Research Square

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# Planned and Unplanned Repeat ERCP After Endoscopic Therapy for Anastomotic Biliary Strictures Following Liver Transplantation: A Retrospective Cohort Study

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## Abstract

# Background

Endoscopic retrograde cholangiopancreatography (ERCP) is the first-line treatment for post-liver transplantation anastomotic biliary strictures. However, repeat ERCP may represent either planned staged treatment or unexpected biliary deterioration. We evaluated the burden, patterns, triggers, adverse events, and endoscopic outcomes of planned and unplanned repeat ERCP.

# Methods

This single-center retrospective cohort study screened 113 post-liver transplantation patients who underwent ERCP between January 2019 and March 2026. After 33 patients were excluded, 80 eligible consecutive patients with anastomotic biliary strictures were included. Repeat ERCP was classified as planned or unplanned. The primary outcome was any repeat ERCP. Secondary outcomes included unplanned repeat ERCP, reasons for unplanned intervention, adverse events, and final endoscopic status.

# Results

During a median follow-up of 39.2 months, 34 patients (42.5%) underwent at least one repeat ERCP. Seventy repeat sessions were recorded, including 56 planned and 14 unplanned sessions. Unplanned repeat ERCP occurred in 12 patients (15.0%) and was triggered by stent dysfunction (n = 5), cholangitis (n = 4), de novo biliary stones (n = 2), or recurrent jaundice (n = 1). Documented stent-free resolution was confirmed in 35 patients (43.8%), whereas 12 patients (15.0%) remained on ongoing endoscopic therapy. Post-ERCP pancreatitis occurred in 10 patients (12.5%); no bleeding or perforation occurred. No variable was independently associated with repeat ERCP in the full-cohort model. In an exploratory plastic-stent subgroup analysis, post-ERCP pancreatitis and biliary stones at index ERCP were associated with a higher hazard of repeat ERCP.

# Conclusions

Repeat ERCP was common, but most repeat sessions were planned components of staged treatment. Unplanned repeat ERCP was mainly related to stent dysfunction, cholangitis, and biliary stones. Planned and unplanned repeat ERCP should be reported separately when assessing endoscopic treatment burden.

## Background

Biliary complications remain an important source of morbidity after liver transplantation, despite improvements in surgical technique, perioperative care, and immunosuppressive therapy. Anastomotic

biliary stricture is one of the most frequent and clinically relevant biliary complications, particularly in recipients with duct-to-duct biliary reconstruction [1]. Because this reconstruction usually allows endoscopic access, ERCP has become the preferred therapeutic approach for most post-liver transplantation anastomotic biliary strictures when anatomy is favorable [2]. Clinically, these strictures may present with cholestatic liver enzyme abnormalities, recurrent jaundice, cholangitis, biliary sludge or stones, and impaired graft function. Although many patients can be treated successfully, management often requires repeated interventions over months or years, creating procedural burden for patients and endoscopy units.

The American Society for Gastrointestinal Endoscopy (ASGE) guideline supports endoscopic management as a central therapeutic option for post-transplant biliary strictures [3]. Conventional ERCP-based therapy generally includes cholangiographic assessment, balloon dilation when indicated, extraction of stones or sludge, placement of one or more biliary stents, and scheduled reassessment or stent exchange. Long-term endoscopic treatment studies have shown that treatment success is often achieved through staged intervention rather than a single ERCP session [4]. Systematic reviews have also emphasized that repeated sessions are intrinsic to many plastic stent-based protocols [5]. Therefore, procedural burden should be considered alongside technical success, stricture resolution, and long-term recurrence when evaluating endoscopic treatment outcomes.

Plastic stent-based therapy remains widely used for benign biliary strictures because of its technical feasibility, removability, and ability to provide progressive dilation across repeated sessions [6]. However, plastic stents have inherent limitations, including limited diameter, progressive occlusion, migration, and the need for timely exchange or removal. Evidence on plastic biliary stent patency indicates that stent dysfunction remains a clinically important problem during follow-up [7]. Delayed stent removal may increase the risk of obstruction, cholangitis, and other biliary events [8, 9]. In the post-transplant setting, these limitations may be amplified by anastomotic narrowing, duct angulation, biliary stasis, sludge formation, and susceptibility to infection.

