Endoscopic and Percutaneous Drainage of Symptomatic Walled-Off Pancreatic Necrosis Reduces Hospital Stay and Radiographic Resources

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Walled off pancreatic necrosis (WOPN), a potentially serious complication of acute severe pancreatitis, has been conventionally managed surgically. Advances in interventional radiology and endoscopy have resulted in development of minimally invasive interventional radiological and endoscopic techniques for management of WOPN. The experience with these new techniques is limited but encouraging. These techniques involve multiple procedures and imaging techniques that adds on to the cost of the treatment. The authors of the current study had earlier described the technical aspects of combined modality therapy (CMT) for patients with symptomatic WOPN that involved combination of percutaneous large-bore catheter drainage with endoscopic transgastric or transduodenal stent placement into the necrotic fluid collection. In the current study the authors retrospectively compared the outcome of CMT (23 patients) with that of standard percutaneous drainage (SPD) alone (43 patients) in patients with symptomatic WOPN.

In patients with SPD group, radiologically guided percutaneous drainage of WOPN was done with aspiration of as much fluid as possible at the time of the drainage. This was followed by placement of 12 F drainage tubes that were irrigated with 10–20 mL of sterile saline 3 times daily. Percutaneous catheters were sequentially upsized to a maximum of 28F. In the CMT group, initially computed tomography (CT) guided drains were placed into the WOPN but in contrast to the SPD group, only 10 ml of the fluid was aspirated and then the drains were clamped. The patients then immediately underwent endoscopic transgastric or transduodenal drainage of the WOPN. Endoscopic ultrasound (EUS) was used when there was no definable luminal bulge. Endoscopic retrograde cholangiopancreatography (ERCP) was performed and if leak was present pancreatic duct stent was inserted. Biliary stent was placed in patients with biliary obstruction. A nasojejunal feeding tube was placed in all the patients. Antibiotics were given as per the culture sensitivity reports. Percutaneous drain tubes were removed when there was no fluid draining from them, clamping them did not cause symptoms and there was no residual collection on CT scan. Endoscopically placed transmural stents were removed if there was no pancreatic duct disruption, the fluid collection had resolved, and removal of percutaneous catheter did not result in fluid reaccumulation. In patients with disconnected pancreatic duct, transenteric stents were left in place indefinitely.

Forty-three patients (25 males) underwent SPD and 23 (18 males) underwent CMT of WOPN. There was no significant difference in the demographic profile of the two groups with biliary pancreatitis being the most frequent cause of acute pancreatitis in both the groups. The mean time until removal of the final percutaneous drain was significantly shorter in the CMT group in comparison to the SPD group (84 days versus 189 days respectively; \( p < .006 \)). Three patients in the SPD group developed pancreatic cutaneous fistulae that needed surgery whereas none of the patients in the CMT group developed external pancreatic fistulae or needed surgery. Three patients in the SPD group died during the course of therapy with drainage catheters in place (2 because of respiratory failure and 1 of multisystem organ failure) whereas only one patient in the CMT died (because of esophageal carcinoma). Five patients in the SPD group had pseudoaneurysmal bleed whereas none of the patients in the SPD group had pseudoaneurysmal bleed. Patients in the CMT group had significantly decreased length of hospitalization (26 vs. 55 days, \( p < .0026 \)), number of computed tomography scans (8.95 vs. 14.3, \( p < .002 \)), and percutaneous drain exchanges (6.5 vs. 13, \( p < .0001 \)).

Commentary

Surgical necrosectomy has been the accepted treatment modality for pancreatic necrosis. However, recently minimally invasive endoscopic and radiological therapeutic modalities have also been shown to be effective in treating WOPN. Endoscopic or radiological drainage alone has been shown to be safe and effective in treating patients with WOPN. However, these techniques are time consuming and require long hospitalization periods thus putting strain on limited hospital resources. Along with this, percutaneous drainage alone is associated with risks and complications like external pancreatic fistulae as well as repeated exposure to ionizing radiations. The authors of the current study have demonstrated that by combining the two techniques ie percutaneous drainage with endoscopic transmural drainage
Randomized Study

LBD or ML for the Management of Large Bile Duct Stones: A Prospective Randomized Study


