

# Extension of a Prior Biliary or Pancreatic Sphincterotomy: Efficacy, Outcomes, and Adverse Events



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## INTRODUCTION

**E**ndoscopic sphincterotomy (ES) is one of the most fundamental maneuvers performed in ERCP, with over 150,000 biliary sphincterotomies performed annually in the United States.<sup>1</sup> ES is a complex procedure performed under direct endoscopic observation. Facilitating the removal of common bile duct stones is the most common indication, but ES is performed for a variety of both biliary and pancreatic disorders, including the treatment of biliary and pancreatic leaks, to facilitate the placement of biliary or pancreatic stents, as a precursor to cholangioscopy and/or pancreatoscopy, and to treat suspected sphincter of Oddi dysfunction, among others (see Table 1).<sup>2,3</sup>

ES, also known as sphincterotomy or papillotomy,

involves retrograde cannulation of the bile or pancreatic duct via the ampulla of Vater. In the vast majority of sphincterotomies, ES is performed after deep access to the desired duct has been achieved and a guidewire is in place in the duct. The biliary or pancreatic sphincter is then incised by a sphincterotome via electrocautery delivered through the cutting wire incorporated into the sphincterotome itself.

Less commonly, a needle knife instead of a sphincterotome is used in order to perform ES, usually in cases where standard techniques to achieve ductal access have failed. Other variations of the technique include a precut sphincterotomy (cutting with a sphincterotome without deep access already established) as well as transpancreatic sphincterotomy also known as a trans-septal sphincterotomy. In rare cases, an interventional radiologist can assist in a combined percutaneous-endoscopic procedure by passing a guide-wire in an antegrade manner through the bile duct and into the duodenum to allow the endoscopist to achieve ductal access and perform sphincterotomy.<sup>1</sup>

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### Complications of Initial Biliary Sphincterotomy

Complications related to performing ES vary greatly, from approximately 6-22% in multiple studies.<sup>4,5,6</sup> Freeman et al. conducted the largest prospective study, consisting of 2347 patients analyzing complications of ES. They identified difficult cannulation of the duodenal sphincter, use of precut sphincterotomy, suspected sphincter of Oddi dysfunction and presence of cirrhosis as significant factors associated with an increased odds ratio of procedure-related complications. The authors concluded that complications were related to the technical skill of the endoscopist, indicating that these procedures may be safest in centers in that perform ES on a regular basis.<sup>1</sup> Complications are likely less common with high volume providers.

A different study that investigated the risk of post-ERCP pancreatitis (PEP) in the setting of ES identified a relative increase in risk in younger patients and patients who received an increased number of contrast injections into the pancreatic duct.<sup>7</sup> More recent retrospective data has identified the co-morbid conditions of chronic kidney disease (possibly with associated platelet dysfunction from uremia), hypertension and ischemic heart disease as risk factors in post-procedural bleeding after ES.<sup>8</sup>

The type of current used for electrocautery has also been described as a risk factor for complications related to ES. Pure current provides better tissue cutting quality, whereas mixed current combines pure current with low-voltage coagulating current in alternating short bursts, achieving cutting and coagulation simultaneously.<sup>9,10</sup> Multiple prospective randomized trials have been unable to identify a clearly superior method of electrocautery in relation to specific side-effects.<sup>11,12</sup> A meta-analysis of 4 trials and over 800 patients identified no significant difference in rate of pancreatitis, however pure current was noted to be associated with more episodes of bleeding compared to the mixed current technique.<sup>13</sup>

Specific complications related to performing ES are most commonly classified as early (occurring within 30 days of the procedure) or late (occurring > 30 days after the procedure). The overall rate of early complications has been quoted around 7-10% in various studies, and most commonly includes bleeding (both immediate and delayed hemorrhage), pancreatitis, and rarely, duodenal perforation.<sup>1,13,14</sup> A major late complication of ES is papillary restenosis, which can occur months to years after initial ES. This complication is rare but has been

Table 1.