Fully covered self-expandable metal stents have been investigated as an alternative to multiple plastic stents, with the potential advantages of a larger effective diameter and fewer scheduled procedures [10]. Comparative evidence has reported heterogeneous findings regarding stricture resolution, recurrence, migration, adverse events, and treatment burden [11]. A meta-analysis restricted to randomized trials likewise found no uniform superiority of one stent strategy across clinically relevant outcomes [12]. Thus, the optimal endoscopic strategy remains institution- and patient-dependent. Newer stent designs and advanced endoscopic techniques have not eliminated the need to characterize repeat ERCP burden in real-world plastic-stent practice.

Most available evidence have focused on technical success, stricture resolution, recurrence, or comparisons between plastic and metal stents. Less attention has been paid to the clinical meaning of repeat ERCP itself. In routine practice, repeat ERCP may represent two distinct scenarios. Planned repeat ERCP is part of an intended treatment strategy, such as scheduled stent exchange, progressive dilation,

or stent removal. In contrast, unplanned repeat ERCP usually reflects unexpected biliary deterioration, including stent dysfunction, cholangitis, recurrent jaundice, or biliary stones. Prior studies have examined early repeat ERCP after liver transplantation, but they did not consistently distinguish planned from unplanned repeat procedures [13]. Another study suggested that repeat intervention may be influenced by treatment-related and patient-related factors [14]. Current ERCP-related guidelines emphasize adverse event prevention and management, but do not specifically address planned versus unplanned repeat ERCP after transplant strictures [15].

Therefore, this retrospective cohort study aimed to evaluate the burden, patterns, clinical triggers, adverse events, and final endoscopic outcomes of repeat ERCP after initial endoscopic therapy for post-liver transplantation anastomotic biliary strictures. We specifically distinguished planned from unplanned repeat ERCP and explored factors associated with time to repeat intervention.

## Methods

# Study design and participants

This was a single-center retrospective cohort study conducted at the Second Affiliated Hospital of Guangxi Medical University. Consecutive patients who underwent therapeutic ERCP for anastomotic biliary strictures after liver transplantation were screened. The index ERCP was defined as the first therapeutic ERCP performed for post-liver transplantation anastomotic biliary stricture during the study period. The index ERCP dates ranged from January 17, 2019 to March 10, 2026, and follow-up data were censored on May 24, 2026.

Patients were eligible if they had a history of liver transplantation and underwent therapeutic ERCP for an anastomotic biliary stricture. Patients were excluded if they had a non-anastomotic biliary stricture, isolated postoperative bile leakage without anastomotic biliary stricture, non-anastomotic strictures, non-therapeutic ERCP, or incomplete key procedural information were excluded. For patients with multiple ERCP procedures, only the first therapeutic ERCP for anastomotic biliary stricture was considered the index procedure; subsequent ERCPs were analyzed as follow-up or repeat ERCP sessions. All eligible consecutive patients treated during the study period were included; no formal sample size calculation was performed.

The study protocol was reviewed and approved by the Ethics Committee of the Second Affiliated Hospital of Guangxi Medical University [approval No. 2018–KYL (003)]. The requirement for written informed consent was waived because of the retrospective nature of the study.

## ERCP procedures and index-treatment variables

ERCP procedures were performed by experienced endoscopists using standard techniques. Treatment decisions were based on cholangiographic findings, stricture morphology, bile duct drainage status, and

the endoscopist's clinical judgment. Endoscopic therapy included biliary plastic stent placement, endoscopic nasobiliary drainage (ENBD), or combined plastic stent placement and ENBD. All biliary stents used in this cohort were plastic stents. Balloon dilation, stone or sludge extraction, and stent exchange or removal were performed when clinically indicated.