Endoscopic common bile duct (CBD) stone removal is difficult in patients with large stones (>12 mm), multiple stones, barrel-shaped stones, and tapering course of CBD. Traditionally these patients have been either treated surgically or endoscopic removal of these stones has been attempted after mechanical lithotripsy (ML). Advent of endoscopic large balloon dilatation (LBD) of the papilla following endoscopic sphincterotomy (EST) has offered an alternative for removal of difficult CBD stones. However, the initial enthusiasm with this technique of LBD dampened because of reports of increased risk of pancreatitis.[3] Despite this risk of pancreatitis, LBD is an effective alternative for management of patients with difficult CBD stones. The authors of the current study therefore conducted a prospective randomized controlled trial to compare the therapeutic benefits and complications of EST followed by LBD or ML for the management of large bile duct stones.

A total of 90 patients with large bile duct stones (12 – 20 mm) were randomized to EST followed by LBD (n = 45) or EST followed by ML (n = 45) [no significant difference in the stone size as well as the CBD diameter between the two groups]. Randomization was performed using the sealed envelope technique and all the ERCP’s were performed by a single operator. Patients needing precut for CBD access, with stones more than 20 mm or with accidental pancreatogram were excluded from the study. In both the groups, complete EST was accomplished by extending the cut up to the major horizontal fold crossing the intramural portion of the bile duct. The patients in the LBD group underwent balloon dilatation with CRE Esophageal/Pyloric balloon, maximum diameter 15, 18, or 20 mm; length 5 cm. (Boston Scientific, Natick, MA). The size of the balloon used was chosen according to the diameter of the bile duct stones and care was taken that it should not exceed the maximum diameter of the bile duct. The balloons were gradually inflated till the waist was obliterated and after that the balloons remain inflated for 10 to 12 seconds. The mechanical lithotripsy was done using a mechanical lithotriptor (BML-4Q, Lithocrush 201 or 202Q; Olympus Optical).

Out of 45 patients in the LBD group, complete CBD clearance was possible in 44 patients (97.7%) whereas complete CBD clearance was possible in 41 out of 45 (91.1%) patients in ML group and this difference was not statistically significant. A subgroup analysis, taking into account the bile duct stone size also did not reveal a statistical significant difference in the success rate between the two groups. Presence of a very tortuous CBD resulted in failure of removal of CBD stones in the LBD group whereas failure in ML group was due to basket being broken on a hard stone (1 patient) or inability to capture the stone (3 patients). Significantly more number of complications were noted in the ML group in comparison to the LBD group (9 vs. 2 patients; p = 0.049). One patient in each group developed post-ERCP pancreatitis which was mild and self-limiting and was managed conservatively. Six patients in the ML group developed cholangitis whereas none in the LBD group developed cholangitis (p = 0.026). Post ERCP bleeding was noted in one patient in each group. One patient in ML group developed CBD perforation whereas none of the patients in LBD group developed it.

Commentary

The authors of the current study have shown that EST followed by LBD is equally effective as EST followed by ML for the removal of large bile duct stones, but is associated with fewer complications. This is a prospective randomized study that has shown that LBD is safe and effective and the risk of pancreatitis is low (a feared side effect that has limited its use). The authors believe that the low risk of pancreatitis in their study could be because of the expertise of the endoscopists performing the ERCPs, as well as by the fact that the authors excluded patients at increased risk of pancreatitis (>5 accidental pancreatograms or use of needle knife precutting).
Also some other studies have also shown that LBD is safe with low risk of pancreatitis as the biliary and pancreatic orifices are separated by previously performed EST.[4] The authors also left the balloon inflated for 10 to 12 seconds only after obliteration of the waist and they believed that this shorter time of inflation could also have decreased the risk of pancreatitis. However, this hypothesis is contrary to an earlier published randomized study comparing 1 minute vs. 5 minute of endoscopic balloon dilatation of intact biliary sphincter where the authors have shown that 5 minute balloon dilatation is associated with better efficacy of stone extraction and reduced risk of pancreatitis.[5] The authors of this study hypothesized that post-ERCP pancreatitis is primarily related to postprocedure papillary edema and outflow obstruction rather than intraprocedural occlusion of the pancreatic sphincter by the balloon and therefore dilations of up to 1 minute, as is typically done, are inadequate and produce excessive postprocedure edema.