Common Indications for Endoscopic Sphincterotomy
Treatment of Choledocholithiasis
Treatment of Pancreaticolithiasis
Papillary Stenosis
Sphincter of Oddi Dysfunction
Choledochocele
Access to biliary or pancreatic ducts for:
Balloon dilation
Stent placement across benign or malignant strictures
Facilitate repair of postoperative biliary leaks
Tissue sampling
Fistulae repair
Pseudocyst drainage

noted in 1-4% of patients, and can be successfully treated with repeat ERCP and ES.<sup>2,3,15</sup> Ascending cholangitis is another late ES complication managed by repeat ERCP.<sup>3</sup> Recurrent stones can also be seen in these patients, but it is unclear if this represents a procedure-related complication or the natural course of stone-related disease.<sup>15</sup>

Throughout the literature there is mention of the long-term risk of patients with ES developing cholangiocarcinoma, presumably through chronic inflammation resulting in malignant transformation or through sample error as those undergoing ERCP are more likely to have underlying biliary disease in the first place. However, several studies with long-term follow up (greater than 10-15 years) have been unable to confirm this suspected link.<sup>5,15,16,17</sup>

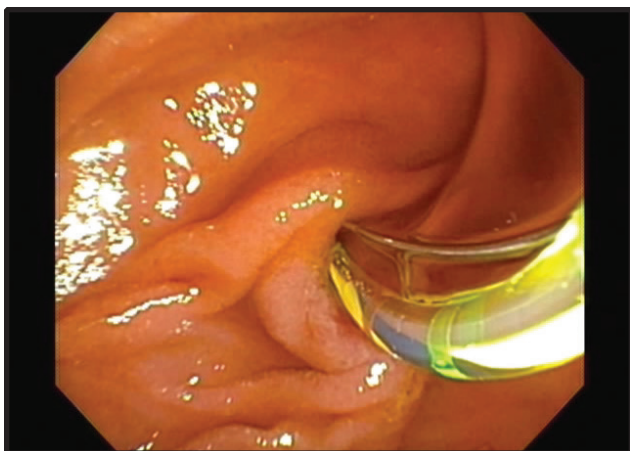
### Repeat Biliary Sphincterotomy When and Why?

A problem for any endoscopist who performs ERCP is the occasional need to extend a previous sphincterotomy. This can occur at any time, from days to years after the initial procedure.

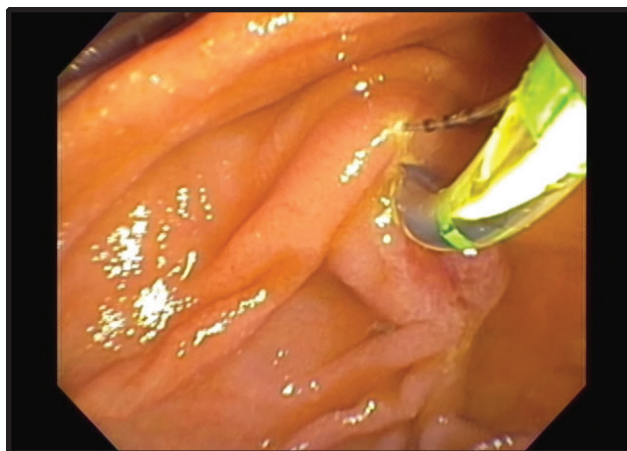
The need for a repeat procedure can be divided into the “early” and the “late” time period, although

**Figure 1. Late Extension of Prior Biliary Sphincterotomy**

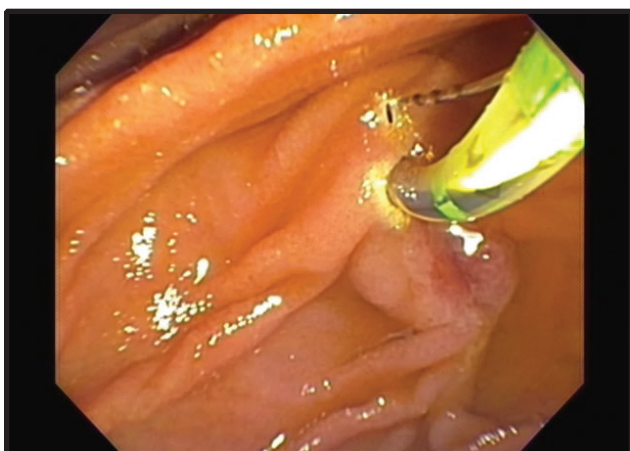
Figures 1a. - 1d. Four image series of extension of an old, healed prior biliary sphincterotomy for the purpose of stone extraction.



