Comparison of Adverse Events for Endoscopic vs Percutaneous Biliary Drainage in the Treatment of Malignant Biliary Tract Obstruction in an Inpatient National Cohort

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**IMPORTANCE** Nonsurgical biliary drainage in malignant biliary tract obstruction can be performed endoscopically by endoscopic retrograde cholangiopancreatography (ERCP) or by percutaneous transhepatic biliary drainage (PTBD). The published body of literature to support either approach is surprisingly sparse, is conflicting on the preferred approach, and is limited by small studies with heterogeneous groups.

**OBJECTIVE** To evaluate the procedure-related adverse event rate with endoscopic vs percutaneous drainage in patients with malignant biliary tract obstruction.

**DESIGN, SETTING, AND PARTICIPANTS** This was a retrospective analysis from the National Inpatient Sample (NIS) database from 2007 through 2009. Data analysis was performed in 2015. Patients from the NIS database are representative of the US population and are included from both community and tertiary care hospitals in the United States.

**MAIN OUTCOMES AND MEASURES** Procedure-related adverse event rates.

**RESULTS** A total of 7445 patients were included for ERCP and 1690 for PTBD. The overall adverse event rate was 8.6% for endoscopic drainage (640 events) and 12.3% for percutaneous biliary drainage (208 events) ($P < .001$). When analyzed by type of malignant neoplasm, ERCP was associated with a lower rate of adverse events compared with PTBD for pancreatic cancer (2.9% vs 6.2%; odds ratio [OR], 0.46 [95% CI, 0.35-0.61]; $P < .001$) and cholangiocarcinoma (2.6% vs 4.2% OR, 0.62 [95% CI, 0.35-1.10]; $P = .10$). For pancreatic cancer, endoscopic procedures were associated with a lower rate of adverse events regardless of the volume of percutaneous procedures performed by a center. For cholangiocarcinoma, centers that performed a low volume of percutaneous biliary drainage procedures were more likely to have adverse events compared with endoscopic procedures performed at the same center (5.7% vs 2.5%; OR, 2.28 [95% CI, 1.02-5.11]; $P = .04$). In centers that performed a high volume of percutaneous drainage procedures, rates of adverse events were similar to those of endoscopic adverse events (3.5% vs 3.0%; OR, 1.18 [95% CI, 0.53-2.66]; $P = .68$).

**CONCLUSIONS AND RELEVANCE** Our results support the finding that endoscopic biliary drainage for malignant biliary obstruction is a first-line intervention. Endoscopic drainage is superior to percutaneous drainage, in regard to adverse event rate, for patients with pancreatic cancer. For patients with cholangiocarcinoma, endoscopic drainage is superior in centers that perform a low volume of percutaneous biliary drainage procedures.

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Biliary drainage is the cornerstone of treatment of various malignant biliary disorders, such as pancreatic cancer and cholangiocarcinoma. Biliary drainage allows for symptom relief of jaundice and pruritus, for normalization of liver function tests, and, in addition, allows for a diagnosis by biopsy or cytology brushing.

Biliary drainage can be achieved by both surgical and nonsurgical means. Nonsurgical means are usually preferable given the minimally invasive nature of these approaches. In addition, a nonsurgical method results in shorter inpatient stays and fewer initial complications. The 2 best established nonsurgical methods are an endoscopic approach by endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic biliary drainage (PTBD) performed by interventional radiology.

