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# Endoscopic Sphincterotomy Increases the Risk of Pyogenic Liver Abscess: A Retrospective Study Using Real-World Data

Abdellatif Ismail[1], Bisher Sawaf[2], Pinghsin Hsieh[1], Khalid Aloum[3], Shahem Abbarh[4], Mhd Kutaiba Albuni[5], Mohammed Al-Aquily[6,*], Mostafa Suhail Najim[7], Amir Humza Sohail[8], Saurabh Chandan[9,10]

1-Department of Internal Medicine, University of Maryland Medical Center, Midtown Campus, Baltimore, MD, USA
2-Department of Internal Medicine, University of Toledo, Toledo, Ohio, USA
3-Department of Internal Medicine, St Barnabas Hospital, Bronx, NY, USA
4-Department of Internal Medicine, MedStar Health, Baltimore, MD, USA
5-Department of Internal Medicine, TriHealth, Good Samaritan Hospital, Cincinnati, Ohio, USA
6-Department of Internal Medicine, Norwalk Hospital/Yale University Program, Norwalk, CT, USA
7-Department of Internal Medicine, Rochester Regional Health - Unity Hospital, Rochester, NY, USA
8-Department of Surgery, University of New Mexico, Albuquerque, NM, USA
9-Center for Interventional Endoscopy, Advent Health, Orlando, FL, USA
10-Advanced Endoscopy, Houston Methodist West Hospital, Houston, TX, USA

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ABSTRACT

**Introduction:** Pyogenic liver abscess (PLA) after Endoscopic Retrograde Cholangiopancreatography (ERCP) is a rare infectious adverse event. The association between post-ERCP PLA and endoscopic sphincterotomy has not been extensively studied.
**Methods:** We conducted a retrospective study using the TriNetX platform by including patients without history of PLA who received ERCP between October 2015 and December 2020. Two groups were made: the endoscopic sphincterotomy (ES) group (patients who received ES during ERCP) and the control group (patients who did not receive ES). The primary outcome was the risk of developing PLA within 1 year of the index ERCP. The secondary outcomes included sepsis, broad-spectrum antibiotics use, need for PLA drainage, and post-ERCP mortality within one year of the index ERCP.
**Results:** There were 169 patients (1.43%) in the ES group who developed PLA compared to 123 patients (1.04%) in the control group, Relative Risk (RR): 1.37, P-value = 0.007. A total of 241 patients (2.05%) in the ES group developed sepsis compared to 176 patients (1.49%) in the control group, RR: 1.37, P-value = 0.001. A total of 2,954 patients (25.1%) in the ES group received treatment with broad-spectrum antibiotics compared to 2,132 patients (18.1%) in the control group, RR: 1.5, P-value < 0.0001. There was no statistically significant difference in the need for PLA drainage (RR: 1.19, P-value = 0.34) or mortality (RR: 0.969, P-value = 0.49).
**Conclusion:** ES during ERCP was associated with an increased risk for PLA, sepsis, and broad-spectrum antibiotics use. No mortality difference was found.

## 1. Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a procedure done with an endoscope that aims to diagnose hepatobiliary conditions, with the ability to intervene when required [1, 2]. The endoscope is inserted through the mouth into the second part of the duodenum. Once the sphincter of Oddi is visualized, another arm from the scope is inserted through the sphincter to gain access into the ampulla of Vater to reach for the common bile duct (CBD) or the pancreatic duct while being visualized under x-ray [3].

During ERCP, some patients undergo endoscopic sphincterotomy (ES), which involves cutting the sphincter of Oddi to open either the common bile duct or the pancreatic duct. ES serves several purposes, including the extraction of CBD stones and treating papillary stenosis and Sphincter of Oddi dysfunction [1, 2, 3]. While this procedure has great benefits and is considered safe, various adverse events (AE) can occur, including bleeding, pancreatitis, cholangitis, and perforation [4]. However, one less common and overlooked AE is pyogenic liver abscess (PLA). PLA is an infected fluid collection in the liver that could be caused by biliary diseases, the spread of bacteria from blood or the GI tract, intrahepatic rupture of cholecystitis, or superinfection of necrotic tissue [5, 6, 7]. Gram-negative microorganisms, such as Escherichia coli, Klebsiella pneumoniae, and other anaerobic microorganisms, are the predominant organisms isolated from PLA [8].