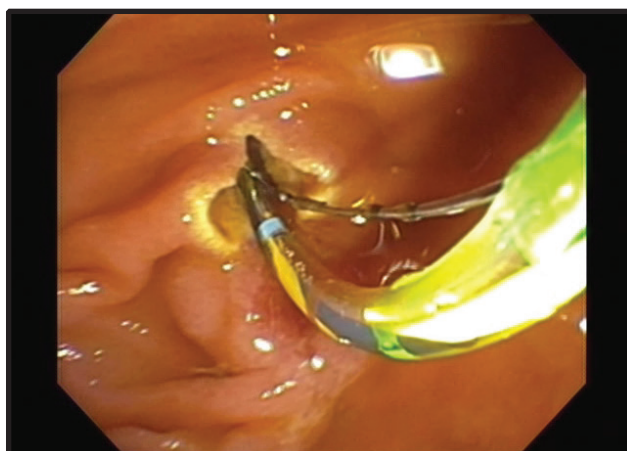
**Figure 1a.**



**Figure 1b.**



**Figure 1c.**



**Figure 1d.**

what exactly is meant by these terms has been variably defined in the literature. A retrospective review of 248 patients defined an early post-procedure period of 1-3 days, and differentiated it from the period 4-10 days after the original sphincterotomy.<sup>18</sup> Although seemingly arbitrary and not based on rigorous evidence, this division was made because of the anecdotal experience that re-intervention within 3 days may be met with increased technical difficulty. This increase in difficulty is thought to be related to persistent edema from recent trauma, as well as the potential presence of an adherent clot, which can obscure vision and carries with it a higher risk of bleeding.<sup>19</sup> Alternatively, Mavrogiannis et al conducted the largest prospective study to date and used 0-8 days as the early re-intervention group, whereas the late reintervention group had a repeat procedure between 9 days to 7 years from the initial

ES.<sup>20</sup> This was done because several early studies had identified a high risk of bleeding in patients within 8 days of ES, attributed to increased papillary vascularity during that time.<sup>21</sup>

Regardless of the specific timing, early extension of prior ES can be performed for several different indications. The most common reason to extend a biliary sphincterotomy is to facilitate the removal of biliary stones that could not be removed on a prior ERCP. (Figures 1 and 2) Other patients need their sphincterotomy extended and completed after it was interrupted during the initial procedure due to various complications (bleeding, severe edema, periampullary diverticulum, and cardiopulmonary complications related to sedation). Another reason for extension of ES is to complete a sphincterotomy after the precut technique has been used.<sup>19</sup>

Although the exact definition of a “late” extension of previous sphincterotomy may be debated, it is commonly needed in the setting of papillary stenosis which can develop after a prior biliary ES, although true papillary stenosis is a rare development. Sphincterotomy extension can also be necessary to remove common bile duct stones that recur.<sup>20</sup>

Papillary stenosis may cause jaundice or other associated conditions like stone formation and/or cholangitis. The development of stenosis at the site of prior sphincterotomy is thought to be due to inadequate incision of the sphincter muscle or excessive scar tissue formation. It is frequently seen in patients who have had extraction of multiple or large stones compared to patients who have sphincter of Oddi dysfunction or pass single, small stones.<sup>22</sup> It could also be related to fibrotic reaction at the site of incision, as previous studies have shown that mean length of incision does decrease over time, indicating an active area of tissue growth and remodeling.<sup>23</sup> Late extension is sometimes not possible, as Bourke et al first described the phenomenon of a papillary orifice that is seemingly buried in the duodenal wall. In this situation, the papillary stenosis extends along the bile duct beyond the biliary orifice, and the lesion is not amenable to further extension.<sup>24</sup> This situation is, fortunately, extremely uncommon.

