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Review

Advancements in the endoscopic treatment of pancreatic fluid collections

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Abstract

Endoscopic drainage of pancreatic fluid collections (PFCs) with fewer complications and less trauma has gradually replaced surgery or percutaneous drainage to become the first-line treatment for PFCs. In recent years, the differential efficacy of various stent techniques to drain different types of PFCs has been controversial. This review summarizes the clinical applications of endoscopic ultrasound-guided stent placement for PFCs drainage.

Keywords: Pancreatic fluid collections; Pancreatic pseudocyst; Walled-off necrosis; Endoscopic treatment; Stent

Introduction

Pancreatic fluid collections (PFCs) are amylase-rich collections of pancreatic fluid resulting from pancreatic duct injury that accumulate in or surround the pancreas. PFCs usually occur after acute or chronic pancreatitis, pancreatic trauma, and pancreatic surgery. Approximately 15%−20% of acute pancreatitis cases develop PFC-induced pancreatic parenchymal necrosis.[1] A further 18%−40% of chronic pancreatitis cases also developed PFCs. The incidence of pancreatic pseudocyst (PPC) after 3, 5, and 10 years of chronic pancreatitis is 8.41%, 10.06%, and 10.76%, respectively.[2] The revised classification of acute pancreatitis identified two phases of acute PFCs, and local complications are classified into four types: peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), PPC and walled-off necrosis (sterile or infected). The cyst walls of PPC and walled-off necrosis (WON) are both composed of fibrous granulatedion tissue without an epithelial lining. These cyst walls usually take more than 4 weeks to develop. PPC results in homogeneous fluid collections containing non-solid components, and occurs after interstitial edematous pancreatitis. While WON results in a collection of pancreatic and/or peripancreatic necrosis and usually occurs after acute necrotizing pancreatitis.[3]

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PFCs may spontaneously resolve, depending on the size of the cyst and the cyst formation time. The spontaneous resolution rate of PFCs declines after 4 weeks, and the rate of PFC-related complications also increases. Surgical treatment is therefore believed to be most effective after 4 weeks. Delaying surgical interventions properly can reduce the proinflammatory response in critically-ill patients.[4] The updated 2018 European Society of Gastrointestinal Endoscopy (ESGE) guidelines concerning the management of acute necrotizing pancreatitis also suggests the first intervention for infected necrosis should be delayed 4 weeks if tolerated by the patient.[5] Currently, the indications for endoscopic drainage of PFCs are generally considered to be: 1) symptomatic or rapidly-enlarged cysts; 2) a cyst diameter of larger than 6 cm and a cyst formation time of longer than 4 weeks; and 3) complications such as infection or bleeding. The indications for chronic pancreatitis are generally determined by the patient's symptoms (chronic pain, gastric outlet obstruction, biliary compression, etc.).[6]

The developmental history of treatment for PFCs

In the past, surgical drainage was the only treatment for PFCs. Although surgical drainage had a relatively high surgical success rate, postoperative complications resulted in a mortality rate of 5%–10%, as well as a high cost, and caused long hospital stays.[7,8] The more recently developed ultrasound or CT guided percutaneous catheter drainage (PCD) techniques are minimally invasive approaches for treating PFCs, and have the advantages of surgical simplicity and lower cost. However, cysts are susceptible to perforation and bleeding during these operations. These surgeries may also result in long-term complications such as postoperative catheter-related infection, drainage tube blockage, and fistula formation. The success rate of PCD is relatively low, and the recurrence rate of PFCs after these procedures is high.

A description of endoscopic treatment of PFCs was first published in 1996, and the first reports of successful endoscopic ultrasound (EUS)-guided drainage for PPC and pancreatic abscess were published in 2001. In recent years, EUS-guided drainage has become the preferred treatment for PPC. Endoscopic ultrasonography can accurately measure the distance between the cyst and the stomach, identify blood vessels and the optimal puncture point for stent implantation. The entire process of puncture and stent implantation can be clearly displayed in real time using fluoroscopic imaging or EUS. The complication/recurrence rates for EUS-guided drainage are not significantly different than surgical treatment or PCD. Furthermore, EUS-guided drainage causes less trauma, costs less, and allows for faster recovery than previous methods.[9]

Endoscopic clinical application of stents

Reports published in 1998 indicated that use of plastic stents (PS) for EUS-guided drainage resulted in good therapeutic outcomes. However, as plastic stents have limited diameter and can not provide access for endoscopic necrosectomy to treat WON, metal stents have gradually replaced plastic stents for clinical use. Manuel et al[10] reported the first use of a self-expanding biliary metal stent to drain PPC through the intestinal wall in 2007. Large-diameter stents allow an endoscope to be inserted into the cyst to remove necrotic tissue for drainage. At the same time, the radial force exerted by these self-expanding stents can compress local hemorrhages.