A retrospective cohort study done in Taiwan showed an increased risk of PLA in patients undergoing ES to treat choledocholithiasis compared to patients who had ERCP without ES [9]. A case was reported in Portugal for a patient who developed PLA with sepsis

* Corresponding author: Mohammed Al-Aquily, Department of Internal Medicine, Norwalk Hospital/Yale University Program, Norwalk, CT, USA. Email: mohammed.alaquily@nuvancehealth.org

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**Table 1:** ICD-10-CM, ICD-10-PCS, RxNorm, & CPT Codes used in the analysis

| Diagnosis/Medications/Procedure | ICD-10-CM, ICD-10-PCS, RxNorm, & CPT Codes |
|---|---|
| ERCP | CPT codes: 43260-43265, 43273-43278 |
| ES | CPT codes: 43262, 43274, 43276, and 43277 |
| PLA | ICD-10-CM code: K76.82 |
| Sepsis with enteric organisms | ICD-10-CM codes: A41.4, A41.51, A41.52, A41.81 |
| PLA drainage procedures | ICD-10-PCS codes: 0F90, 0F91, 0F92 |
| Meropenem | RXNORM: 29561 |
| Imipenem | RXNORM: 5690 |
| Ertapenem | RXNORM: 325642 |
| Piperacillin | RXNORM: 8339 |
| Cefepime | RXNORM: 20481 |

ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; ICD-10-PCS, International Classification of Diseases, Tenth Revision, Procedure Coding System; CPT, Current Procedural Terminology codes

with Escherichia coli, Streptococcus anginosus, and Enterococcus faecalis three days after he underwent ERCP with ES for choledocholithiasis [10]. In this study, we aim to evaluate the association between ES and PLA development.

## 2. Methods

### 2.1. Design and data source

This was a retrospective study utilizing the TriNetX database, a global federated health research network encompassing electronic health records (EHRs) from 86 healthcare organizations (HCOs) in the United States (US) at the time of analysis. All data were derived from the EHRs through a built-in natural language processing system that extracts variables from clinical documents. The TriNetX interface provides only aggregate counts and statistical summaries to protect patient health information, ensuring the data remains de-identified at all levels.

### 2.2. Study cohorts

Patients were included if they underwent ERCP procedures between October 1, 2015, and December 31, 2020. The start date corresponds to the mandatory adoption of International Classification of Diseases, Tenth Revision, and Clinical Modification (ICD-10-CM) codes in U.S. hospital systems, and the end date ensures adequate follow-up. ERCP was identified through specific Current Procedural Terminology (CPT) codes (43260-43265, 43273-43278). The identified patients were stratified into two cohorts: the ES cohort (intervention group), defined by CPT codes 43262, 43274, 43276, and 43277, and the non-sphincterotomy cohort (control group), defined by all other ERCP CPT codes without any overlapping sphincterotomy codes. We excluded patients under 18 years of age at the time of ERCP and patients with a history of any liver abscess defined by ICD-10-CM codes: K75.0 and A06.4 prior to the index ERCP (**Table 1**).

### 2.3. Outcomes

The analysis setup involved defining the index date and observation time window for each cohort. The index date was set as the first recorded ERCP procedure during the study period. If a patient received ERCP for multiple instances during the study period, only the day of their first instance was counted as the index date. The observation time window began one day after the index date and extended for 365 days, during which primary and secondary outcomes were evaluated. The primary outcome was the development of PLA, identified by the ICD-10 diagnosis code K75.0. The secondary outcomes included the occurrence of sepsis with enteric organisms (ICD-10 codes A41.4, A41.51, A41.52, A41.81), the need for broad-spectrum antibiotics (namely, piperacillin/tazobactam, cefepime, ertapenem, imipenem/cilastatin, or meropenem), the need for PLA drainage (ICD-10 PCS procedure codes 0F90, 0F91, 0F92), and mortality.