### Outcomes, Safety and Adverse Events

The largest prospective study of extending a biliary ES followed 250 patients who underwent sphincterotomy as primary treatment for choledocholithiasis. Of those, 81 (32%) underwent extension of their initial ES. 66 of these patients underwent a “late” extension (9 days to 7 years after initial procedure), while the remaining 15 had an early extension within 8 days of the first ES. 80 out of the 81 patients had successful clearance of stones from the bile duct after repeat ES, with mechanical lithotripsy utilized in one case. The authors concluded that extension of a previous sphincterotomy is an efficient treatment for recurrent biliary stones. It should be noted that the cohort represented a homogenous group of patients with choledocholithiasis, and patients with other indications for repeat ES were excluded.<sup>20</sup>

This study concluded that repeat ES was a safe procedure, with an overall complication rate which was no different when compared to the initial sphincterotomy group (2.5% vs 8.4%,  $p > 0.05$ ). Other common complications, including bleeding, cholangitis and perforation were found to be the same in both groups,

with no deaths reported in either group. The repeat ES group did, however, have statistically significant fewer episodes of pancreatitis (0% vs 4.8%,  $p < 0.05$ ). This suggests that extension of previous sphincterotomies may have less risk of pancreatic injury than initial ES, possibly explained by cutting on the upper edge of the previous cut, thus avoiding the pancreatic orifice. There was a trend (although not statistically significant) towards a higher risk of bleeding in early repeat ES vs late repeat ES. Both cases of bleeding in this cohort occurred when repeat ES was performed within 3 days of initial ES.<sup>20</sup>

A similar study aimed to examine whether repeat ERCP was safe and feasible in treating recurrent choledocholithiasis. Resembling the design of Mavrogiannis et al, the study excluded patients with concomitant hepatolithiasis, choledochal cysts or bile duct strictures. Of 84 patients who underwent repeat ERCP for post-ES recurrent choledocholithiasis, 69 patients received a repeat sphincterotomy. Biliary duct clearance was achieved in 100% of these patients. Early adverse events were noted in 2 (2%) patients. This low complication rate consisted of cases of mild pancreatitis and mild hemorrhage.<sup>25</sup>

In addition to confirming that repeat ES is indeed a safe procedure in the short-term, this study was unique in that it also included long-term follow up (mean 11.7 years) after repeat ERCP. Choledochal complications, consisting of recurrent choledocholithiasis and cholangitis were noted in 30 patients during this follow-up period. While this rate of 36% is higher than the complication rates reported after initial ES (6-22%), the authors explained this by identifying independent risk factors not related to the procedure. Multivariate analysis found that early recurrent choledocholithiasis (within 5 years), a dilated bile duct ( $>15\text{mm}$ ) and periampullary diverticulum were independent risk factors predictive of these recurrent stone disease and cholangitis.<sup>25</sup> While this study confirmed that repeat ERCP and ES are safe and effective means of managing recurrent biliary disease, the simple fact that patients require a repeat procedure seems to put them at increased risk for further complications and future procedures.

A more recent study investigating the safety and efficacy of repeat ES was described by Hisai et al.<sup>26</sup> They describe a series of 76 patients who underwent repeat ES, 25 of whom had a repeat procedure within

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#### Figure 2. Extension of a Very Recent Biliary Sphincterotomy

Figures 2a - 2e. Five image series showing extension of a recent biliary sphincterotomy. The initial sphincterotomy was performed at an outside hospital for the purposes of stone extraction, which was unsuccessful. Note ulceration at apex of prior sphincterotomy in Figure 2a. Upon extension and completion of the sphincterotomy, an impacted distal common bile duct stone was able to be removed using only the sphincterotome.