Index ERCP variables included drainage modality, maximum plastic stent diameter and length, use of multiple plastic stents, and presence of biliary stones or sludge at the index procedure. Pre-ERCP laboratory parameters, including white blood cell count, albumin, creatinine, total bilirubin, direct bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, total bile acids, and amylase, were extracted from the source clinical database when available. The interval from liver transplantation to index ERCP was calculated in months.

## Definitions of repeat ERCP and clinical triggers

Repeat ERCP was defined as any ERCP session performed after the index ERCP during follow-up. Repeat ERCP was classified as planned or unplanned. Planned repeat ERCP referred to scheduled endoscopic reassessment, stent exchange, or stent removal as part of the intended endoscopic treatment strategy. Unplanned repeat ERCP referred to unscheduled or urgent repeat intervention prompted by recurrent biliary symptoms, recurrent jaundice, cholangitis, stent dysfunction, or newly identified biliary stones or sludge.

The primary outcome was any repeat ERCP after index treatment. Secondary outcomes included unplanned repeat ERCP, the number of repeat ERCP sessions per patient, planned and unplanned repeat ERCP sessions, reasons for unplanned repeat ERCP, and final endoscopic outcomes.

## Final endoscopic outcomes

Final endoscopic status was determined by reviewing follow-up ERCP records and subsequent clinical documentation. Final endoscopic status was categorized as resolved with stent-free status, ongoing endoscopic therapy, death before confirmation of resolution, loss to follow-up, or indeterminate. Documented stricture resolution was defined as improvement or resolution of the anastomotic stricture with no requirement for further endoscopic stent therapy at the last available follow-up. Stent-free status at last follow-up was defined as absence of biliary stent, ENBD, or percutaneous drainage at the last available follow-up. Ongoing endoscopic therapy was defined as persistent need for planned ERCP, stent exchange, or continued stent therapy. Need for percutaneous transhepatic biliary drainage, surgical revision, or retransplantation was also recorded.

## Adverse events

Post-ERCP adverse events included post-ERCP pancreatitis, post-ERCP hyperamylasemia, post-ERCP cholangitis, bleeding, and perforation. Post-ERCP pancreatitis was confirmed by manual review of candidate cases identified from the source clinical database and postoperative 24-hour amylase levels. Because severity grading of post-ERCP pancreatitis was not systematically recorded in the source database, post-ERCP pancreatitis was analyzed as a binary adverse event. Post-ERCP cholangitis, bleeding, and perforation were extracted from the clinical database and manually reviewed when needed.

# Statistical analysis

Continuous variables were summarized as medians with interquartile ranges (IQRs), and categorical variables were summarized as numbers and percentages. Patients were compared according to whether they required any repeat ERCP after index treatment. Continuous variables were compared using the Wilcoxon rank-sum test, and categorical variables were compared using Fisher's exact test. Time to repeat ERCP was analyzed from the date of index ERCP to the date of first repeat ERCP. Patients without repeat ERCP were censored at the last follow-up date. Kaplan-Meier analysis was used to describe repeat ERCP-free survival. Cox proportional hazards regression was used to explore factors associated with time to repeat ERCP. Given the limited number of outcome events and sparse categories for some variables, risk factor analyses were considered exploratory. A simplified multivariable Cox model was constructed using clinically relevant variables, including post-ERCP pancreatitis, biliary stones at index ERCP, and the interval from liver transplantation to index ERCP. A separate exploratory Cox model was performed in the plastic-stent subgroup to evaluate the association of maximum plastic stent diameter, post-ERCP pancreatitis, and biliary stones at index ERCP with repeat ERCP. Analyses were performed using available data for each variable; no missing values were imputed. All statistical analyses were performed using R software. A two-sided P value $< 0.05$ was considered statistically significant.

## Reporting guideline

This study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for observational cohort studies.

## Use of AI-assisted tools

No AI-assisted tool was used to generate or alter patient-level data, statistical results, tables, figures, images, or manuscript text.