Also, the authors have demonstrated that ML is associated with more risk of complications like cholangitis when compared to LBD where none of the patients developed cholangitis. The authors believed that higher cholangitis rate in patients in ML group could be because of trauma to the CBD wall by the lithotriptor wires as well as edema at the sphincterotomy site and / or inadequate sphincterotomy could also contribute to the higher cholangitis rate. The current prospective randomized study has shown that LBD is safe and effective and is associated with fewer complications than ML and importantly the risk of pancreatitis is low and comparable between the two groups.

**References**


**Covered versus uncovered self-expandable nitinol stents in the palliative treatment of malignant distal biliary obstruction: results from a randomized, multicenter study**


The first study was a RCT conducted to compare differences in stent patency, patient survival, and complication rates between covered and uncovered nitinol stents. in patients with malignant biliary obstruction. This multicenter trial was conducted between January 2006 and October 2008, at 10 sites in Sweden. A total of 21 endoscopists with 4 to 25 years of experience performing ERCP participated.

The randomization process, was done in blocks of 20 (10:10) when the patient was in the ERCP suite and after the guidewire had passed the stenosis. The endoscopist opened an opaque sealed envelope with computer-generated random numbers. A total of 400 patients with unresectable distal
malignant biliary obstruction were included. The most common cause of obstruction was pancreatic cancer, which occurred in 76% and 77% in the cSEMS group and uSEMS group, respectively. The trial compared a polycarbonate-polyurethane covered nitinol stent with an uncovered nitinol metal stent (Nitinella; ELLA-CS, Hradec Kralove, Czech Republic). The membrane of the covered stent was placed inside of the metal mesh, and only the distal 5 mm of the covered stent was uncovered. The endoscopist decided the length of SEMS to use—either 52 or 72 mm. All stents had an inner diameter of 10 mm.

The criteria for a successful stent insertion included radiological confirmation (at ERCP), and at least a 30% decrease in bilirubin level during the first 5 days after stent insertion. Clinical follow-up was performed once per month, starting at 1 month, and the endpoint was 12 months after randomization.

The investigators found that patient survival times were 116 days and 174 days in the cSEMS and uSEMS groups, respectively (p=0.320). The first quartile stent patency time (the day when 25% of the stents had occluded) was 154 days in the covered stent group and 199 days in the uncovered stent group (p =0.326). There was no difference in the incidence of pancreatitis or cholecystitis between the 2 groups. Stent migration occurred in 6 patients (3%) in the covered group and in no patients in the uncovered group (p=0.030). The majority of patients in both groups died within 12 months with a patent stent. Ten percent of the patients in the cSEMS group and 15% in the uSEMS group were alive at 12 months with a patent stent.

The authors concluded that there was no significant difference in patient survival or stent patency time between cSEMS and uSEMS in the palliative treatment of malignant distal biliary obstruction. There was no increase in risk of cholecystitis or pancreatitis when using cSEMS.

**Commentary**

The primary objective of the study was stent patency, and no difference was found in this end point between the uSEMS and cSEMS. The frequency of observed stent failure also occurred in nearly equal proportion - 24% and 23% for cSEMS and uSEMS, respectively. Important mechanisms causing stent occlusion are tumor overgrowth and ingrowth, which in this series occurred in 27 patients (13%) in the cSEMS group and in 31 patients (15%) in the uSEMS group. However, a significant difference in the frequency of ingrowth was found between cSEMS in 9 patients (5%) and uSEMS in 21 patients (11%), as would be expected. Stent obstruction by sludge formation and encrustation occurred more often with cSEMS (6% vs 2%). This is in agreement with findings by others who have reported sludge formation, with or without food impaction, to be the most common cause of stent occlusion in cSEMS.

One must remember that it is notoriously difficult in most cases to distinguish between overgrowth, ingrowth, and encrustation. In the present study the mechanisms of stent dysfunction was mainly based on cholangiographic findings, which may be subject to observer error.