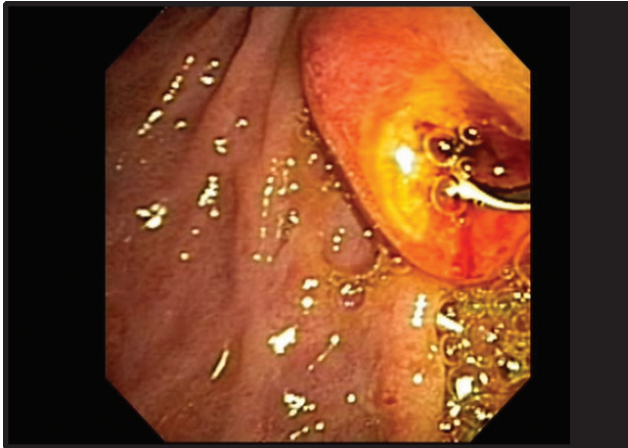


Figure 2a.



Figure 2b.

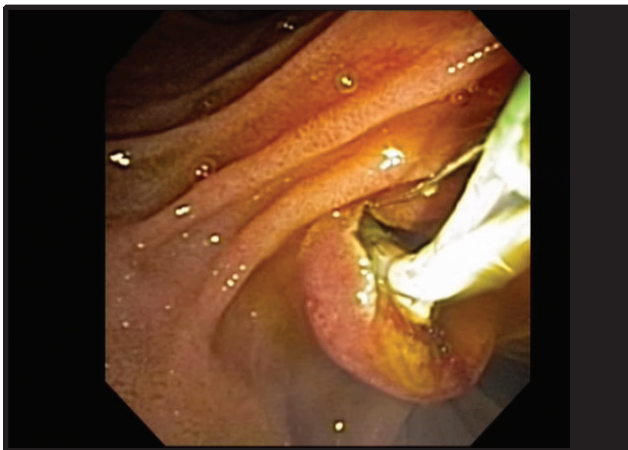


Figure 2c.



Figure 2d.



Figure 2e.

8 days of the initial procedure (“early” extension), and 51 who received a “late” extension (> 9 days after initial procedure). This delineation of early and late was the same as described by Mavrogiannis et al.<sup>20</sup> While recurrent choledocholithiasis was the most common indication for repeat ES (67/81 patients, 83%), this study included patients requiring ES for other indications, including biliary strictures and papillary stenosis. Repeat ES was technically successful in all cases, with an overall complication rate of 5.4%. Complications consisted of bleeding (2 patients), mild pancreatitis (2 patients) and cholangitis (1 patient). The overall complication rate, including pancreatitis, was

**Figure 3. Extension of a Prior Pancreatic Sphincterotomy at the Major Papilla**

Figures 3a - 3e. Five image series demonstrating extension of a prior limited pancreatic sphincterotomy. There is also a guidewire in the bile duct, of note. The prior pancreatic sphincterotomy was quite limited and was both extended and completed to allow pancreatic stone removal.

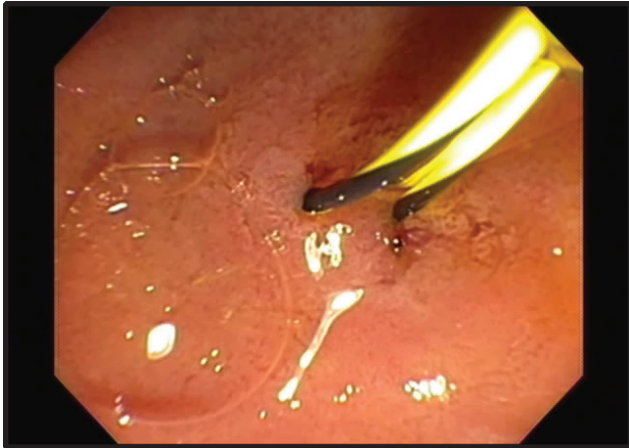


Figure 3a.