## Results

# Study population and baseline characteristics

Among 113 post-liver transplantation patients who underwent ERCP and were assessed for eligibility, 33 were excluded: 7 had non-anastomotic strictures, 12 had postoperative bile leakage without anastomotic biliary stricture, 12 underwent non-therapeutic ERCP or did not meet the target population criteria, and 2 had missing key procedural information. A total of 80 patients with post-liver transplantation anastomotic biliary strictures were included in the final analysis. The median age was 51.0 years (IQR, 45.0–57.0), and 62 patients (77.5%) were male. The median interval from liver transplantation to index ERCP was 3.0 months (IQR, 0.6–5.6). The study flow and repeat ERCP classification are shown in Fig. 1.

At index ERCP, 69 patients (86.2%) underwent plastic stent placement alone, 9 patients (11.2%) underwent ENBD alone, and 2 patients (2.5%) underwent combined plastic stent placement and ENBD. Biliary stones or sludge were present at index ERCP in 24 patients (30.0%). Multiple plastic stents were placed in 20 patients (25.0%). Among patients who received plastic stents, the median maximum plastic stent diameter was 8.5 Fr (IQR, 8.5–8.5), and the median maximum stent length was 9.0 cm (IQR, 9.0–11.0).

Patients who required repeat ERCP tended to be older than those who did not require repeat ERCP, although the difference was not statistically significant (54.0 years [IQR, 49.0–58.0] vs. 49.5 years [IQR, 41.8–57.0], P = 0.191). The median interval from liver transplantation to index ERCP was also numerically longer in the repeat ERCP group than in the no-repeat ERCP group (3.3 months [IQR, 0.8–7.0] vs. 1.7 months [IQR, 0.6–5.0], P = 0.309). There were no statistically significant differences between the two groups in sex, pre-ERCP laboratory parameters, drainage modality, biliary stones at index ERCP, multiple stent placement, or early ERCP-related adverse events (Table 1).

Table 1
Baseline and index ERCP characteristics by repeat ERCP status

| Variable | Level | Overall (n = 80) | No repeat ERCP (n = 46) | Any repeat ERCP (n = 34) | P value | Missing, n |
|---|---|---|---|---|---|---|
| Age, years | | 51.0 (45.0–57.0) | 49.5 (41.8–57.0) | 54.0 (49.0–58.0) | 0.191 | 1 |
| Time from liver transplantation to index ERCP, months | | 3.0 (0.6–5.6) | 1.7 (0.6-5.0) | 3.3 (0.8-7.0) | 0.309 | 0 |
| Pre-ERCP WBC | | 6.0 (4.1–9.1) | 5.5 (4.0-7.9) | 7.1 (4.2–9.8) | 0.306 | 3 |
| Pre-ERCP albumin | | 37.4 (33.7–41.3) | 38.6 (34.7–41.5) | 36.5 (32.6–39.5) | 0.166 | 2 |
| Pre-ERCP creatinine | | 81.5 (64.8–99.2) | 81.5 (64.2-102.8) | 81.5 (65.5–97.2) | 0.817 | 4 |
| Pre-ERCP total bilirubin | | 79.2 (15.3-161.3) | 86.6 (29.9-189.9) | 55.6 (10.5-151.9) | 0.270 | 2 |
| Pre-ERCP direct bilirubin | | 70.8 (10.3–143.0) | 78.4 (23.7-156.8) | 49.7 (6.1-139.4) | 0.275 | 2 |
| Pre-ERCP ALT | | 55.0 (28.0-107.2) | 69.0 (29.0-146.0) | 43.0 (23.0–94.0) | 0.175 | 2 |
| Pre-ERCP AST | | 54.0 (29.2-118.5) | 55.0 (30.0-122.0) | 48.0 (27.0-112.0) | 0.578 | 2 |
| Pre-ERCP ALP | | 251.0 (114.0-462.0) | 251.0 (99.2-470.8) | 251.0 (136.0-436.0) | 0.877 | 3 |
| Pre-ERCP GGT | | 252.5 (111.8-480.8) | 294.0 (158.0-546.0) | 238.0 (107.0-398.0) | 0.324 | 2 |
| Pre-ERCP total bile acids | | 174.0 (50.6–395.0) | 178.3 (54.0-395.8) | 158.0 (57.0-372.6) | 0.844 | 25 |