It is often debated which approach is preferable for patients requiring biliary drainage for malignant biliary tract obstruction (MBTO). The published body of literature to support either approach is surprisingly sparse. Only 3 small randomized clinical trials (RCTs) looking at ERCP vs PTBD in patients with malignant neoplasms have been reported. In 1987 Speer et al observed that ERCP had a significantly higher success rate for relief of jaundice (81% vs 61%; \( P = .02 \)) than PTBD and a significantly lower 30-day mortality (15% vs 33%; \( P = .02 \)). The higher mortality rate after percutaneous stents was related to hemorrhage and bile leaks. The second RCT (Pifó et al) from 2002 compared PTBD with self-expanding metal stents to conventional endoscopic polyethylene stents. The technical success rates of both procedures were similar (PTBDs, 75%; ERCP, 58%; \( P = .29 \)). Major complications were noted to be more common (although they were not statistically significant) in the percutaneous group (61% vs 35%; \( P = .09 \)). The 30-day mortality rates were similar in both procedures (PTBD, 36%; ERCP, 42%; \( P = .83 \)). A third RCT involved only patients with gallbladder cancer with hilar strictures. This study found that PTBD was more successful in providing biliary drainage compared with ERCP (89% vs 41%; \( P < .001 \)) and had less rates of infection (48% vs 11%; \( P = .002 \)).

More recently, Zhao et al published a meta-analysis incorporating 5 retrospective studies and the 3 aforementioned RCTs. A total of 692 patients were included. All of the retrospective studies involved patients with hilar tumors, a factor deemed more favorable for percutaneous drainage. The meta-analysis reported a trend toward advantage for PTBD in regard to technical success (odds ratio [OR], 2.18; 95% CI, 0.73-6.47; \( P = .16 \)) with significantly lower rates of infection in PTBD (OR, 0.59; 95% CI, 0.37-0.93; \( P = .02 \)).

A major deficiency in the published literature is the number of patients enrolled in these studies. The total number of patients combined for all 3 RCTs was only 183. Given the small population of patients in the medical literature and the conflicting data, the evidence base for which approach is preferable remains limited.

Our anecdotal experience suggests that clinical practice in the treatment of these complex patients is variable and seems to be dependent on physician preference, experience, and local availability.

Given the small number of patients studied comparing ERCP and PTBD in MBTO in the current medical literature, the goal of this study was to compare ERCP with PTBD using a large national inpatient database. The primary outcome was to look at adverse event rates for ERCP vs PTBD adjusted for comorbidities and age. Secondary outcomes examined included length of hospital stay, total cost of hospitalization, and referral patterns for ERCP vs PTBD for MBTO.

### Methods

### Data Source

The Nationwide Inpatient Sample (NIS) database is the largest publicly available database in the United States of all-payer inpatient care. This is a part of the Healthcare Cost and Utilization Project (HCUP) sponsored by the Agency for Healthcare Research and Quality (AHRQ). We used the data from this database for 2007, 2008, and 2009. A previous study established the reliability of the NIS database because it concurs with the National Hospital Discharge Survey. The database includes data from approximately 8 million hospital stays every year and represents a 20% sample of all nonfederal US hospital discharges in all 50 states. The data include a unique identifier for the hospitalization and clinical information extracted from inpatient and discharge data (nearly 100 patient- and hospital-related variables). Quality control procedures performed by HCUP have demonstrated reliability and accuracy, specifically when data pertain to the principal diagnosis. Studies have also noted that outcomes calculated from the NIS database are accurate estimates of national outcomes. Thus, this database can be reliably used to represent the population of patients undergoing ERCP and PTBD in the United States.

### Study Population

Our study population consisted of all hospitalized patients 18 years or older with malignant biliary tract obstruction (pancreatic cancer or cholangiocarcinoma) in the NIS database (2007, 2008, and 2009) who underwent inpatient ERCP or PTBD for biliary drainage. The data were extracted from the database and analysis was performed in June 2015. We excluded all patients...
who underwent PTBD after failed ERCP; patients with gallbladder cancer, because their presentation is variable; and patients who had more than 1 kind of cancer leading to obstruction to avoid selection bias.

The study population was selected based on procedural coding in accordance with the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*. Patients who underwent ERCP were identified with diagnostic ERCP codes 51.10, 51.11, 51.14, 52.13, and 52.14 and therapeutic ERCP codes 51.84, 51.85, 51.86, 51.87, 52.93, 52.94, 52.97, and 52.98; patients who underwent PTBD were identified using codes 51.98, 51.96, 51.43, and 51.12. Most of these codes have been previously validated and have been shown to have good sensitivity and positive predictive value. The sampling design used for the study is shown in the *Figure*.