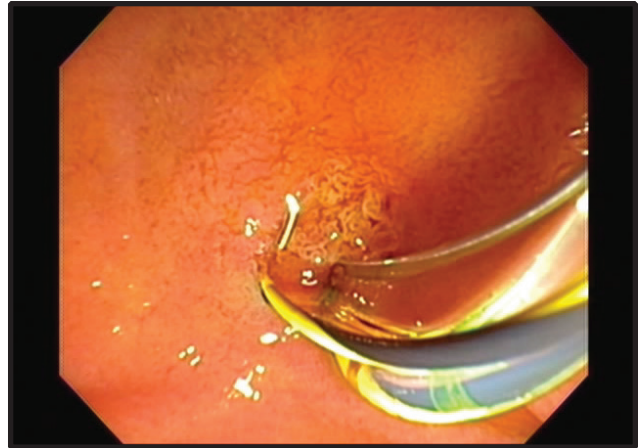


Figure 3b.



Figure 3c.



Figure 3d.

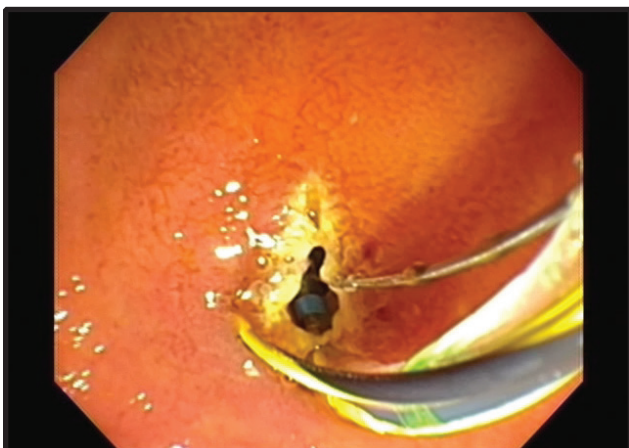


Figure 3e.

no different between the two groups, and there were no procedure-related deaths. The authors concluded that repeat ES is safe, effective and was not associated with an increased risk of bleeding as they had hypothesized.<sup>26</sup>

**Pancreatic Sphincterotomy**

***Indications for and Complications of Initial Pancreatic Sphincterotomy***

The sphincter of Oddi can be anatomically divided into the bile duct (biliary) sphincter, the pancreatic duct sphincter, and the ampullary sphincter, encompassing the distal most portion of the ampulla. In biliary

endoscopic sphincterotomy, the pancreatic sphincter is left intact.<sup>27</sup> Pancreatic sphincterotomy was first described in 1976 and can be performed in conditions such as pancreas divisum, chronic pancreatitis, to perform pancreatoscopy, to facilitate the evaluation of pancreatic malignancy, to enable the removal of pancreatic stones (pancreaticoliths), and to treat suspected pancreatic sphincter of Oddi dysfunction.<sup>28,29</sup>

Pancreas divisum is a relatively common congenital abnormality of the pancreatic ductal system, occurring in about 7% of the population in the United States.<sup>29</sup> While typically asymptomatic, it can be associated with recurrent acute or chronic pancreatitis, as well as chronic abdominal pain. Most studies evaluating the success of pancreatic ES in these patients consist of retrospective case series measuring pain burden, and the success rates vary widely from 32%-86%.<sup>30,31</sup> Of note, pancreatic sphincterotomy in patients with pancreas divisum is performed on the minor papilla, which is distinct from pancreatic ES for other indications.

Pancreatic ES of the major papilla is useful in chronic pancreatitis, as it can improve pancreatic drainage via facilitating the removal of stones and endoscopic of strictures in the pancreatic duct.<sup>29</sup> While technical success rates of the procedure are high (> 85%), the number of patients who clinically improve after the procedure is lower, around 50% in several studies.<sup>32,33</sup>

A more controversial indication, the treatment of sphincter of Oddi dysfunction, is another indication for pancreatic ES, biliary ES, or both. In patients with abnormal sphincter manometry, clinical improvement after ES has been quoted as 85%-95% in earlier studies.<sup>34,35</sup> A recent, widely publicized, randomized sham controlled, multicenter trial studied over 200 patients with sphincter of Oddi type III dysfunction. Their results were far less enthusiastic and demonstrated that in these patients, pancreatic and/or biliary ES does not improve outcomes, and sphincter manometric pressure is not predictive of pain relief, lessening the enthusiasm for this procedure in some circles.<sup>36</sup>

