Improved Stent Characteristics for Prophylaxis of Post-ERCP Pancreatitis

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Background & Aims: Pancreatic stenting is an effective method to prevent post–endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis in high-risk patients. This retrospective study evaluated the impact of modified stent characteristics on the rate of post-ERCP pancreatitis, spontaneous stent dislodgment, and stent-related sequelae.

Methods: A total of 2283 patients underwent 2447 ERCPs over a 6-year period with placement of 3–4F diameter, unflanged pancreatic stents. The indication for stenting was pancreatitis prophylaxis predominantly in suspected sphincter of Oddi dysfunction (SOD), pancreas divisum therapy, and precut sphincterotomy. An abdominal radiograph was obtained 10–14 days later to assess spontaneous stent passage. Post-ERCP pancreatitis was defined according to established criteria. A total of 479 patients underwent repeat ERCPs after an initial ERCP with pancreatic stent placement. The prestenting pancreatogram was then compared with follow-up studies.

Results: The pancreatitis rate with 3F, 4F, 5F, and 6F stents was 7.5%, 10.6%, 9.8%, and 14.6%, respectively (3F vs. 4F, 5F, 6F: P = 0.047). Spontaneous stent dislodgment was 86%, 73%, 67%, and 65%, respectively (3F vs. 4F, 5F, 6F: P < 0.0001). The frequency of ductal changes was 24% in patients with 3–4F stents compared with 80% with 5-6F stents. Ductal perforation from the stents occurred in 3 patients (0.1%). Conclusions: Small diameter (3–4F), unflanged pancreatic stents are more effective than the traditionally used stents (5–6F) in preventing post-ERCP pancreatitis. Stent-induced ductal changes and the need for endoscopic removal are also significantly less with 3–4F stents. The 3F stent appears to be superior in all aspects studied. Additional studies are needed to define the ideal method to eliminate post-ERCP pancreatitis.

Materials and Methods

Small-diameter 3F and 4F polyethylene pancreatic stents with a single duodenal pigtail (Wilson-Cook, Winston-
Salem, NC) became commercially available in the 1990s. From January 1997 to October 2002, 7383 consecutive patients underwent 11,178 ERCPs at our institution. Of those, 2283 (31%) patients underwent 2447 ERCPs with placement of a 3F or 4F diameter, 4–12 cm long (median length 8 cm, intraductal length 3–8 cm), three-quarter duodenal pigtail polyethylene pancreatic duct stent at the discretion of the endoscopist. The flange of the 4F stent was always removed. The 3F stent had no internal flange (Figure 1). Indications for stenting were predominantly for pancreatitis prophylaxis in manometrically documented or suspected SOD dysfunction, pancreas divisum therapy (minor papilla sphincterotomy), and as a guide for needle-knife precut papillotomy or pancreatic sphincterotomy (Table 1). The 3F and 4F stents were placed predominantly over a 0.018-in diameter guidewire (Roadrunner wire; Wilson-Cook). When a 0.025-in diameter guide wire was used, a 4F diameter stent was necessary to accommodate the larger guide wire. Patients only were observed overnight in the hospital if there was a clinical suspicion of post-ERCP pancreatitis, other complications, or if they were in the hospital for ongoing treatment. A plain abdominal radiograph (kidney ureters bladder [KUB]) was obtained for all patients 10–14 days after stent placement to ensure spontaneous passage of the stent. If the stent did not exit the pancreas, endoscopic removal was undertaken. Follow-up pancreatography at the time of stent removal was performed at the discretion of the endoscopist.

The prospectively recorded ERCP database from January 1997 to October 2002 was reviewed regarding the frequency and severity of post-ERCP pancreatitis in patients who underwent prophylactic 3F or 4F stent placement, and was compared with patients who had 5F or 6F stents. The diagnosis of post-ERCP pancreatitis and the grading of its severity were based on established criteria. The occurrence of post-ERCP pancreatitis and its severity was correlated with the prevalence of SOD in the same population group.