**Outcome and Predictor Variables**

The aim of this study was to evaluate the adverse event rate associated with ERCP and PTBD in patients with MBTO. The primary outcomes evaluated were ERCP-related complications (bleeding, infection, perforation, and pancreatitis) and PTBD-related complications (bleeding, infection/peritonitis/bile leak, and perforation). The secondary outcomes evaluated included length of stay and total cost of hospitalization. We evaluated the baseline medical status using the Elixhauser comorbidity index. The Elixhauser comorbidity index is well established and validated in predicting in-patient mortality in previous studies. The NIS database contains 29 QHRQ comorbidity measures used by Elixhauser et al. We used the Comorbidity Software created by HCUP for the creation and analysis of these comorbidities. We identified facilities that performed a high volume of PTBD procedures. This was defined as a facility where at least 20% of all the patients who needed biliary drainage for malignant obstruction underwent PTBD. Inpatient all-cause mortality was not included in the analysis because it cannot be determined from the data set if the cause of death was directly related to the procedure, or related to another coexisting disease process (eg, pulmonary embolism, infection).

**Statistical Analysis**

Data analysis was performed using SAS statistical software (version 9.2; SAS Institute Inc). We accounted for the stratified 2-stage cluster design by using SAS's proc survey commands and incorporating individual discharge-level weights during data analysis. Statistical analysis using the chi-square test for categorical data and t test for continuous data were performed. P < .05 was considered statistically significant. Univariate and bivariate analysis were performed to assess adverse events for ERCP and PTBD. We also used logistic regression to assess the association between adverse events and type of procedure (ERCP vs PTBD) while adjusting for age, race/ethnicity, health insurance, comorbidity, teaching hospital status, and presence of sepsis.

**Ethical Considerations**

The analysis of the NIS sample uses completely unidentified data with no risk of loss of confidentiality. We completed a data user agreement with the AHRQ prior to using the NIS database. According to the data user agreement, any individual table cell counts of 10 or lower cannot be presented to preserve patient confidentiality. In such instances, data are designated by the abbreviation IS, meaning information suppressed. The present study was exempt from institutional review board review by North Shore Long Island Jewish Health System.

**Results**

**Patient Characteristic and Demographics**

There were total of 9135 patients included in the study, of whom 7445 (81.5%) underwent ERCP, whereas 1690 (18.5%) underwent PTBD. The eTable in the *Supplement* presents the comparison of patient and hospital characteristics among inpatients in the NIS database who underwent either ERCP or PTBD from 2007 to 2009. The mean age of patients who underwent ERCP was similar to that of patients who underwent PTBD. No difference was found between the 2 groups with respect to sex. The ERCP group was 49.6% male, whereas the PTBD group was 50.6% male.
Most of the patients in both groups (74.0%) were white. Patients in both groups were more likely to be admitted on a weekday. Patients undergoing PTBD (16.0%) were more likely to have sepsis in comparison with patients undergoing ERCP (10.0%). The mean Elixhauser index was similar in both ERCP and PTBD groups (P = .45), with 55.0% in ERCP group compared with 57.0% in the PTBD group having 3 or more comorbidities.

There was a significantly greater number of days from admission to performing PTBD (mean, 3.0 days) compared with number of days from admission to performing ERCP (mean, 2.7 days) (P < .001) and also a greater length of stay for patients who underwent PTBD (mean, 10.4 days) in comparison with those who underwent ERCP (mean, 7.6 days) (P < .001).