The major early complications associated with pancreatic ES are bleeding, cholangitis and pancreatitis.<sup>29</sup> As would be expected, the overall rate of pancreatitis in patients undergoing pancreatic ES is higher than the risk after ERCP without pancreatic ES. Overall, the rate of pancreatitis following pancreatic ES is around 10-12%, while the rate of post-ERCP pancreatitis has been quoted at approximately 3% in

expert hands, and is likely higher in the hands of low volume providers.<sup>37,38,39</sup> The incidence of pancreatitis after pancreatic ES can be affected by other factors, including pancreatic duct stent placement, difficulty of cannulation of the pancreatic duct, and whether the pancreatic sphincterotomy was performed on the major or minor papilla.<sup>40</sup> Stent-related complications, including parenchymal changes, infection, perforation, occlusion and stone formation can be seen in follow-up if stents are left in the pancreatic duct too long, but are not related to the sphincterotomy itself.<sup>41</sup> Late complications such as papillary stenosis and proximal ductal strictures are exceedingly rare, and can similarly be treated with repeat pancreatic ES.

### Repeat Pancreatic Sphincterotomy

Pancreatic ES is performed far less frequently than biliary ES. This is due to less commonly encountered indications for the procedure, as well as operator concern regarding the technical difficulties and the perceived increased occurrence of complications.<sup>40</sup> As a result, the literature is sparse regarding incidence, safety and specific complications in regards to repeat endoscopic pancreatic sphincterotomy. Still, repeat pancreatic sphincterotomy is a valid procedure that is sometimes clinically indicated, most commonly to allow removal of pancreatic duct stones. (Figure 3)

Jakobs et al. retrospectively identified 171 patients who underwent pancreatic ES for therapy of chronic pancreatitis over the span of 11 years.<sup>42</sup> The procedure was technically successful on the first attempt in 147 patients (86%). In the remaining 24 patients, repeat pancreatic ES (maximum of 3 attempts) was successful in 20 (83%) patients. During the long-term follow-up period, a repeat pancreatic sphincterotomy was necessary in 17/167 patients (10%), and was successful in all patients. Indications for repeat sphincterotomy were an inadequate pancreatic duct orifice for removal of pancreatic duct stones (13 patients), retrieval of a pancreatic duct stent (2 patients) or transpapillary insertion of a larger pancreatic stent (2 patients).<sup>42</sup>

A similar retrospective study by Joo et al. identified 46 patients who underwent pancreatic ES.<sup>40</sup> While a majority (26/46 or 57%) of patients received pancreatic ES for the indication of chronic pancreatitis, 10/46 (22%) were undergoing evaluation for possible malignancy, for cases of pancreas divisum (4/46) (9%), and for treatment of pancreatic pseudocyst (3/46) (7%). The

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procedure was successful in 96% (44/46) of patient, and the authors only reported one late complication of re-stenosis of the pancreatic duct, which developed after 38 months. The need for repeat sphincterotomy in only 2% (1/46) of patients is explained by the authors as being due to the heterogenous characteristics of the study cohort, as well as the relatively large amount of patients (12/46 or 26%) that were lost to follow-up.<sup>40</sup>

A recent large prospective study examining the effectiveness of ES in patients with chronic pancreatitis prospectively followed a 41 patient sub-set who received a pancreatic ES in addition to ductal dilation and/or stent placement. The mean follow-up period was 4.8 years, and there were no reported long-term complications that required repeat pancreatic ES. While the study's primary aim was to compare outcomes in patients who underwent different modalities of treatment, it contributes to the conclusion that pancreatic ES is a safe and effective procedure without significant long-term complications.<sup>32</sup>