Follow-up pancreatograms were available for review in 479 patients who previously had either a 3F or 4F stent placed. The indications for repeat study were for stent removal if it failed to dislodge spontaneously after 2 weeks of placement (mean = 24 days; range = 10–59 days), or for recurrent symptoms long after the stent migration or removal (mean = 14 mo; range = 2–67 mo). Patients whose initial pancreatogram showed moderate to severe pancreatitis, malignancy involving the pancreas, or those patients who underwent interval pancreatic surgery were excluded. Baseline pancreatograms were read and classified as normal or abnormal according to the Cambridge criteria.

Ductographic abnormalities were recorded with emphasis on their location and type and degree of change. The location of main pancreatic ductal changes was specified to the stented portion of the duct (i.e., stented zone) or the upstream duct (i.e., remote zone), and involvement of the pancreatic side branches. The morphologic ductal changes were noted as ductal irregularity, narrowing, or dilatation. The degree of narrowing was graded subjectively as follows: grade I: <20% luminal narrowing; grade II: 20% to 50% luminal narrowing; grade III: >50% luminal narrowing.

![Figure 1](image1.png)

**Figure 1.** (A) Polyethylene duodenal pigtail pancreatic stents (Wilson-Cook): 3F stent (top), 4F stent (middle), and 5F stent (bottom). (B) Three-quarter duodenal pigtail stents, 3F stent (top), and 4F stent, internal flange removed (bottom).

<table>
<thead>
<tr>
<th>Stent</th>
<th>n</th>
<th>M/F</th>
<th>Mean age (range)</th>
<th>SOD</th>
<th>PDiv</th>
<th>CP</th>
<th>Others</th>
<th>PAN</th>
<th>DES</th>
<th>MIES</th>
<th>Others</th>
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<tbody>
<tr>
<td>3F</td>
<td>1353</td>
<td>293/1060</td>
<td>47 (10–89)</td>
<td>994</td>
<td>165</td>
<td>75</td>
<td>110</td>
<td>110</td>
<td>912</td>
<td>174</td>
<td>167</td>
</tr>
<tr>
<td>4F</td>
<td>930</td>
<td>207/723</td>
<td>45 (5–91)</td>
<td>656</td>
<td>119</td>
<td>37</td>
<td>108</td>
<td>108</td>
<td>661</td>
<td>130</td>
<td>139</td>
</tr>
<tr>
<td>Total</td>
<td>2283</td>
<td>500/1783</td>
<td>1650</td>
<td>284</td>
<td>112</td>
<td>218</td>
<td></td>
<td>1573</td>
<td>304</td>
<td>306</td>
<td></td>
</tr>
</tbody>
</table>

CP, chronic pancreatitis; DES, dual (biliary and pancreatic) endoscopic sphincterotomy; MIES, minor papilla sphincterotomy; PDiv, pancreas divisum.

*Sphincter of Oddi dysfunction: basal sphincter pressure > 40 mm Hg.

*Normal SOM, precut sphincterotomy, ampullary tumor resection.

*No therapy, orifice (biliary/pancreatic) dilatation.
grade III: >50% luminal narrowing (Figures 2–4). Ductal perforations were recorded. The degree of resolution of stent-induced changes was determined by comparing the latest available pancreatograms with baseline study (Figure 5). All studies were performed at our institution. Two endoscopists experienced in ERCP who were blinded to the patient’s clinical condition graded the pancreatograms. Differences in pancreatogram interpretation were resolved by mutual discussion between the investigators. The frequency of stent-induced changes was correlated with stent size, duration of follow-up, patency of the removed stents, and whether or not the baseline pancreatogram was normal or abnormal. This study was approved by the Institutional Review Board at Indiana University Medical Center.

**Statistical Methods**

Logistic analysis was used to model binary responses such as severity of pancreatitis and stent-induced ductal changes to examine the effects of different stent diameters on these outcomes, with or without adjusting for other risk factors and to conduct pairwise comparisons between the different stent diameters after controlling for type I error. Pearson’s $\chi^2$ test and exact version of the Pearson’s $\chi^2$ test when the sample sizes were small were used to test for association between the baseline pancreatogram and the development of stent-induced ductal changes, as well as for association between different stent diameters and stent spontaneous dislodgment. Statistical tests with a $P$ value $<0.05$ were considered significant. Statistical analyses were performed using the statistical software package SAS version 8.2 (SAS Institute, Cary, NC).