A variety of stents have been used for EUS-guided drainage, including uncovered self-expandable metal stents, partially covered self-expandable metal stents, and fully covered self-expandable metal stents (FCSEMS).[11] These stents are mainly used for recanalization of blocked passages such as the bile duct. Barresi et al[12] found that local tissue can grow into both ends of a partially-covered self-expandable metal stent, preventing stent displacement. However, buried stent syndrome prevented removal of the stent in some patients, which necessitated the surgical removal of the stent. The stents listed above can also cause liquid leakage into the peritoneum without the use of an anchor structure between the cyst and the stomach. In addition, both ends of the stent may cause tissue injury and hemorrhaging in the cyst wall, and the stent may migrate into the gastric lumen or cyst.

Use of new lumen-apposing metal stents (LAMS) was described in 2011.[13] A LAMS has flanges shaped like dumbbells at both ends, making the stent easier to fix on both sides of the stomach wall. Meanwhile, the large diameter of a LAMS allows for the insertion of endoscopes to perform necrotic tissue debridement in WON. Currently, the widely-used LAMS subtypes include Axios stents (Boston Scientific, United States), Nagi[14] and Spaxus stents[15] (Taewoong Medical, South Korea), and HANARO stents[16] (MI-Tech, South Korea). These stents with different specifications allow clinicians to choose according to the specific patient's condition. Currently, a domestic LAMS from Micro-Tech Co. (Nanjing, China) is undergoing clinical trials in China.

Reports indicate that FCSEMS and LAMS have similar clinical efficacies.[17−19] The rates of adverse reactions between FCSEMS and LAMS have yet to be studied, and researchers should specifically examine rates of early severe bleeding after metal stent implantation.[19] Ryan et al[20] speculated that with rapid decompression of the cyst, the wide-bore flanges of the LAMS could impinge on the cyst wall and damage the adjacent vessels, resulting in bleeding. They further speculated that the outer flange of the stent could migrate into the lumen, leading to buried stent syndrome. Recently, a novel LAMS with an anti-reflux valve has been developed to prevent food reflux into the cyst cavity.[21]

A novel electrocautery-enhanced LAMS (EC-LAMS) delivery system (Hot Axios, Boston Scientific Corporation, United States) was recently developed. This one-step approach facilitates the passage of the LAMS deployment device without first dilating the fistulous tract, which streamlines the procedure. Yoo et al[22] and Lakhtakia et al[23] report that single-step EUS-guided drainage of PFCs without fluoroscopic guidance using the novel EC-LAMS is a safe and effective method for draining PFCs. The method has good technical and clinical success rates, and causes no complications. However, another study[24] reported that using an electrocautery-enhanced delivery system may lead poor therapeutic outcomes in WON, but not PPC. The researchers speculated that the balloon required to dilate the puncture channels during non-EC-LAMS procedures might facilitate stent expansion and the drainage of necrotic debris. Because EC-LAMS requires no such dilation, it may provide fewer therapeutic benefits for WON.

Comparison of clinical efficacy between metal stents and plastic stents

Several non-Chinese studies have shown that the technical success rate of EUS-guided plastic stent drainage of PPC is 86%−92%.[25,26] The clinical success rate is 59%−89%,[26,27] and the incidence of complications is 31%.[26] However, Chinese studies show the technical success rate of the procedure is 94.4%−95.0%, the clinical success rate is 84.0%−97.1%, and the incidence of complications is 19.5%.[28−30]

Reports show that FCSEMS and LAMS drainage of PFCs is safe and effective. Ang et al[31] state that recent studies that used either NAGI, SPAXUS or AXIOS stents reveal the technical success rate of PFCs was 91%−100%, in fact, a series of experiments showed that the clinical success rate of LAMS drainage for PFCs treatments, including PPC and WON, was 77%−100%. A recent systematic review including 344 patients who had PFCs drained with metal stents (including FCSEMS and LAMS), showed that the technical success rate, clinical success rate and mortality rate of the procedure were 100%, 98.3% and 1.7% respectively. The post-operative complications were mainly stent displacement, bleeding, and infection.[32]

There are few studies examining the efficacy of metal stent drainage on PFCs in China, especially LAMS. Jin et al[33] conducted the first study examining FCSEMS drainage of pancreatic pseudocyst in 2013. This retrospective study involved 11 patients, and found that the technical and clinical success rate of FCSEMS drainage were 100% and 73.7% respectively. Two patients experienced subsequent infection, while one patient experienced stent migration. Jin et al also suggest that adjusting the placement of the metal stents after procedure can prevent stent migration. Currently, a multicenter randomized controlled trial[34] examining the clinical efficacy of LAMS compared to double pigtail plastic stents (DPPS) in WON is being conducted and is expected to include 256 patients, which is designed to verify whether LAMS are superior to DPPS for WON.

