ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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ERCP and Mortality

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G&H What are the most common indications for the use of endoscopic retrograde cholangiopancreatography?

SH Endoscopic retrograde cholangiopancreatography (ERCP) is an advanced endoscopic procedure. Although initially developed as a diagnostic modality, ERCP is now primarily a therapeutic procedure. The many indications for ERCP broadly involve diseases of the biliary tree and pancreas. The most common indications among biliary diseases include removal of stones from the biliary tract, assessment and treatment of benign and malignant biliary strictures, treatment of postoperative bile leaks, and assessment and treatment of select patients with suspected sphincter of Oddi dysfunction (SOD). Of note, based on the recent EPISOD trial, ERCP should not be used in those with postcholecystectomy biliopancreatic pain without objective findings (type 3 SOD). Common indications among pancreatic diseases include assessment and treatment of pancreatic duct stones, strictures, and pancreatic pseudocysts related to acute and chronic pancreatitis. ERCP can also be used to evaluate those with unexplained recurrent acute pancreatitis.

G&H What are the risks and benefits of ERCP?

SH ERCP is a powerful tool. It permits nonsurgical management of a wide spectrum of benign and malignant biliopancreatic diseases. It has been shown to be effective as well as cost-effective for many indications.

However, ERCP is associated with real and significant risks to patients. These risks include cardiopulmonary complications, bleeding, perforation, and—typically the most feared complication—pancreatitis. Although generally quoted to complicate 5% of all ERCP procedures, there is, in fact, a wide range of risk for post-ERCP pancreatitis, which can be higher than 20% in patients with suspected SOD. Interventions such as prophylactic pancreatic duct stenting and rectal indomethacin can lower this risk significantly. Nevertheless, post-ERCP pancreatitis can result in tremendous morbidity and can even result in death. It is, therefore, critical that the procedure be reserved for those most likely to benefit.

G&H What was previously known about ERCP and patient mortality?

SH A number of studies have evaluated the impact of ERCP on mortality and health care utilization among patients with acute cholangitis, choledocholithiasis, and acute pancreatitis. Early ERCP has been shown to reduce mortality in patients with acute cholangitis but not among patients with acute pancreatitis in the absence of obstructive jaundice. A meta-analysis of randomized trials also concluded that ERCP performed within 72 hours reduced mortality in patients with cholangitis but not in patients with acute pancreatitis without biliary obstruction. Early ERCP has also been shown to improve morbidity in patients with acute biliary conditions, whereas delays in ERCP increase hospital length of stay and health care costs.

However, many of the studies performed to date in this field have been limited by small sample size, short-term follow-up, and an inability to account for key confounders such as patient comorbidity. Furthermore, nationwide population-based studies evaluating the effect of ERCP on mortality in real-world settings have been lacking.

G&H What did you expect to find in your recent study on ERCP and mortality?

SH Given the evolution of ERCP from a diagnostic to a primarily therapeutic procedure as well as advancements in ERCP techniques and interventions to reduce the risk of pancreatitis, my colleagues and I hypothesized that in-hospital mortality from acute pancreaticobiliary conditions requiring ERCP has decreased over time. Furthermore, we hypothesized that improvements in mortality would be independently associated with ERCP treatment success.

G&H Could you discuss your study design, source of data, and measured outcomes?

SH We conducted a cohort study using administrative data from the Nationwide Inpatient Sample (NIS) database for the years 1998 to 2008. The NIS is the largest all-payor database in the United States and employs stratified random sampling to ensure that it is representative of the US population, accounting for approximately 90% of all hospitalizations. We then used the International Classification of Diseases, 9th Revision, to identify adult patients hospitalized with a primary diagnosis of cholangitis, acute pancreatitis, or choledocholithiasis between 1998 and 2008. Patients who did not undergo same-stay ERCP were excluded to ensure that only patients with suspected biliary obstruction were captured.

The primary outcome was in-hospital mortality from 2003 to 2008 compared with 1998 to 2002, but we also looked at hospital length of stay and charges. Although the primary exposure was time period, we also examined the effect of a number of patient and procedural variables on the outcomes of interest. In addition, a number of sensitivity analyses were completed, including propensity-score matched analyses to control for confounding by indication.

G&H What were your study findings?

SH Between 1998 and 2008, there were 166,438 admissions that met our inclusion criteria for analysis. Mortality decreased from 1.1% in 1998 to 0.6% in 2008, and there was a 30% reduction in mortality between the time periods 2003 to 2008 and 1998 to 2002 after adjusting for age, sex, race, health insurance, comorbidities, and hospital and procedural characteristics. This is a significant finding, especially given that the proportion of patients with multiple comorbidities increased over time. Of note, unsuccessful ERCPs and the need for an open cholecystectomy were associated with increased mortality. Furthermore, unsuccessful ERCPs, open cholecystectomies, and ERCPs performed later than 3 days after admission were linked to significant increases in hospital length of stay and costs of hospitalizations.