Values are presented as median (interquartile range) or number (%). Continuous variables were compared using the Wilcoxon rank-sum test and categorical variables using Fisher's exact test. Maximum plastic stent diameter and length were assessed among patients who received plastic stents. ALT, alanine aminotransferase; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ENBD, endoscopic nasobiliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; GGT, gamma-glutamyl transferase; WBC, white blood cell count.

| Variable | Level | Overall (n = 80) | No repeat ERCP (n = 46) | Any repeat ERCP (n = 34) | P value | Missing, n |
|---|---|---|---|---|---|---|
| Pre-ERCP amylase | | 55.0 (35.0–87.0) | 56.0 (38.2–71.5) | 54.0 (29.0-87.5) | 0.570 | 23 |
| Maximum plastic stent diameter, Fr | | 8.5 (8.5–8.5) | 8.5 (8.5–8.5) | 8.5 (8.5–8.5) | 0.360 | 9 |
| Maximum plastic stent length, cm | | 9.0 (9.0–11.0) | 9.0 (9.0–11.0) | 9.0 (9.0–11.0) | 0.167 | 9 |
| Sex | Female | 18 (22.5%) | 12 (26.1%) | 6 (17.6%) | 0.427 | 0 |
| | Male | 62 (77.5%) | 34 (73.9%) | 28 (82.4%) | | |
| Index drainage modality | ENBD only | 9 (11.2%) | 8 (17.4%) | 1 (2.9%) | 0.084 | 0 |
| | Plastic stent only | 69 (86.2%) | 37 (80.4%) | 32 (94.1%) | | |
| | Plastic stent plus ENBD | 2 (2.5%) | 1 (2.2%) | 1 (2.9%) | | |
| Biliary stones or sludge at index ERCP | No | 56 (70.0%) | 35 (76.1%) | 21 (61.8%) | 0.219 | 0 |
| | Yes | 24 (30.0%) | 11 (23.9%) | 13 (38.2%) | | |
| Multiple plastic stents | No | 60 (75.0%) | 37 (80.4%) | 23 (67.6%) | 0.205 | 0 |
| | Yes | 20 (25.0%) | 9 (19.6%) | 11 (32.4%) | | |
| Post-ERCP pancreatitis | No | 70 (87.5%) | 42 (91.3%) | 28 (82.4%) | 0.310 | 0 |
| | Yes | 10 (12.5%) | 4 (8.7%) | 6 (17.6%) | | |
| Post-ERCP cholangitis | No | 79 (98.8%) | 46 (100.0%) | 33 (97.1%) | 0.425 | 0 |
| | Yes | 1 (1.2%) | 0 (0.0%) | 1 (2.9%) | | |
| Post-ERCP bleeding | No | 80 (100.0%) | 46 (100.0%) | 34 (100.0%) | 1.000 | 0 |

Values are presented as median (interquartile range) or number (%). Continuous variables were compared using the Wilcoxon rank-sum test and categorical variables using Fisher's exact test. Maximum plastic stent diameter and length were assessed among patients who received plastic stents. ALT, alanine aminotransferase; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ENBD, endoscopic nasobiliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; GGT, gamma-glutamyl transferase; WBC, white blood cell count.

| Variable | Level | Overall (n = 80) | No repeat ERCP (n = 46) | Any repeat ERCP (n = 34) | P value | Missing, n |
|---|---|---|---|---|---|---|
| | Yes | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | | |
| Post-ERCP perforation | No | 80 (100.0%) | 46 (100.0%) | 34 (100.0%) | 1.000 | 0 |
| | Yes | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | | |

Values are presented as median (interquartile range) or number (%). Continuous variables were compared using the Wilcoxon rank-sum test and categorical variables using Fisher's exact test. Maximum plastic stent diameter and length were assessed among patients who received plastic stents. ALT, alanine aminotransferase; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ENBD, endoscopic nasobiliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; GGT, gamma-glutamyl transferase; WBC, white blood cell count.