### 2.4. Statistical analysis

All statistical analyses were conducted in the TriNetX software with the browser-based real-time analytics feature, TriNetX Live (TriNetX LLC, Cambridge, MA). Baseline characteristics of all groups were described with means ± standard deviation for continuous data and counts and percentages for categorical data. Covariates based on demographics, comorbid diseases, prior procedures, and medications were identified.

To address potential confounding, propensity score matching (PSM) was performed to balance baseline characteristics between cohorts. The variables included in the matching process were age (categorized as 18–65 and >65), gender, race, underlying biliary diseases, hepatobiliary, pancreatic, or colorectal malignancy, prior antibiotic use, proton pump inhibitor or histamine-2 receptor blocker use, and most recent total bilirubin levels on chart (categorized as 0–2 mg/dL, 2–4 mg/dL, and >4 mg/dL). Propensity scores were calculated, and patients were matched in a 1:1 ratio using the nearest neighbor (greedy) method without replacement, with a caliper of 0.10 standard deviations. Cohorts were randomly shuffled prior to matching to minimize selection bias.

For each outcome, a Measure of Association Analysis was conducted to compare the fractions of patients in each cohort who experienced the outcome during the observation period. Results included the number of patients in each cohort, the number of patients with the outcome, the fraction of affected patients within each cohort, and the relative risk (RR) between the ES and the control groups. The 95% confidence interval (CI) of the relative risk was also reported. A two-sided p-value <0.05 was considered statistically significant for all analyses.

## 3. Results

### 3.1. Baseline Characteristics

A total of 137,522 patients underwent ERCP during the study period (October 1, 2015, to December 31, 2020). After excluding

**Table 2:** Participants' baseline characteristics before and after propensity score matching, including demographic factors, comorbidities, and medications