The difference in clinical efficacy between metal stents and plastic stents for PFCs drainage is still the subject of controversy. Several studies reported no significant difference between mental stents and PS in their technical success rates, clinical success rates, or complication incidence rates.[19,35,36] However, three subsequent meta-analyses[37−39] have shown that metal stents have a higher clinical success rate and cause fewer complications than plastic stents. Mental stent placement requires a significantly shorter surgery than PS placement, but costs several times as much. Walter et al[40] speculate that while the initial cost of mental stents may be higher than PS,[18] the total cost of treatment is lower due to reduced operating time and a reduced number of necessary postoperative interventions (i.e. endoscopic necrospectomy).[41,42] Overall, these studies suggest that mental stents are superior to plastic stents for PFCs drainage.

Comparison of the clinical efficacy of stents between pancreatic pseudocyst and walled-off necrosis

Varadarajulu et al[43] suggest that plastic stent drainage is more efficacious in patients with PPC than in patients with WON. Watanabe et al[44] also suggest EUS-guided

plastic stent drainage has poor efficacy in WON due to the proportion of necrotic tissue in the cyst. They also propose that the enzyme levels in the cyst cavity may predict cyst recurrence. Thus one double-pigtail plastic stent is generally used for PPC, while multiple double-pigtail plastic stents are used for WON to reduce the risk of stent blockage. However, in some patients multiple plastic stents are not effective due to their limited diameter, as well as the difficulty and cost of placement.[45] For simple pancreatic cysts, there is no significant difference in drainage between 7-Fr and 10-Fr PS.[27]

Proper treatment for WON requires more effective drainage than PS, as well as access for direct endoscopic necrosectomy (DEN). LAMS may simplify and streamline EUS-guided treatment of WON. If necessary, a nasal cyst drainage tube or plastic stent can be placed inside the metal stent to assist in draining and flushing the cyst.[33] Hydrogen peroxide (H_2O_2) irrigation is an effective means of facilitating debridement and extracting debris in patients undergoing DEN as a preliminary means of managing WON. Siddiqui et al suggest that using LAMS to treat WON is both safe and feasible, having both a good success rate and a minimal rate of adverse events.[46,47] A LAMS with a diameter of 15 mm is six times more efficacious at treating WON than a LAMS with a diameter of 10 mm.[47] Another study from Siddiqui et al showed that the use of FCSEMSs and LAMSs for EUS-guided drainage/debridement of WON is superior to the use of DPPS.[48]

Endoscopic drainage should be performed when clinicians suspect the presence of liquid necrosis. More study is needed to determine whether endoscopic interventions are more effective than surgery for treating critical cases of WON involving large amounts of solid debris. Studies should specifically investigate the relationship between the quality/quantity of solid debris and clinical outcomes. EUS is better than computed tomography (CT) for defining the morphological characteristics of PFCs and quantifying solid debris.[49] If WON contains higher proportions of solid debris, conventional drainage involving the endoscopic implantation of a FCSEMS may not be effective. Clinicians should consider alternatives such as multiple transluminal gateway drainage.[50] However, some researches suggest no significant difference in the clinical efficacy of endoscopy between PPC and WON.[18,37,51] However, inconsistencies in PFCs differentiation between endoscopists may have been responsible for these negative results. Petrone et al[52] reported that the adverse event rate in the WON group was higher than the PP group. Therefore, complications related to endoscopic operations should be further studied.

The timing of stent removal

The appropriate time for stent removal has also been the subject of study. The time of stent removal has generally been determined using the absorption of the cyst, abdominal pain relief, the reduction of abdominal distension. Studies show that most stent placements last 1–3 months. A newly published meta-analysis shows that it is appropriate to remove the stent after 1 month, which is consistent with ESGE guidelines. Additional large-scale prospective cohort studies may be needed to further validate the proper time of stent removal, and to identify LAMS-related adverse reactions such as bleeding and buried stent syndrome.[53] Zhu et al[54] report a case in which the LAMS implantation time was extended to prevent the recurrence of a cyst. When the stent was removed after five months, they found that serious tissue adhesion made removing the stent difficult. Therefore, while extending the stent implantation time could reduce rate of cyst recurrence, it could also lead to difficult removal. Some experts suggest that patients should be imaged every three weeks after stent implantation to identify those suited for early stent removal to avoid these complications.[55]

Conclusion

For the endoscopic treatment of PFCs, the older DPPS has been replaced by FCSEMS, as well as LAMS. Although FCSEMS and LAMS are easier and faster to implant than DPPS, they may not be the best options for draining PPC due to their cost. However, for WON mainly composed of solid necrosis, metal stents are more suitable for drainage while also allowing access for direct endoscopic necrosectomy. Further studies are needed to verify the difference in clinical efficacy of endoscopic ultrasound-guided treatments between PPC and WON.

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Conflicts of interest

None.

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