Table 1 shows the comparison between ERCP and PTBD among inpatients based on the type of malignant neoplasm in our study. Most of the patients in this study had pancreatic cancer. Both the ERCP group and the PTBD group had high percentages of patients who underwent biliary drainage for pancreatic cancer (78.5% vs 75.8%). Table 1 also summarizes the adverse events among patients undergoing ERCP or PTBD. The PTBD group had a higher adverse event rate than the ERCP group (12.3% vs 8.6%; P < .001). We performed subgroup analyses of adverse events between younger (≤85 years) and older (>85 years) patients undergoing ERCP and PTBD. We found no differences between the younger and older groups for both ERCP and PTBD. We also performed subgroup analyses of adverse events after excluding patients with cholangitis undergoing ERCP and PTBD. We found no differences in the results after excluding patients with cholangitis.

Pancreatic Cancer

As noted in Table 2, patients with pancreatic cancer had a significantly higher (P < .001) adverse event rate when they underwent PTBD (6.2%) compared with ERCP (2.9%). The total cost of hospitalization and length of stay were also found to be significantly higher in the PTBD group compared with the ERCP group (cost: $73 151.40 vs $ 53 881.10; length of stay: 10.4 days vs 7.6 days) (P < .01 for both comparisons). On multivariate analysis, we found a higher rate of adverse events (OR, 1.8; 95% CI, 1.3-2.5) among patients who underwent PTBD compared with ERCP. In an attempt to control for center expertise, we evaluated adverse event rates of percutaneous biliary drainage in centers performing a high-volume of procedures vs those performing a low volume and compared it with the adverse event rate of endoscopic procedures performed in the same center. Most PTBD procedures for pancreatic cancer were performed in high-volume centers (72.0%). We found that both low-volume and high-volume centers for PTBD had increased adverse event rates vs ERCP (7.6% vs 2.9%; P < .001 and 5.6 vs 3.1%; P = .001, respectively).

On subgroup analysis for comorbidities, using the mean Elixhauser comorbidity index, we found that patients with less than 5 comorbidities, those in the ERCP group had significantly lower adverse events (2.8% vs 6.2%; P < .001), length of stay (mean, 7.3 days vs 10.3 days), and total cost of hospitalization compared with those in the PTBD group. For patients with more than 5 comorbidities, those who underwent ERCP had significantly lower event rates.

### Table 1. Comparison Between Endoscopic Retrograde Cholangiopancreatography (ERCP) and Percutaneous Transhepatic Biliary Drainage (PTBD) Among Inpatients Based on Type of Malignant Neoplasm and Adverse Events

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Procedure, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ERCP (n = 7445)</td>
</tr>
<tr>
<td>Pancreatic malignant neoplasmab</td>
<td>78.47</td>
</tr>
<tr>
<td>Cholangiocarcinomab</td>
<td>21.53</td>
</tr>
<tr>
<td>All adverse events, %c</td>
<td>8.57</td>
</tr>
<tr>
<td>ERCP-related adverse events</td>
<td></td>
</tr>
<tr>
<td>Post-ERCP pancreatitis</td>
<td>4.66</td>
</tr>
<tr>
<td>ERCP-associated hemorrhage</td>
<td>1.84</td>
</tr>
<tr>
<td>Perforation</td>
<td>IS</td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>1.52</td>
</tr>
<tr>
<td>PTBD-related adverse events</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>NA</td>
</tr>
<tr>
<td>Perforation</td>
<td>NA</td>
</tr>
<tr>
<td>Peritonitis and/or bile leak</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: IS, information suppressed (according to the data user agreement, any individual table cell counts of ≤10 cannot be presented to preserve patient confidentiality); NA, not applicable.

