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Sphincterotomy to Prevent PEP After FCSEMS placement

ENDOSCOPY

Mohammad Bilal, MD, FACG

Associate Professor of Medicine, University of Colorado Anschutz Medical Center, Aurora, CO

Mohammad Bilal, MD, FACG
Associate Editor

This summary reviews Onnekink AM, Gorris M, Bekkali NL on behalf of the Dutch Pancreatic Cancer Group, *et al.* Endoscopic sphincterotomy to prevent post-ERCP pancreatitis after self-expandable metal stent placement for distal malignant biliary obstruction (SPHINX): A multicentre, randomised controlled trial. *Gut* 2025;74:246-254.

Correspondence to Mohammad Bilal, MD, FACG. Associate Editor. Email: EBGI@gi.org

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STRUCTURED ABSTRACT

Question: Does endoscopic sphincterotomy prior to fully covered self-expanding metal stent placement (FCSEMS) reduce the risk of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) in patients with suspected distal malignant biliary obstruction (MBO)?

Design: Multicenter, randomized, open-label, controlled superiority trial.

Setting: Seventeen hospitals (16 Dutch and 1 Spanish hospital including academic and teaching centers).

Patients: Adults aged 18 years or older with suspected distal MBO undergoing

ERCP with FCSEMS placement. Two hundred and ninety-seven patients were randomized (156 to sphincterotomy and 141 to control). Exclusion criteria included benign biliary stenosis, prior sphincterotomy, hilar obstruction, prior pancreatic duct (PD) stenting, coagulopathy, or inability to stop anticoagulants.

Exposure or Interventions: Patients were randomized to either undergo endoscopic sphincterotomy or no sphincterotomy prior to FCSEMS placement. All patients received standard FCSEMS 10 mm in diameter and the majority of patients received stents 6 cm in length. However, 4 cm and 8 cm in length stents were also placed depending on anatomical considerations. Patients also received rectal nonsteroidal anti-inflammatory drugs for PEP prophylaxis. Procedures were performed under direct supervision of expert endoscopists.

Outcomes: The primary outcome was PEP within 30 days, as defined per modified Cotton criteria: (1) onset of new or worsened abdominal pain requiring new or prolonged hospital admission and (2) an elevation of pancreatic enzymes (amylase and/or lipase) of ≥3 times upper limit of normal at more than 24 hours after the procedure.[1] Secondary outcomes included severity of PEP, technical success, bleeding, perforation, cholangitis, cholecystitis, stent-related morbidity, and 30-day mortality.

Data Analysis: Intention-to-treat and per-protocol analyses were conducted. Categorical variables were compared using Fisher's exact test, and continuous variables compared with Student's *t*-test or Mann-Whitney U test. Relative risk (RR) with 95% confidence intervals (CIs) were reported. Interim analysis was performed and the study was terminated early due to futility.

Funding: Cook Medical Europe partially reimbursed stents but had no role in the study design, data collection, analysis, or manuscript preparation.

Results: Overall, 297 patients were included in the intention-to-treat analysis, with 156 in the sphincterotomy group and 141 in the control group. PEP occurred in

17% of sphincterotomy vs 21% of control patients (RR 0.78, 95% CI 0.49–1.26; *P*=0.37). There were no significant differences in bleeding, perforation, cholangitis, or cholecystitis. 30-day mortality was 6% vs 4%. The study was terminated early after interim analysis showed futility.

COMMENTARY

Why Is This Important?

PEP is the most common adverse event of ERCP, and rates are high—especially due to FCSEMS placement. This is hypothesized to be the result of pancreatic outflow obstruction caused by the radial forces of the FCSEMS on the orifice of the PD.[2] While endoscopic sphincterotomy is frequently performed to reduce this risk, high-quality prospective evidence validating its benefit in the context of FCSEMS placement is lacking. The SPHINX trial attempts to address this gap through a randomized controlled design and provides important data to inform best practices in managing patients with distal MBO undergoing ERCP.

Key Study Findings

The trial demonstrated that endoscopic sphincterotomy before FCSEMS placement did not significantly reduce the risk of PEP compared to no sphincterotomy. The rates of PEP were 17% vs. 21% (RR 0.78, *P*=0.37), and no significant differences were found in adverse events such as bleeding, perforation, cholangitis, or cholecystitis.

Caution

The results of the study need to be interpreted with the following caveats. This study was terminated early due to futility and slower-than-expected enrollment, which reduced statistical power to detect more modest differences. Additionally, patients who could not undergo randomization due to technical difficulties during ERCP (e.g., pre-cut sphincterotomy or prophylactic PD stenting) were excluded, potentially limiting generalizability. In addition to these factors, the rate of PEP in this study are extremely high (17% and 20% in both groups). These rates are high especially considering the population included in this study, patients with suspected distal MBO, are typically not considered as high-risk patients for PEP. Also, incidental PD cannulation was seen in 33% of patients in the sphincterotomy group compared to 28% of patients in the control group, which is a known risk factors for PEP.[3]

There was no mention of PD stent placement in these patients which is a critical intervention shown to reduce the rates of PEP.[4] It would have been interesting to see if PD stents were placed in patients where deep PD guidewire cannulation was achieved, and if there was any difference in PEP rates. Also, a subgroup analysis excluding patients where PD cannulation was achieved would have also provided valuable insight. Lastly, the risk of biliary sphincterotomy in this cohort of patients is low. The main risks of biliary sphincterotomy are bleeding and perforation and both these adverse events can be treated with FCSEMS placement.[5,6] Therefore, whether the performance of sphincterotomy in the vast majority of these patients with MBO adds additional risks is unclear.

My Practice

My practice for patients with MBO who need a FCSEMS does not change significantly with the results of this trial. The high rates of PEP in this trial are unclear and could be attributed to the fact that only <50% of ERCPs were characterized as easy cannulations. Another factor highlighted by the authors is variable operator experience of endoscopists performing ERCP. My practice in these cases where PD is cannulated is to place a small caliber PD stent with features that would allow spontaneous passage of PD stent to reduce the risk of PEP.

In addition, as this randomized controlled trial shows that there was no difference in rate of other adverse events in both groups, my practice of performing a biliary sphincterotomy in these patients unless sphincterotomy is higher risk (in patients with coagulopathy, bleeding disorders or those in which anticoagulation cannot be stopped) will not change. Lastly, 4% of patients who developed PEP in this study died of severe acute pancreatitis. Therefore, in summary, this study reinforces that placement of FCSEMS in MBO carries a higher risk of PEP and this should be incorporated in consent considerations.

For Future Research

Future research is needed to compare the impact of PD stent placement on reduction of PEP in patients with MBO undergoing FCSEMS placement.

Conflict of Interest

Dr. Bilal is a consultant for Boston Scientific, Steris Endoscopy, Aspero Medical and Cook Medical.

Abbreviations

CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography; FCSEMS, covered self-expanding metal stent placement; MBO, malignant biliary obstruction; PD, pancreatic duct; PEP, Post-ERCP pancreatitis; RR, relative risk.

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