| Variable | ERCP with ES before matching | ERCP alone before matching | P-value | ERCP with ES after matching | ERCP alone after matching | P-value |
|---|---|---|---|---|---|---|
| N | 70,319 | 11,751 | | 11,751 | 11,751 | |
| **Demographics** | | | | | | |
| Age at index (Mean, SD) | 58.6 +/- 16.7 | 58.5 +/- 16.5 | 0.547 | 58.2 +/- 16.7 | 58.5 +/- 16.5 | 0.089 |
| Female N% | 36,622 (52.1%) | 6,259 (53.3%) | 0.017 | 6,328 (53.9%) | 6,259 (53.3%) | 0.367 |
| Male N% | 30,545 (43.4%) | 5,091 (43.3%) | 0.818 | 5,024 (42.8%) | 5,091 (43.3%) | 0.377 |
| White N% | 50,405 (71.7%) | 7,959 (67.7%) | <0.001 | 8,041 (68.4%) | 7,959 (67.7%) | 0.251 |
| Black N% | 6,349 (9.0%) | 951 (8.1%) | 0.001 | 957 (8.1%) | 951 (8.1%) | 0.886 |
| Hispanic N% | 8,047 (11.4%) | 1,273 (10.8%) | 0.054 | 1,255 (10.7%) | 1,273 (10.7%) | 0.705 |
| Asian N% | 2,171 (3.1%) | 530 (4.5%) | <0.001 | 470 (4.0%) | 530 (4.5%) | 0.052 |
| **Baseline Comorbidities and Diagnoses** | | | | | | |
| Obstruction of the bile duct N% | 27,882 (39.7%) | 2,988 (25.4%) | <0.001 | 2,886 (24.6%) | 2,988 (25.4%) | 0.124 |
| Other specified diseases of the biliary tract N% | 28,760 (40.9%) | 3,651 (31.1%) | <0.001 | 3,636 (30.9%) | 3,651 (31.1%) | 0.832 |
| Cholelithiasis N% | 37,162 (52.8%) | 5,428 (46.2%) | <0.001 | 5,471 (46.6%) | 5,428 (46.2%) | 0.574 |
| Malignant neoplasm of the pancreas N% | 8,342 (11.9%) | 761 (6.5%) | <0.001 | 688 (5.9%) | 761 (6.5%) | 0.048 |
| Malignant neoplasm of liver and intrahepatic bile ducts N% | 3,366 (4.8%) | 365 (3.1%) | <0.001 | 323 (2.7%) | 365 (3.1%) | 0.104 |
| Malignant neoplasm of other and unspecified parts of the biliary tract N% | 2,444 (3.5%) | 210 (1.8%) | <0.001 | 210 (1.8%) | 210 (1.8%) | 1 |
| Malignant neoplasm of colon N% | 1,293 (1.8%) | 129 (1.1%) | <0.001 | 118 (1.0%) | 129 (1.1%) | 0.482 |
| Malignant neoplasm of gallbladder N% | 576 (0.8%) | 40 (0.3%) | <0.001 | 30 (0.3%) | 40 (0.3%) | 0.231 |
| Cholangitis N% | 9,572 (13.6%) | 1,477 (12.6%) | 0.002 | 1,331 (11.3%) | 1,477 (12.6%) | 0.003 |
| **Baseline Medications** | | | | | | |
| Beta-lactam antibacterial agents N% | 21,025 (29.9%) | 3,105 (26.4%) | <0.001 | 3,007 (25.6%) | 3,105 (26.4%) | 0.145 |
| Beta-lactam antibacterial agents, penicillins N% | 19,333 (27.5%) | 3,182 (27.1%) | 0.351 | 3,073 (26.2%) | 3,182 (27.1%) | 0.108 |
| Quinolone antibacterial agents N% | 16,891 (24.0%) | 2,962 (25.2%) | 0.005 | 2,774 (23.6%) | 2,962 (25.2%) | 0.004 |
| Other antibacterial agents N% | 13,958 (19.8%) | 2,332 (19.8%) | 0.991 | 2,178 (18.5%) | 2,332 (19.8%) | 0.011 |
| Proton pump inhibitors N% | 26,459 (37.6%) | 4,329 (36.8%) | 0.103 | 4,240 (36.1%) | 4,329 (36.8%) | 0.228 |
| H2-receptor antagonists N% | 12,499 (17.8%) | 1,832 (15.6%) | <0.001 | 1,773 (15.1%) | 1,832 (15.6%) | 0.286 |

ERCP, Endoscopic Retrograde Cholangiopancreatography; ES, Endoscopic Sphincterotomy

the patients with a prior diagnosis of liver abscess (n=55,452), we identified 82,070 patients and included them in the study. After stratification based on receiving sphincterotomy during the ERCP procedure, 70,319 patients were included in the "ES group", while 11,751 patients were included in the "ERCP-alone group". After propensity score matching, 11,751 patients were included in each group, achieving a balance in demographics, hepatobiliary comorbidities, baseline biochemistry, and medication use. The mean age was 58.2 ± 16.7 years for the ES group and 58.5 ± 16.5 years for the ERCP-alone group, with no significant difference (P-value = 0.089). The proportion of females in both groups was similar (53.9% in ES vs. 53.3% in ERCP-alone; P = 0.367). Other characteristics were well-matched, with no significant differences between the groups **(Table 2)**.

### 3.2. Primary Outcome

A total of 169 patients (1.43%) in the ES group developed PLA within the 5-year observation period compared to 123 patients (1.04%) in the ERCP alone group. The risk of developing PLA within one year of the index ERCP was slightly but significantly higher in the ES group (n= 169, 1.43%) compared to the ERCP-alone group (n= 123, 1.04%), Relative Risk (RR): 1.37, 95% CI: 1.09–1.73; P-value = 0.007, **(Table 3)**.