### Table 2. Adjusted Outcomes of Percutaneous Transhepatic Biliary Drainage (PTBD) Compared With Endoscopic Retrograde Cholangiopancreatography (ERCP)

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>ERCP (n = 5842)</th>
<th>PTBD (n = 1281)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All adverse events, %</td>
<td>2.94</td>
<td>6.17</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Length of stay, d</td>
<td>7.6</td>
<td>10.4</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Total charges, $</td>
<td>53 881.10</td>
<td>73 151.40</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Coefficient, OR (95% CI)</td>
<td>1.80 (1.32-2.45)</td>
<td>&lt; .001</td>
<td></td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All adverse events, %</td>
<td>2.62</td>
<td>4.16</td>
<td>.10</td>
</tr>
<tr>
<td>Length of stay, d</td>
<td>7.5</td>
<td>10.5</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Total charges, $</td>
<td>52 855.70</td>
<td>78 904.60</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Coefficient, OR (95% CI)</td>
<td>1.42 (0.76-2.67)</td>
<td>.27</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviation:** OR, odds ratio.
length of stay (mean, 9.3 days) and nonsignificantly lower rates of adverse events (3.5% vs 5.9%; \( P = .14 \)) and total cost of hospitalization (mean, $63 229.00 vs $72 515.00; \( P = .10 \)).

### Cholangiocarcinoma

Similar to patients with pancreatic cancer, patients in the PTBD group with cholangiocarcinoma had a higher incidence of adverse events vs those in the ERCP group, but this was not statistically significant (Table 2). However, when accounting for the PTBD volume of the centers, a significant trend was seen. Most PTBD procedures for cholangiocarcinoma were performed in high-volume centers (70.0%). Low-volume centers for PTBD were more likely to have adverse events compared with ERCP procedures performed at the same center (5.7% vs 2.5%; \( P = .04 \)). In high-volume centers for percutaneous drainage, the rate of adverse events was similar to that of endoscopic adverse events (3.5% vs 3.0%; \( P = .68 \)). The total cost of hospitalization and length of stay were also found to be significantly higher in the PTBD group (Table 3).

On subgroup analysis based on the mean Elixhauser comorbidity index, we found that for patients with more than 4 comorbidities, there was a significantly lower adverse events rate (\( P = .05 \)). ERCP was associated with significantly lower length of stay (low-comorbidity ERCP vs PTBD: mean days, 7.2 vs 10.2, \( P < .001 \); high-comorbidity ERCP vs PTBD: mean days, 9.2 vs 13.5; \( P = .01 \)) and total cost of hospitalization (low-comorbidity ERCP vs PTBD: mean, $51 507.00 vs $76 526.00; \( P < .001 \); high-comorbidity ERCP vs PTBD: mean, $61 704.00 vs $104 155.00; \( P = .01 \)) compared with PTBD for patients with both low and high amounts of comorbidities.

### Discussion

In this study, we aimed to determine which approach to biliary drainage in malignant obstruction resulted in fewer adverse events in patients admitted to hospitals in the United States. To our knowledge, this was the largest study to date to address this question and included 9135 patients who underwent biliary drainage for malignant biliary tract obstruction from a large sample of patients of various age groups, ethnicities, socioeconomic backgrounds, geographic regions, and type of hospital. These data are representative of the entire population of the United States, which is a primary goal of the NIS.

Overall, ERCP is associated with fewer adverse events than PTBD. The pancreatic cancer subgroup had the most striking results, with statistically significant fewer rates of adverse event in ERCP vs PTBD. The PTBD volume of centers did not affect this result. This suggests that ERCP may be the preferential procedure of choice for biliary drainage in pancreatic cancer. In addition, length of stay and total charges were also less for the ERCP group for pancreatic cancer.

The cholangiocarcinoma subgroup did not show a difference in adverse events between ERCP and PTBD. However, when controlling for PTBD volume of centers, low-volume centers had significantly higher adverse event rates compared with endoscopic procedures performed at the same center. This trend was not seen in high-volume PTBD centers. This study suggests that PTBD for cholangiocarcinoma should be performed only in centers that perform a high volume of this procedure. Biliary drainage for cholangiocarcinoma is challenging, and our study supports this. Patients undergoing PTBD also had a longer length of stay and higher cost of hospitalization. It is unclear if this is related to the procedure itself or to other factors; however, the difference is striking and warrants future research.

