded after a few months, resulting in a recurrence of symptoms. Although pancreatic stent placement probably is not needed “life long” and the majority of stents can be removed without being replaced after a few years, the need for regular stent exchange during this period of time represents a significant source of morbidity. Therefore, having stents that would provide longer patency would be extremely useful for the management of these patients.

A better understanding of the mechanisms that lead to stent occlusion might allow for improving stent components and design to offer prolonged effective pancreatic drainage. It, however, is amazing to note that, despite biliary and pancreatic endoscopic drainages being performed for more than 20 years and the mechanism of their occlusion having been studied, no material that dramatically changes the duration of patency in this “low pressure” environment has become available. For palliation of malignant jaundice, the problem has been partially solved with the availability of self-expandable metal stents (SEMS) that render the task even more challenging for newly designed plastic stents which offer only slightly better results than the usual ones. SEMS, however, have been extremely disappointing when used in benign strictures.

Even if biliary and pancreatic stents are placed in a similar environment, at least on the duodenal side, the analysis presented by Farnbacher et al. further demonstrates that the mechanism of pancreatic stent occlusion differs from that of biliary stents. If adherence of bacteria and the formation of a biofilm that consists of these bacteria and their derived glycoproteins is a key early event that promotes biliary stent occlusion, the formation and the adherence of an organic matrix, predominantly of proteic origin, appears to be the major event, inducing pancreatic stent occlusion. Bacterial colonization and plant debris accumulation come later, predominantly at the duodenal side, as a marginal secondary event. This is important when seeking new materials potentially able to prevent stent occlusion. Hydrophilic coatings of ultrasmooth surfaces might be useful for both pancreatic and biliary stents, whereas policies based on treatment or stent impregnation with antibiotics (or even stents with antireflux valves) will probably not help to maintain patency of pancreatic stents. The relevance of this finding, however, is probably limited, because almost all antibiotic-based policies have been disappointing for preventing biliary stent occlusion, and it is clinically evident that pancreatic juice is a less favorable environment than bile for growth of bacteria.

The ideal pancreatic stent would be a hydrophilic, ultra-smooth and soft, large diameter stent without side holes.

The protein content of pancreatic-stent obstructing material is qualitatively similar in the 3 studies published so far. In this current issue of Gastrointestinal Endoscopy, Farnbacher et al. have been able to identify, by Western blot, two 66 and 46 KDA bands that correspond to albumin and its proteolytic fragments and a 14 KDA band identified by mass spectrometry as consisting almost exclusively of lithostatin. Albumin was consistently found as a major component of this protein matrix, and its presence, because it is not a component of pancreatic juice, probably illustrates the leakage of serum proteins. Placing a stent into the pancreas and through a pancreatic stricture induces a chronic inflammatory process responsible for this leakage of proteins. This propensity to develop an inflammatory reaction and secondary fibrosis in the presence of a foreign body is more pronounced in the pancreas than in the bile ducts and may take place even when the stents are placed in the absence of a tight stricture that had been previously dilated. Clinically, this ongoing inflammatory reaction may be illustrated by the fact that a pancreatic stricture is more difficult to “calibrate” than a biliary stricture by transient placement of stents. This is probably also important for the process of stent occlusion, because albumin discloses hydrophobic sites that may promote its adhesion to the stent surface and development of the protein matrix.
Lithostatin also was found consistently as a major component of the proteic material found inside occluded stents.\textsuperscript{5,7} It probably comes from the pancreatic juice but also can be derived from the surface of stones, of which lithostatin is a major component.\textsuperscript{9} It is tempting to speculate that extracorporeal shock wave lithotripsy (ESWL), by fragmenting the stones and exposing a larger surface, may increase the amount of lithostatin initially available for precipitation into the stents. In the same line, although they do not report about the use of ESWL in their patients, Farnbacher et al.\textsuperscript{5} describe the presence of visible calculi in a third of their stents, a feature often observed in our experience during the first stent placement period after ESWL and probably related to the migration of fragments from secondary ducts or the uncompleted endoscopic clearance after ESWL, before stent placement. A common observation in these patients is that the relapse of symptoms, because of stent occlusion occurs earlier, during the first stent-placement period than during the following ones.\textsuperscript{10}

The design of the stents apparently is also important. Although not confirmed in the current study, which was not designed for this purpose, larger stents have a prolonged patency compared with smaller ones.\textsuperscript{11} A larger amount of material was observed at the level of the proximal and the distal side holes and flaps,\textsuperscript{9} highly suggesting that surface irregularities promote adhesion and occlusion. This is important to note, because, for reasons that are unclear to me, there are still pancreatic stents with multiple side holes that are commercialized; the only utility of these side holes is to potentially shorten the duration of stent patency.

Which would be the ideal stent for pancreatic drainage? Apparently, an hydrophilic ultrasmooth stent without side holes, soft enough to prevent impaction and tissue damage, would deserve evaluation. It also should not be too expansive. Chronic pancreatitis is a rare disease with limited marketing potential; it, however, is unlikely that major development will be conducted by the industry and, if new materials and designs become available, the clinical evaluation will be under the responsibility of the clinicians.

Another way to decrease the clinical problem related to stent occlusion might be to reduce the duration of stent placement needed by placement of multiple large bore plastic stents for a limited period of time. Mutignani et al.\textsuperscript{12} reported encouraging results of this policy of aggressive calibration for a period of less than 1 year. Long-term results are awaited to know if this “calibration,” and, more importantly, the pain relief will be long lasting. Additional information we have from this multiple-stent-placement policy is that many patients present themselves at the time of stent removal with all the stents occluded and no pain relapse, maybe because pancreatic juice flow can still go through the space located between the plastic tubes. Interestingly, this space is rarely the site of accumulation of the typical creamy white material found in the stents, probably because the respective stents are in perpetual movement to each other, bringing another factor potentially delaying adherence of proteins.

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\textbf{REFERENCES}