**Results**

**Post-ERCP Pancreatitis**

Overall, post-ERCP pancreatitis occurred in 7.5%, 10.6%, 9.8%, and 14.6% of patients stented with 3F, 4F, 5F, and 6F stents, respectively. Table 2 shows the frequency and severity of post-ERCP pancreatitis corre-
lated with stent size. The frequency of post-ERCP pancreatitis was significantly lower with the 3F stent than the 4F stent ($P = 0.0043$). The 3F and the 4F stents were associated with significantly lower post-ERCP pancreatitis rates than the 5F and 6F stents ($P = 0.0471$). However, when comparing the severity of pancreatitis rates between 3F or 4F stents with 5F or 6F stents, the difference was not statistically significant ($P = 0.19$). Seventy-five percent of patients with post-ERCP pancreatitis and 93% of patients with moderate to severe post-ERCP pancreatitis had manometrically documented SOD.

**Stent Dislodgment**

Data regarding the spontaneous dislodgment rate of the 3–4F stents were tallied on 1371 patients and were compared with our previous experience with the 5–6F stents (Figure 6). The 3F stent had the highest spontaneous passage rate ($P < 0.0001$).

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**Figure 4.** (A) Baseline normal pancreatogram. A prophylactic 3F 10-cm pancreatic stent was placed. (B) Pancreatogram at stent removal showing grade III narrowing in the stented zone (arrow, >50% luminal narrowing).

**Figure 5.** (A) Baseline normal pancreatogram. A prophylactic 4F 8-cm pancreatic stent was placed. (B) Pancreatogram at stent removal showing grade I narrowing in the stented zone (arrow <20% luminal narrowing). (C) Resolution of the stent-induced changes seen on a pancreatogram performed 8 months later (arrow, no residual narrowing present).
Ductographic Changes

Of the 479 patients who had serial pancreato-grams available for review, 166 (24%) were found to have morphologic changes of their pancreatic duct compared with their baseline pancreatogram (Table 3). The ductal changes were most commonly grade I (90%), and were typically found within the stented zone. Involvement of the remote zone and the side branches were seen in patients with grade II or III ductal abnormalities. These changes were seen more frequently during the short-term follow-up period (i.e., at stent pull), but were found less commonly on long-term follow-up evaluation (i.e., recurrent symptoms). The 3F stents had significantly less short-term as well as long-term stent-induced morphologic changes \((P = 0.0006)\). At presentation, 355 (74%) patients had a normal pancreatogram, and 124 (26%) had features of mild chronic pancreatitis. Of the patients with stent-induced ductal alterations, 99/116 (85%) had a normal baseline pancreatogram, whereas patients with underlying mild chronic pancreatitis were less prone to have stent-induced ductal changes (17/116, 15%; \(P = 0.002\)), as shown in Table 4. All the stent-induced changes were grade I in patients with baseline chronic pancreatitis. Correlation of stent-induced changes between 3, 4, 5, and 6F stents is summarized in Figure 7.

The degree of resolution of stent-induced changes was assessed in 22 patients who had remote follow-up pancreatograms (Table 5). The indications for pancreatic stent insertion in these patients were as follows: 11 SOD, 7 pancreas divisum, 3 chronic pancreatitis, and 2 ampullary adenoma resections. The mean duration of follow-up evaluation was 8.4 months, the range was 3–20 months. The indication for further follow-up ERCP in this group was continuing or recurrent pain or pancreatitis and surveillance for ampullary tumor recurrence. The degree of long-term resolution appeared similar in patients with normal and abnormal baseline pancreatograms. Nine of the 22 patients (42%) had stent-induced changes noted at the time of stent removal (failure to dislodge spontaneously after 2 weeks of placement). Six of the 9 patients (67%) had complete resolution of the stent-induced abnormalities with longer follow-up evaluation. The remaining 13 patients (58%) had stent-induced changes noted at long-term follow-up. There was no significant difference seen in the mean follow-up interval between the patients who had complete and incomplete resolution. All 8 patients who had no improvement of their stent-induced ductal changes had grade II–III changes of the stented zone, associated with main duct and side branch dilations at the remote zone. One patient with grade III ductal changes had partial resolution after repeated stenting and stricture dilation. The remaining 13 patients with complete or partial resolution had only mild ductal narrowing and irregularity of the stented zone.