In an attempt to control for potential confounders, we analyzed the data of adverse events by age for each group. We did not find a difference in adverse events and in hospital mortality with regard to age for ERCP or PTBD. This finding is discordant with those of a recent meta-analysis showing that patients older than 80 years who undergo ERCP are at higher risk of adverse events. We speculate that the excess morbidity associated with ERCP in elderly individuals may relate to benign disease (eg, cholelithiasis) alone. Another potential confounder is the presence or absence of comorbidities. We therefore tried to control for this and analyzed the data using the Elixhauser comorbidity index. The results revealed that even when adjusted for comorbidities, ERCP remained safer with respect to lower adverse event rates for pancreatic cancer. The results were equivocal for cholangiocarcinoma (Table 3).

It is unclear what drives referral patterns to ERCP vs PTBD. It is interesting to note that 80% of all the biliary drainage procedures in this study for MBTO were endoscopic. However, there are clearly high-volume centers that performed most of the PTBD procedures in this study, which suggests that referrals for primary PTBD are also based on local expertise. For pancreatic cancer, our data support the contention (and ob-
served practice) that ERCP should be the first-line treatment approach for biliary drainage in pancreatic cancer. However, patients undergoing biliary drainage in cholangiocarcinoma fare well, in regard to adverse events, with both modalities if performed in experienced centers.

Our study does have certain limitations. As with all retrospective studies, care must be taken when interpreting data of this nature owing to the inherent limitations of retrospection. For instance, one can never truly account for why a patient underwent PTBD vs ERCP. Factors such as degree of local expertise for one method over the other or patient-specific clinical issues (eg, the presence of local invasion and/or gastric outlet obstruction that may have precluded endoscopy, postsurgical anatomy) clearly play a role in clinical decision making. This cannot be captured in this large data set. We try to account for this by providing hospital volume data. However, the large numbers in this data set are compelling enough to support the use of ERCP as the primary approach in pancreatic cancer.

While we believe the data in the pancreatic cancer subgroup are robust, we would advise a word of caution in regard to the cholangiocarcinoma subgroup. Because of data set limitations, we were unable to determine the tumor stage, presence of metastasis, and Bismuth classification of the cholangiocarcinoma and specifically the hilar involvement of disease. It has been previously acknowledged that complex hilar tumors may be best treated by PTBD.4,6,7 The previous studies4,6,7 in the literature were not able to address this either.

Our study analyzes adverse event rates and not technical success rates as the other RCTs did for MBTO. It is not possible to calculate success rates from this database. We did, however, exclude patients who underwent both procedures, our assumption being that one of the procedures was unsuccessful (eg, a patient who underwent unsuccessful ERCP subsequently underwent PTBD for biliary drainage). It is possible that our data set (as a consequence of our assumption) does not include patients who failed treatment and did not proceed to another intervention for a variety of reasons (eg, the primary procedure caused a clinically significant complication precluding another procedure, lack of local clinician expertise, or transfer to another institution for the other procedure). Finally, the type of anesthesia (conscious sedation vs endotracheal anesthesia) used for the procedures cannot be abstracted from the NIS data set. However, this should not affect the adverse events measured in this study. The adverse events measured in this study are related to the procedure and not the anesthesia.

Conclusions

Despite its limitations, we believe our study adds considerably to the limited published literature. Our study shows that patients who undergo ERCP for biliary drainage in malignant biliary obstruction have lower procedure-related adverse event rates compared with those who undergo PTBD in pancreatic cancer in all centers and cholangiocarcinoma in low-volume centers. Our data support the contention that ERCP should be the first-line treatment consideration for MBTO in pancreatic cancer and low-volume centers for PTBD in cholangiocarcinoma. Larger prospective RCTs are still needed to expand on our experience and to address specific clinical scenarios (eg, hilar cholangiocarcinoma).

REFERENCES