There has been an apprehension that cSEMS might increase the prevalence of cholecystitis and pancreatitis by blocking the cystic duct and the pancreatic duct orifice. However in this study cholecystitis occurred in 2 patients (1%) in each group, which is similar to previously reported incidence. Similar findings were reported in the second study described below.

Migration of cSEMS has been reported to occur in 6% to 12% of cases, more often with stents made of stainless steel than in those made with nitinol. In this series also migration of cSEMS occurred in 6 of 200 patients (3%) compared with none in the uSEMS group—a significant but small difference.

**References**


**A randomized trial comparing uncovered and partially covered self-expandable metal stents in the palliation of distal malignant biliary obstruction**


This second multicenter RCT was conducted in 4 teaching hospitals in Canada and US. Adults with inoperable distal malignant biliary obstruction were included. From
October 2002 to May 2008, 129 patients were randomized. Distal obstruction was defined in this study, as being ≥1 cm distal to the biliary hilum. As in the previous study, subjects were randomized at the time of the ERCP after successful placement of a guidewire across the malignant stricture, using sealed envelopes. Either an uncovered Wallstent or a Permalume membrane partially covered Wallstent (Boston Scientific Corporation, Natick, Mass, USA) was used. Follow-up data were collected by telephone interview conducted by a research assistant, 1 week after stent insertion and then monthly until patient death. The primary study outcome was time to recurrent biliary obstruction, and secondary outcomes of interest were patient survival, serious adverse events, and the mechanism of recurrent biliary obstruction.

Recurrent biliary obstruction was observed in 11 of 61 uSEMS (18%) and 20 of 68 cSEMS (29%). The median times to recurrent biliary obstruction were 711 days and 357 days for the uSEMA and cSEMS groups, respectively (p = 0.530). Median patient survival was 239 days for the uSEMS and 227 days for the cSEMS groups (p = 0.997). Serious adverse events occurred in 27 (44%) and 42 (62%) patients in the uSEMS and cSEMS groups, respectively (p = 0.046). None of the uncovered and 8 (12%) of the partially covered SEMS migrated (p = 0.0061). Cholecystitis developed in 3 patients in each treatment group.

The authors concluded that there was no significant difference in time to recurrent biliary obstruction or patient survival between the partially covered and uncovered SEMS groups. Partially covered SEMS were associated with more serious adverse events, particularly migration.

Commentary

A previously published randomized trial in 2004 demonstrated improved stent patency and an absence of tumor ingrowth with a cSEMS compared with an uSEMS.[1] However, the cSEMS used in this study is not commercially available. A subsequent retrospective cohort study[2] and a prospective cohort with a retrospective comparison group[3] did not demonstrate a difference in stent patency between uncovered and partially covered SEMS. Hence although there is some suggestion that covering a SEMS may increase the duration of stent patency, there is no firm data in this regards. In addition, there is some concern that cSEMS may be associated with an increased incidence of cholecystitis, pancreatitis, and distal migration due to lack of tissue embedding.

The planned sample size for this study was 136 patients, but the study was closed before reaching this goal because of slow accrual. The results of this study did not demonstrate a difference in the time to recurrent biliary obstruction or patient survival between the two stents, but did demonstrate a higher incidence of serious adverse events in those patients who received a cSEMS. Migration of the covered stents contributed to recurrent biliary obstruction in 6 cases.

Migration caused duodenal perforation in two cases and contributed to upper GI hemorrhage in one. Duodenal perforation secondary to biliary SEMS migration has not been reported previously. Cholecystitis after cSEMS placement may occur in up to 10% of patients, but was not seen at an increased rate in this study (7% in both cSEMS and uSEMS groups).

In an accompanying editorial in the same issue Willingham states that although not currently indicated for late removal, it is possible that the covered stents, with their inherent propensity to migration and prevention of ingrowth, could be of benefit when the quality of late removability is desired, and the diagnosis of malignancy is not definitely established.[4] In conclusion, the message from these two studies is that cSEMS, although safe, offer no real advantage for patients with distal biliary obstruction.