G&H What were the limitations of your study?

SH In the NIS database, because each record represents a single hospitalization, not a person, there can be multiple records for an individual if he or she has several hospitalizations. Given that the NIS database is unable to link individual patients within or between hospitals, we could not adjust for within-patient correlations. Similarly, we had to exclude patients transferred to other institutions, as we could not determine their survival status, diagnoses, or interventions before transfer. This represented a minority of the excluded cases. In addition, many of the diagnostic and procedure codes that were used in our study have not been validated. As well, given that the dates of diagnoses were not available, we could not identify cases of post-ERCP pancreatitis to examine its effect on mortality. Finally, our conclusions are limited to in-hospital same-stay deaths.

Despite these limitations, the study also has important strengths. Our sample size was very large, and using the NIS allowed for nationwide, population-based study of important and relatively uncommon outcomes, such as mortality in a real-world setting.

G&H Do you think that the transition from a largely diagnostic to an almost exclusively therapeutic modality has affected mortality from ERCP?

SH Unfortunately, our study did not address this issue specifically. However, we did look at ERCP type (diagnostic vs therapeutic) over time and found that the proportion of purely diagnostic ERCPs dropped from nearly 29% in 1998 to 10% in 2008. Therapeutic ERCPs for acute biliary diseases have a greater chance of being beneficial to patients during a hospital stay than a diagnostic procedure in which the risks may in fact outweigh the benefits.

G&H Did you form an impression of the effect of endoscopic ultrasound on ERCP utilization and, by extension, mortality?

SH Unfortunately, this question cannot be directly answered by our study. One might predict that the decrease

in proportion of diagnostic ERCPs observed over time was accompanied by an increase in the use of less invasive diagnostic modalities, such as endoscopic ultrasound (EUS) and magnetic resonance cholangiopancreatography (MRCP). This is certainly hoped. However, despite the unproven validity of the procedure codes used, it was surprising that only approximately one-third of patients undergoing ERCP for acute cholangitis, choledocholithiasis, and acute pancreatitis were coded as having removal of gallstones. This suggests that many patients, even in the later time period, underwent ERCP after spontaneous passage of stones. Therefore, if anything, our study suggests that EUS continues to be underutilized in cases of intermediate biliary stones and that many additional ERCPs could be avoided. Whether this might translate into further reductions in mortality needs to be explored.

G&H How can the rate of unsuccessful ERCPs be reduced, and how can the use of ERCP in general be further optimized?

SH Our study suggests that unsuccessful ERCPs increase the risk of in-hospital mortality. Why this relationship exists is not entirely clear. Do hospitalized patients requiring ERCP who have unsuccessful procedures have more severe disease? Or does a failed ERCP lead to iatrogenic complications that subsequently increase the risk of death? Further work in this area is warranted. ERCP is a highly specialized procedure that requires dedicated training and maintenance of competency. We have to respect this. Although my colleagues and I did not demonstrate an association between hospital ERCP procedural volume and mortality, this does not mean that volume standards for ERCP are unimportant. It is paramount to stress that other researchers have demonstrated relationships between ERCP volumes and patient outcomes. Moreover, we could not explore procedural volumes at an individual provider level, which are likely important. It has previously been shown that patients who undergo ERCP at high-volume centers experience a shorter hospital length of stay. Furthermore, ERCP failure rates are higher among lower-volume ERCP endoscopists. When taken together, the literature points to volumes being important. We should strive as subspecialists to respect this and prioritize the provision of the highest-quality procedures to our patients.

It is encouraging that diagnostic ERCPs are declining. However, our study does suggest that patients with passed stones continue to undergo ERCP. Serial clinical and laboratory data obtained during active patient follow-up, combined with less invasive yet highly sensitive diagnostic interventions, including EUS and MRCP, need to be emphasized. Readily available EUS and MRCP for indeterminate cases or, better yet, combined same-procedure EUS immediately followed by ERCP when indicated should arguably be the standard.

Those performing ERCP should take pause and only perform the procedure when the need for therapeutic intervention is believed to be high. Furthermore, in my opinion, ERCP services should be focused in centers offering the full complement of diagnostic and therapeutic strategies where expert high-volume endoscopists practice.

G&H What are the next steps in research in this area?

SH Many ERCPs are performed in outpatient settings for less urgent indications than we examined in our study. We need to look at the impact of ERCP on patient outcomes, including mortality, while exploring the factors we have discussed in outpatient populations, where the margin of benefit to risk is lower. Further research evaluating ERCP performance characteristics and the role of the endoscopist on patient outcomes is also needed.

Dr Heitman has no relevant conflicts of interest to disclose.

Suggested Reading

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