# Repeat ERCP burden and patterns

During a median follow-up of 39.2 months (IQR, 27.3–55.2) after index ERCP, 34 patients (42.5%) underwent at least one repeat ERCP. A total of 70 repeat ERCP sessions were recorded, including 56 planned and 14 unplanned sessions. The median total number of ERCP sessions per patient was 1.0 (IQR, 1.0–2.0), and the median number of repeat sessions per patient was 0.0 (IQR, 0.0–1.0). The median number of planned repeat sessions per patient was 0.0 (IQR, 0.0–1.0), whereas the median number of unplanned repeat sessions per patient was 0.0 (IQR, 0.0–0.0), reflecting that most patients did not undergo unplanned reintervention (Table 2). The Kaplan-Meier curve for time to first repeat ERCP is shown in Fig. 2. Forty-six patients (57.5%) had no repeat ERCP, 22 (27.5%) underwent planned-only repeat ERCP, 4 (5.0%) underwent unplanned-only repeat ERCP, and 8 (10.0%) underwent both planned and unplanned repeat ERCP (Table 3; Fig. 3).

Table 2
Endoscopic treatment burden

| Variable | Value |
|---|---|
| Follow-up duration after index ERCP, months | 39.2 (27.3–55.2) |
| Total ERCP sessions per patient | 1.0 (1.0–2.0) |
| Repeat ERCP sessions per patient | 0.0 (0.0–1.0) |
| Planned repeat ERCP sessions per patient | 0.0 (0.0–1.0) |
| Unplanned repeat ERCP sessions per patient | 0.0 (0.0–0.0) |
| Patients with any repeat ERCP, n (%) | 34 (42.5%) |
| Patients with unplanned repeat ERCP, n (%) | 12 (15.0%) |
| Total repeat ERCP sessions, n | 70 |
| Planned repeat ERCP sessions, n | 56 |
| Unplanned repeat ERCP sessions, n | 14 |

Values are presented as median (interquartile range) unless otherwise indicated. Total ERCP sessions included the index ERCP and all follow-up ERCP sessions. Planned repeat ERCP comprised scheduled reassessment, stent exchange, or stent removal. Unplanned repeat ERCP comprised unscheduled intervention for recurrent symptoms, cholangitis, stent dysfunction, recurrent jaundice, or biliary stones. ERCP, endoscopic retrograde cholangiopancreatography.

Table 3
Repeat ERCP patterns and first unplanned repeat ERCP reasons

| Section | Category | n (%) |
|---|---|---|
| Repeat ERCP pattern | No repeat ERCP | 46 (57.5%) |
| | Planned-only repeat ERCP | 22 (27.5%) |
| | Unplanned-only repeat ERCP | 4 (5.0%) |
| | Both planned and unplanned repeat ERCP | 8 (10.0%) |
| Reason for first unplanned repeat ERCP | Stent dysfunction | 5 (41.7%) |
| | Cholangitis | 4 (33.3%) |
| | De novo biliary stones | 2 (16.7%) |
| | Recurrent jaundice | 1 (8.3%) |

Values are number (%). Percentages for reasons for first unplanned repeat ERCP were calculated among the 12 patients who required unplanned repeat intervention. ERCP, endoscopic retrograde cholangiopancreatography.

# Reasons for unplanned repeat ERCP

Twelve patients (15.0%) underwent unplanned repeat ERCP. The dominant reasons for the first unplanned repeat procedure were stent dysfunction in 5 patients (41.7%), cholangitis in 4 (33.3%), de novo biliary stones in 2 (16.7%), and recurrent jaundice in 1 (8.3%) (Table 3; Fig. 4). Thus, unplanned repeat ERCP was mainly driven by stent-related dysfunction, infection, and recurrent biliary obstruction.