### 3.3. Secondary Outcomes

Sepsis with enteric organisms occurred in 241 patients (2.05%) of the ES group and in 176 patients (1.49%) of the ERCP-alone group, with a statistically significant increased risk in the ES group (RR: 1.37, 95% CI: 1.29–1.66; P-value = 0.001). Similarly, broad-spectrum antibiotic use was more frequent in the ES group (n= 2,954, 25.1%) compared to the ERCP-alone group (n= 2,132, 18.1%), RR: 1.38, 95% CI: 1.31–1.45; P-value < 0.001) **(Table 3)**.

**Table 3:** Primary and secondary outcomes post-ERCP and ES

| Outcome | Cohort | N | (%) | RR | 95% CI | P-value |
|---|---|---|---|---|---|---|
| Pyogenic liver abscess | ERCP with ES | 169 | 1.43% | 1.37 | (1.09-1.73) | 0.007 |
| | ERCP-alone | 123 | 1.04% | - | - | - |
| Sepsis with enteric organisms | ERCP with ES | 241 | 2.05% | 1.37 | (1.29-1.66) | 0.001 |
| | ERCP-alone | 176 | 1.49% | - | - | - |
| Broad-spectrum antibiotic use | ERCP with ES | 2,954 | 25.1% | 1.38 | (1.31-1.45) | < 0.001 |
| | ERCP-alone | 2,132 | 18.1% | - | - | - |
| Procedure for drainage of pyogenic liver abscess | ERCP with ES | 62 | 0.52% | 1.19 | (0.82-1.72) | 0.34 |
| | ERCP-alone | 52 | 0.44% | - | - | - |
| Mortality | ERCP with ES | 994 | 8.4% | 0.972 | (0.894-1.05) | 0.49 |
| | ERCP-alone | 1,023 | 8.7% | - | - | - |

ERCP, Endoscopic Retrograde Cholangiopancreatography; ES, Endoscopic Sphincterotomy; CI, Confidence Interval; N, Number; RR, Relative Risk

There was no significant difference between the two groups in the rate of procedures for drainage of PLA (n= 62, 0.52% in ES vs. n= 52, 0.44% in ERCP-alone; RR: 1.19, 95% CI: 0.82–1.72; P-value= 0.34) or mortality within one-year post-ERCP (n= 994, 8.4% in ES vs. n= 1,023, 8.7% in ERCP-alone; RR: 0.972, 95% CI: 0.89–1.05; P = 0.49). Overall, ES was associated with increased risks of PLA, sepsis with enteric organisms, and broad-spectrum antibiotic use. However, no differences were observed in mortality between the ES and ERCP-alone groups.

## 4. Discussion

In this retrospective cohort study, we found that ES was associated with an increased risk of post-ERCP PLA compared to ERCP without ES (RR: 1.37, 95% CI: 1.09–1.73; P = 0.007). This also corresponded to a higher incidence of sepsis with enteric organisms (RR: 1.37, 95% CI: 1.29–1.66; P = 0.001) and use of broad-spectrum antibiotics (RR: 1.38, 95% CI: 1.31–1.45; P < 0.001), thereby increasing the burden on the healthcare system. Despite the higher morbidity, we did not observe a statistically significant difference in the rates of procedural abscess drainage or mortality within one year following ERCP. To the best of our knowledge, this is the first study examining this association in the US and Western Hemisphere population, as earlier studies originated mainly from Taiwan.