References


Prediction of drainage effectiveness during endoscopic stenting of malignant hilar strictures: the role of liver volume assessment


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The optimal endoscopic approach to the drainage of malignant hilar strictures remains controversial, especially with regards to the extent of desirable drainage and unilateral or bilateral stenting. In this study the records of all 188 patients who underwent endoscopic stenting for malignant
hilar strictures between January 1996 and December 2005, at two academic tertiary referral centers in the greater Paris area (Cochin Hospital and Bicêtre Hospital), were reviewed. Among these, the authors included 107 patients for whom a CT scan performed during the week before ERCP, and clinical and biological data on the day of ERCP and 30 days later, were available. Bismuth I strictures were excluded, as the authors felt that a single stent was sufficient in these cases. All 107 included patients had Bismuth type II-IV strictures. The objective of the study was to identify useful criteria for predicting successful endoscopic drainage.

The volumetry of the 3 main hepatic sectors (left, right anterior, and right posterior) was assessed on CT scans. The liver volume drained was estimated and classified into one of three classes: < 30%, 30% to 50%, and >50% of the total liver volume. The primary study outcome was effective drainage, which was defined as a decrease in the bilirubin level of >50% at 30 days after drainage. Secondary outcomes were early cholangitis rates, and survival.

The main factor associated with drainage effectiveness was a liver volume drained of >50% (odds ratio 4.5, \( p=0.001 \)), especially in Bismuth III strictures. Intubating an atrophic sector (<30% of liver volume) was useless and increased the risk of cholangitis (odds ratio 3.04, \( p=0.01 \)). A drainage volume >50% was associated with a longer median survival (119 vs. 59 days, \( p=0.005 \)).

The key conclusion of this study was that draining more than 50% of the liver volume, which frequently requires bilateral stent placement, was an important predictor of drainage effectiveness in malignant hilar strictures, especially Bismuth III. A pre-ERCP assessment of hepatic volume distribution on cross-sectional imaging may optimize the endoscopic procedures.

**Commentary**

Draining of only 25% of the liver has been believed to be the minimal requirement for relief of jaundice.[1] This dogma has been challenged by the current study, which concludes that draining > 50% of liver volume is a major predictor of drainage effectiveness and prolonged survival in malignant hilar strictures, especially Bismuth type III. Drainage of > 50% of the liver volume, generally involves drainage of at least two plastic stents to drain two hepatic sectors. It is to be noted that patients with Bismuth I strictures were excluded from the current study. The only RCT found that unilateral stenting was more efficient, but in this study one-third of patients had Bismuth I stricture.[2]

The volume of the liver drained was estimated from a review of the CT scans performed during the week before ERCP. Each sector (left, right anterior, and right posterior) was classified as <30%, 30% to 50%, or >50% of the total liver volume. A sector was considered atrophic if it accounted for < 30% of the whole liver volume. If the tumor extended to > 75% of a sector volume, this sector was also considered as having <30% volume. Normalization of serum bilirubin was achieved in 32% of the patients at day 30.

Several limitations of the current study need to be highlighted. First, this was a retrospective study encompassing a 10-year period. Only 60% of the 188 patients with malignant hilar strictures treated during the study period were included. The authors state that the Bismuth type was defined based on the preoperative MRCP ‘when available’ and confirmed or otherwise established during ERCP. However, in a separate section it is stated that contrast was ‘selectively’ injected, and injection into atrophic segments was avoided. This discrepancy casts doubts on the accuracy of Bismuth staging. If complete opacification of the intrahepatic segments was attempted, it would incur significant risks of cholangitis. As such cholangitis developed in 37% of cases overall. The method of volumetry was also very rudimentary, but practical for a clinical study. There are now several automated liver volumetry protocols available like MeVis systems. Use There is currently a limited role for plastic stent placement in malignant hilar strictures. In an accompanying editorial on the paper, Kozarek explicitly states that ‘in 2010, the treatment of unresectable hilar malignancies has evolved into placement of one or more metal prostheses, particularly in patients with the potential for prolonged survival.[3] The only possible exceptions would be patients for whom endoscopically facilitated photodynamic therapy or brachytherapy is planned.

Despite these limitations, there are important messages in this study. It reiterates that injecting contrast into undrained ducts is associated with cholangitis, and a decreased survival rate. It therefore reinforces, the importance of preoperative staging and procedural planning, particularly with MRCP, before any attempted endoscopic approach to a hilar lesion.

**References**


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