Three of the 2283 patients (0.1%) developed a perforation of the pancreatic duct at the intraductal stent tip.

<table>
<thead>
<tr>
<th>Stent</th>
<th>Reason for repeat pancreatogram</th>
<th>N</th>
<th>Frequency of stent-induced changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>3F</td>
<td>Stent pull</td>
<td>24</td>
<td>9 (37%)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Symptoms&lt;sup&gt;b&lt;/sup&gt;</td>
<td>219</td>
<td>23 (10%)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>4F</td>
<td>Stent pull</td>
<td>68</td>
<td>39 (57%)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Symptoms&lt;sup&gt;b&lt;/sup&gt;</td>
<td>168</td>
<td>45 (26%)&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>479</td>
<td>116 (24%)</td>
</tr>
</tbody>
</table>

Note. a vs. d: \(P = 0.0006\); c vs. e: \(P < 0.0001\).

<sup>a</sup>Refers to repeat pancreatograms for persistent and/or recurrent symptoms long after stent migration or removal.
(two 4F and one 3F), which manifested 1–3 days after stent placement. All 3 patients remained in the hospital and were treated for severe pancreatitis. One patient was managed successfully with conservative therapy; the other patients underwent surgical debridement followed by full recovery.

**Discussion**

Acute pancreatitis is the most common complication of ERCP. The underlying pathogenesis of post-ERCP pancreatitis is almost certainly multifactorial,1 with pancreatic outflow obstruction15–18 and thermal and hydrostatic injury19–26 frequently implicated. Impaired pancreatic drainage after ERCP may be caused by ampullary edema from papillary manipulation, pancreatic sphincter dysfunction, and transpapillary biliary stenting.24,27–29 Augmentation of pancreatic drainage by placement of pancreatic stents has been documented in a number of studies to reduce post-ERCP pancreatitis in a selected group of patients (Table 6).15,29–35 Despite promising therapeutic results of pancreatic stenting, their use is not risk free, with reported complications including ductal and parenchymal alterations, pain exacerbation, flare of acute pancreatitis, duodenal wall erosion, stent migration, and pancreatic pseudocyst and abscess formation.2–10,36–39

To date, the application of pancreatic stents smaller in diameter than 5F has received little evaluation. The present study shows that 3–4F stents are more effective than traditionally used stents in prevention of post-ERCP pancreatitis. Moreover, stent-related complications, particularly stent-induced pancreatic ductal changes as well as the need for endoscopic removal, are remarkably less with 3F and 4F stents. When comparing 3F with 4F, the 3F stent was superior in all aspects studied (Tables 2, 3; Figures 6, 7). These results strongly support our theory that smaller-diameter stents provoke less ductal irritation and spontaneously dislodge more frequently than larger ones. It is not clear if the diameter of the stent alone explains the lower incidence of procedure-induced pancreatitis with 3–4F stents. More likely, this benefit is multifactorial, secondary to a combination of other factors including improved endoscopic and prophylactic skills (less pancreatic duct injections, less papillary manipulation, and combined biliary/pancreatic sphincterotomy).

It is not known exactly how long a stent should stay intraductally to minimize pancreatitis risk and yet avoid ductal damage. Stents placed in the pancreas of normal dogs caused ductal and parenchymal fibrosis of increasing severity with more than 8 weeks of stenting.40 On the other hand, stents left in place for shorter periods of time (2–4 wk) may develop ductal changes.2 Because only 24% of patients who had a 3F or 4F stent placed had follow-up pancreatograms available for review in this study, the actual incidence of stent-induced pancreatic ductal changes is unknown. However, because we mainly study highly symptomatic individuals, it might be speculated that such patients would have more ductal changes (stent-induced or reflection of underlying primary process) than asymptomatic subjects. Nevertheless, if such changes can be avoided it seems preferable. It is uncertain how stents cause ductal changes. Stent length, patency, side branch obstruction, and ductitis as a result of direct stent irritation or reaction to the stent material have been thought to be the potential reasons.3 Of note, in the present study, almost all the stents were occluded.