# Final endoscopic outcomes

At the last available follow-up, documented stricture resolution with stent-free status was achieved in 35 patients (43.8%). Twelve patients (15.0%) remained on ongoing endoscopic therapy. Eighteen patients (22.5%) died before confirmation of stricture resolution, 1 patient (1.2%) was lost to follow-up, and 14 patients (17.5%) had indeterminate final endoscopic status because available documentation was insufficient to confirm resolution.

When analyzed by outcome category, documented stricture resolution was recorded as yes in 35 patients (43.8%), no in 12 patients (15.0%), and indeterminate in 33 patients (41.2%). Stent-free status at last follow-up was achieved in 35 patients (43.8%), whereas 12 patients (15.0%) were not stent-free and 33 patients (41.2%) had indeterminate stent-free status. Ongoing stent therapy was present in 12 patients (15.0%). One patient (1.2%) required percutaneous transhepatic biliary drainage, and 1 patient (1.2%) required surgical revision. No patient required retransplantation for biliary stricture-related treatment failure (Table 4; Fig. 5).

Table 4
Final endoscopic outcomes

| Outcome | Category | n (%) |
|---|---|---|
| Final endoscopic status | Resolved stent-free | 35 (43.8%) |
| | Ongoing endoscopic therapy | 12 (15.0%) |
| | Death before confirmation of resolution | 18 (22.5%) |
| | Indeterminate | 14 (17.5%) |
| | Lost to follow-up | 1 (1.2%) |
| Documented stricture resolution | Yes | 35 (43.8%) |
| | No | 12 (15.0%) |
| | Indeterminate | 33 (41.2%) |
| Stent-free at last follow-up | Yes | 35 (43.8%) |
| | No | 12 (15.0%) |
| | Indeterminate | 33 (41.2%) |
| Ongoing stent therapy | Yes | 12 (15.0%) |
| | No | 35 (43.8%) |
| | Indeterminate | 33 (41.2%) |
| Need for PTBD | Yes | 1 (1.2%) |
| | No | 79 (98.8%) |
| Need for surgical revision | Yes | 1 (1.2%) |
| | No | 79 (98.8%) |
| Need for retransplantation | Yes | 0 (0.0%) |
| | No | 80 (100.0%) |

Values are number (%). Documented stricture resolution was defined as improvement or resolution without further endoscopic stent therapy at the last available follow-up. Stent-free status was defined as absence of a biliary stent, endoscopic nasobiliary drainage, or percutaneous drainage. Death before confirmation of resolution should not be interpreted as stricture-related mortality. PTBD, percutaneous transhepatic biliary drainage.

# ERCP-related adverse events

Post-ERCP pancreatitis occurred in 10 patients (12.5%). Post-ERCP hyperamylasemia was also recorded in 10 patients (12.5%). Post-ERCP cholangitis occurred in 1 patient (1.2%). No post-ERCP bleeding or perforation was observed in this cohort (Table 5).

Table 5
ERCP-related adverse events

| Adverse event | n (%) |
|---|---|
| Post-ERCP pancreatitis | 10 (12.5%) |
| Post-ERCP hyperamylasemia | 10 (12.5%) |
| Post-ERCP cholangitis | 1 (1.2%) |
| Post-ERCP bleeding | 0 (0.0%) |
| Post-ERCP perforation | 0 (0.0%) |

Post-ERCP pancreatitis was analyzed as a binary adverse event because severity grading was not systematically recorded. ERCP, endoscopic retrograde cholangiopancreatography.

# Exploratory risk-factor analysis for repeat ERCP

In univariable Cox regression analysis for time to any repeat ERCP, no baseline or index-procedure factor was significantly associated with repeat ERCP in the full cohort. In the simplified multivariable Cox model including post-ERCP pancreatitis, biliary stones at index ERCP, and the interval from liver transplantation to index ERCP, none of these variables remained independently associated with time to repeat ERCP. The hazard ratio was 1.877 for post-ERCP pancreatitis (95% confidence interval [CI], 0.748–4.710; P = 0.180), 1.510 for biliary stones at index ERCP (95% CI, 0.719–3.168; P = 0.276), and 1.027 per month for the interval from liver transplantation to index ERCP (95% CI, 0.974–1.083; P = 0.327).