### Initial and Repeat Sphincterotomy of the Minor Papilla

In contrast, pancreatic ES performed on the minor papilla in patients with pancreatic divisum (PD) is considered a separate clinical and technical entity. For patients with symptomatic PD, it is postulated that obstruction at the site of the accessory pancreatic duct, or minor papilla, is an important predisposing factor for symptomatic disease. By receiving therapy to relieve the obstruction and improve pancreatic drainage, it is thought that symptoms such as pain and recurrent acute pancreatitis may be relieved.<sup>43</sup> Successful endoscopic therapy via pancreatic ES, which consists of resolved pain and decreased instances of pancreatitis, has been reported to occur in up to 60-80% of patients in some studies. This varies based on patient characteristics and this number is likely elevated due to some degree of publication bias.<sup>44,45</sup>

Pancreatic ES at the minor papilla incurs similar risks of acute complications, including pancreatitis, bleeding and perforation.<sup>46</sup> The rate of pancreatitis, however, has been noted to be higher in patients undergoing pancreatic ES of the minor papilla, with some studies citing an incidence in over 30% of patients.<sup>47</sup> More recent studies have shown that if the intervention is performed by an experienced endoscopist at a large referral volume center, the rate of pancreatitis

may decrease significantly, to below 10%.<sup>44,48</sup> The rate of re-stenosis in these patients is a significant long-term complication, ranging from 16-20%. This results in the need for re-intervention, often with repeat pancreatic ES.<sup>45,49</sup>

In a large retrospective review of 184 patients, Atwood et al compared differences in outcomes between needle-knife sphincterotomy and standard pull-type sphincterotomy of the minor papilla.<sup>44</sup> Complication rates and outcomes were the same in both groups, with the authors indicating that endoscopist preference and comfort plays a large role in which technique is safest. Re-stenosis rates were around 20%, and were not different between the two groups. In this study, median follow-up over the span of 5-6 years identified 28 patients (21%) who required repeat pancreatic ES. A majority of these patients received their repeat procedure within a year of the index procedure, and the need for a repeat ES did not seem to be a risk factor for further complications.<sup>44</sup>

Another retrospective study that included 113 patients attempted to evaluate long-term clinical outcomes in patients who underwent ES of the minor papilla. Over a median follow-up range of 47 months, the overall success rate was 62%. While primary success (no need for repeat procedure) was noted in 49/113 (43%) patients, another 47/113 (42%) patients required at least one more ERCP. While the authors did not publish data regarding how many of those patients needed a repeat or extension of minor papilla ES, they did mention restenosis as a complication seen in follow-up that was safely treated via a repeat ES.<sup>50</sup>

Maple et al. described a retrospective study of 64 patients undergoing minor papilla ES to compare a wire-assisted technique compared to the aforementioned needle-knife or pull-type sphincterotomies. While no significant difference existed between the techniques, the published data included a sub-set of patients who required re-intervention. The authors reported 11/64 (17%) patients who required a repeat intervention on the minor papilla. No complications were reported in these procedures, and all were technically successful.<sup>51</sup>

### CONCLUSION

Endoscopic sphincterotomy remains a fundamental maneuver during ERCP, and the need for repeat sphincterotomy can arise in clinical practice and interventionalists should be prepared to perform this when it is needed. Complications of extension of an

ES tend to be linked to characteristics of the patients, the indication for the procedure, and the technical skill and experience of the endoscopist. Patients who undergo biliary ES tend to be at risk to undergo further endoscopic therapy, likely related to their underlying disease process and not the sphincterotomy itself. Distinct “early” and “late” re-interventions are well described in the setting of biliary ES, and studies have shown that these repeat procedures are safe and effective. While the field still lacks multiple prospective clinical trials to confirm this, repeat biliary ES is a necessary procedure that can be performed without excessive risk of adverse events.

Although sparse and lacking randomized prospective data, the summation of the literature regarding extension of a prior pancreatic ES supports the fact that it can also achieve good outcomes when patients are properly selected. Some pancreatic ES patients do require repeat procedures, and while re-intervention is also relatively safe, it is a fact that should be taken into account when deciding on initial therapy. ■

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