Our findings align with and expand upon the existing literature regarding post-ERCP PLA risk. Prior studies have reported a similar association between ES and subsequent PLA. For instance, Peng et al. (2018) conducted a population-based cohort study in Taiwan and found that the incidence of PLA was significantly higher after ES than in those without ES (4.20 vs 0.94 per 1000 person-years), with an adjusted hazard ratio of 4.5, P-value < 0.001 [9]. They concluded that patients receiving ES have a markedly increased risk of liver abscess, which is consistent with our observation of increased risk in the ES group [9]. Another large retrospective cohort study from Taiwan by Wu et al. [11] also demonstrated a higher cumulative incidence of PLA in patients who underwent sphincterotomy for choledocholithiasis compared to those who had ERCP without ES where on multivariate analysis, the ES increased the risk of PLA by an adjusted hazard ratio [aHR] of 1.49; 95% CI=1.12-1.98; p-value = 0.0058). These epidemiological findings reinforce earlier clinical reports, including multiple case reports [6, 7, 10] that had flagged PLA as a potential AE following ERCP with sphincterotomy. Notably, the magnitude of risk observed in our study (approximately 1.4-fold increase) is more modest than that reported in some of the Asian cohort studies, for instance, in Peng et al., who reported a fourfold or greater relative risk [9]. This discrepancy could stem from differences in study design (e.g., our analysis was limited to one-year outcomes and controlled via propensity matching, whereas Peng et al. examined longer-term hazard), variations in patient populations, or differences in baseline biliary disease severity. Additionally, geographic and practice differences – such as the microbiological spectrum (Klebsiella pneumoniae is a more common cause of PLA in East Asia [12]) or thresholds for performing sphincterotomy – might contribute to the varying effect sizes. Importantly, no prior research to our knowledge has shown a decreased risk of PLA with sphincterotomy; the trend across studies consistently supports our core finding that ES is a risk factor for PLA. Finally, while earlier studies primarily focused on the occurrence of PLA, our work adds nuance by examining outcomes like sepsis by gut derived organisms, PLA drainage and mortality. The lack of mortality difference we observed is in line with the notion that, if recognized early, PLA can be managed effectively [13, 14].

Several mechanisms might explain why ES increases the likelihood of PLA. Physiologically, an intact sphincter of Oddi serves as a barrier between the duodenum and the biliary system. When a sphincterotomy is performed, this barrier is compromised, potentially allowing duodenal contents – including bacteria – to reflux into the bile ducts more freely [15]. This duodeno-biliary reflux can lead to ascending bacterial colonization of the biliary tree and, in susceptible individuals, the seeding of infection in the liver parenchyma. In essence, ES creates an open conduit for enteric microbes to access the intrahepatic biliary ducts, providing a direct path for infection that can result in liver abscess formation [15, 9]. The bacterial ascent theory is further supported by the fact that ES increases the risk of acute cholangitis as well [16, 17]. In a Swedish population-based study, Langerth et al found a significantly increased risk of acute cholangitis following ES (HR: 36, P <0.001), and noted that most of these episodes developed during the first four years following ES [18].

Additionally, the act of performing an ES (and ERCP in general) may introduce bacteria or cause transient bacteremia. Minor

mucosal trauma or papillary edema from the cut could facilitate bacterial translocation into the bloodstream or bile ducts during the procedure, thereby increasing the risk of hepatic seeding. The organisms involved in post-ERCP abscesses are typically enteric Gram-negative flora and anaerobes, supporting this mechanism. Common isolates from PLA include Escherichia coli, Klebsiella pneumoniae, Streptococcus anginosus, and Enterococcus species, which are all gut-derived microbes [19, 20, 11]. The predominance of these organisms in PLA following ERCP/ES strongly implicates the gut as the source and is consistent with bacterial reflux or translocation after sphincterotomy. Another contributing factor is the alteration of biliary flow dynamics after ES. By widening the biliary outflow tract, ES reduces the tone that normally prevents bacteria from ascending, especially in the presence of biliary stasis [21]. Pre-existing biliary pathologies – such as choledocholithiasis, strictures, or malignancy – can compound this risk. This mechanistic understanding – duodenal bacterial entry combined with biliary stasis & injury – explains why ES, while facilitating bile drainage, also facilitates biliary and hepatic infections.