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**Table 4. Correlation of Baseline Pancreatogram and the Frequency of Stent (3–4F)-Induced Ductal Changes**

<table>
<thead>
<tr>
<th>Baseline pancreatogram</th>
<th>n</th>
<th>Stent-induced ductal injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>355</td>
<td>99a</td>
</tr>
<tr>
<td>Abnormalb</td>
<td>124</td>
<td>17b,c,d</td>
</tr>
<tr>
<td>Total</td>
<td>479</td>
<td>116</td>
</tr>
</tbody>
</table>

**Table 5. Correlation of Long-Term Resolution of Stent-Induced Ductal Changes and Baseline Pancreatogram**

<table>
<thead>
<tr>
<th>Baseline pancreatogram</th>
<th>n</th>
<th>Complete (%)</th>
<th>Partial (%)</th>
<th>None (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>17</td>
<td>7 (41)</td>
<td>3 (18)</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>5</td>
<td>3 (60)</td>
<td>1 (20)</td>
<td>1 (20)</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>10 (45)</td>
<td>4 (18)</td>
<td>8 (37)</td>
</tr>
</tbody>
</table>

**Figure 7.** Polyethylene stent-induced pancreatic ductal changes. Data on 5F stent from Smith et al.2
at the time of removal, but ductal changes were noted in 37% of 3F stent and 57% of 4F stents. This may suggest that the mechanical pressure from the stent, which is proportional in magnitude to the size of the stent, is the most likely contributing factor because larger stents (5–10F) are known to induce more ductal alterations (80% to 100%).

This retrospective study shows that unflanged, small-diameter (preferably 3F), polyethylene stents have superior protection and substantially fewer complications compared with traditional larger-diameter stents. Concerns about stent-induced ductal damage remain. Placement of pancreatic stents can be challenging, particularly in patients with a tortuous main pancreatic duct in the head. We recommend placement of the guidewire around the genu and into the body main duct if possible. This allows placement of a 6- to 8-cm stent securely into the duct, such that it rarely is dislodged accidentally during ERCP. Care must be exercised when maneuvering the guidewire in the pancreatic duct to prevent inadvertent duct branch tracking and perforation. The endoscopist and his assistant must be familiar with small-diameter guidewires, which are necessary to place such stents. As noted earlier, 3 patients experienced duct perforation requiring hospitalization.

Our initial brief experience with 3F diameter and 2- to 2.5-cm long stents showed that they exited the duct during sphincterotomy and therefore were unsatisfactory. We substituted an increased length of the stent in the duct for an internal flange. This seems satisfactory because 86% of 3F stents exited without endoscopic removal. In addition to pancreatic stenting, we previously showed that using a needle-knife to perform a combined pancreaticobiliary sphincterotomy over a pancreatic duct stent has significantly decreased pancreatitis rates in patients with SOD. In the present study, 72% (1650/2283) of our patients had manometrically documented SOD, and 95% (1573/1650) underwent combined pancreaticobiliary sphincterotomy over a temporary 3–4F pancreatic duct stent (Table 1). Although the post-ERCP pancreatitis rates remain high in this high-risk population (7.5% to 10.6%), the rates are lower than those in the historic control. Without pancreatic stenting, the incidence of post-ERCP pancreatitis in suspected SOD patients occurred in 18% to 33% in prospective randomized studies from our institution as well as others. However, whether the temporary pancreatic stenting, the endoscopic sphincterotomy, or a combination of both is the optimal protection desired awaits further studies. We acknowledge that a randomized prospective trial still is needed to better define the benefit of these lesser-diameter stents. However, a self-dissolving stent or perhaps a stent programmed to migrate out of the duct in 2–5 days would be of interest.

References