Given the increased risk of serious infection (PLA, cholangitis, and sepsis) associated with ES, several clinical precautions should be considered. While routine antibiotic prophylaxis for ERCP remains debated [22], our findings suggest it may be beneficial in high-risk cases, such as patients with biliary obstruction, cholangitis, diabetes, or immunosuppression. Peri-procedural antibiotics could reduce PLA risk, but should be balanced against antibiotic stewardship concerns. Endoscopists should carefully assess the necessity of ES and consider alternatives, such as endoscopic papillary balloon dilatation, when feasible. Ensuring complete biliary clearance and using stents in cases of incomplete drainage can further reduce the infection risk [23].

The management of PLA generally requires both antimicrobial therapy and source control. According to Rismiller et al., only a small proportion of patients (4 out of 64 in their study) were successfully treated with antibiotics alone, whereas the majority required percutaneous drainage (PD) or surgery for effective management [24]. Similarly, Lo et al. identified that patients with PLA secondary to endoscopic interventions are at a higher risk of therapy failure (Odds ratio: 3.22, P-value: 0.01) when treated with antibiotics alone, emphasizing the need for early PD in these cases [25]. On the other hand, Du et al. reported a 100% success rate in treating small liver abscesses (<5 cm in diameter) with antibiotics alone (53 of 125 cases in their retrospective study) [26]. In summary, clinicians should implement preventive, procedural, and post-ERCP strategies to mitigate infection risk and ensure appropriate & timely treatment.

Our study has several limitations, mainly due to its retrospective design and reliance on the TriNetX database, EHRs, and ICD-10 codes, which may have introduced misclassification errors [27]. While PSM helped balance confounders, residual confounding remains possible because factors such as ERCP urgency and biliary stone characteristics were not captured. Additionally, patients undergoing ES may have had more complex pathology, inherently increasing PLA risk. The retrospective nature of the study prevents establishing causation, and selection bias may have influenced outcomes. Variability in practice patterns across centers may affect generalizability, and our one-year follow-up may not have captured late PLA cases. Furthermore, we lacked granular data on PLA management. Despite these limitations, our large dataset and robust matching enhance validity. Furthermore, this is the first study that evaluates this important association in the US.

Future prospective studies are needed to confirm these results under controlled conditions. Future research should focus on confirming the ES-PLA association and identifying ways to reduce this risk. Prospective studies and trials are needed to determine whether administering prophylactic antibiotics lowers PLA incidence in ES patients and whether its benefit outweighs its risk.

## 5. Conclusions

Our study demonstrated that endoscopic sphincterotomy (ES) during ERCP was associated with an increased risk of pyogenic liver abscess (PLA), sepsis with enteric organisms, and the need for broad-spectrum antibiotics. However, it did not significantly impact mortality or the need for invasive abscess drainage. These findings reinforce the importance of recognizing PLA as a potential complication of ES and highlight the need for preventive strategies, including careful patient selection, procedural optimization, and enhanced post-ERCP care.

## Conflicts of Interest

The authors declare no competing interests that could have influenced the objectivity or outcome of this research.

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None.

## Large-Language Model

None.

## Authors' Contribution

AI and PH conceived the study and designed it. AI extracted the data and ran the analysis. AI, BS, PH, SA, KA, MA, MN, AS, and MA wrote the manuscript draft. SC reviewed and critically edited the draft. All the authors contributed to the intellectual component of the manuscript. All the authors reviewed the final version and approved it for submission.

## Data Availability

The data used in this study were obtained from the TriNetX platform, which compiles de-identified electronic health records from participating healthcare organizations. Due to privacy regulations, the raw data cannot be shared publicly. Access to the TriNetX platform could be granted to researchers through institutional subscriptions or collaborations with participating institutions. Please contact the corresponding author if you have any questions.

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