In the plastic-stent subgroup, which included 71 patients and 33 repeat ERCP events, post-ERCP pancreatitis and biliary stones at index ERCP were associated with a higher hazard of repeat ERCP in the exploratory multivariable model. Post-ERCP pancreatitis was associated with an HR of 2.651 (95% CI, 1.063–6.612; P = 0.037), and biliary stones at index ERCP were associated with an HR of 2.317 (95% CI, 1.143–4.700; P = 0.020). Maximum plastic stent diameter was not significantly associated with repeat ERCP (HR, 1.130; 95% CI, 0.559–2.284; P = 0.734). The full-cohort and plastic-stent subgroup models are summarized in Table 6.

Table 6
Exploratory Cox regression for time to repeat ERCP

| Model | Variable | HR (95% CI) | P value |
|---|---|---|---|
| Full cohort simplified multivariable model | Post-ERCP pancreatitis | 1.877 (0.748–4.710) | 0.180 |
| | Biliary stones or sludge at index ERCP | 1.510 (0.719–3.168) | 0.276 |
| | Interval from liver transplantation to index ERCP, months | 1.027 (0.974–1.083) | 0.327 |
| Plastic-stent subgroup multivariable model | Maximum plastic stent diameter, Fr | 1.130 (0.559–2.284) | 0.734 |
| | Post-ERCP pancreatitis | 2.651 (1.063–6.612) | 0.037 |
| | Biliary stones or sludge at index ERCP | 2.317 (1.143-4.700) | 0.020 |

Hazard ratios were estimated using Cox proportional hazards regression for time from index ERCP to first repeat ERCP. Patients without repeat ERCP were censored at the last available follow-up. The plastic-stent subgroup included 71 patients and 33 repeat ERCP events. Because of the modest sample size and limited number of events, all risk factor analyses were exploratory. CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography; HR, hazard ratio.

Exploratory analyses for unplanned repeat ERCP were interpreted cautiously because only 12 patients experienced unplanned repeat intervention and some model categories were sparse.

# Discussion

In this single-center retrospective cohort study of patients undergoing ERCP for post-liver transplantation anastomotic biliary strictures, repeat ERCP was common but clinically heterogeneous. During a median follow-up of 39.2 months, 42.5% of patients required at least one repeat ERCP. A total of 70 repeat ERCP sessions were recorded, including 56 planned and 14 unplanned sessions. Importantly, 27.5% of patients underwent planned-only repeat ERCP, whereas 15.0% required unplanned repeat ERCP. The main triggers for unplanned repeat intervention were stent dysfunction, cholangitis, de novo biliary stones, and recurrent jaundice. Documented stricture resolution with stent-free status was achieved in 43.8% of the total cohort, whereas 15.0% remained on ongoing endoscopic therapy. Only one patient required percutaneous transhepatic biliary drainage, one required surgical revision, and no patient required retransplantation. These findings suggest that repeat ERCP after post-transplant anastomotic biliary stricture should not be interpreted as a uniform endpoint. Rather, planned and unplanned repeat interventions represent different clinical processes and should be analyzed separately.

Anastomotic biliary stricture after liver transplantation is a well-recognized complication and remains a major indication for post-transplant ERCP [1]. Current guideline-based management emphasizes

individualized selection among endoscopic, percutaneous, and surgical strategies according to biliary anatomy, stricture features, and procedural feasibility [16]. The present results fit within this management framework: although the median total number of ERCP sessions per patient was 1.0, more than 40% of patients required repeat ERCP, indicating that procedural burden cannot be fully captured by technical success or final stricture resolution alone.

A key feature of the present study is the distinction between planned and unplanned repeat ERCP. In conventional plastic stent-based therapy, repeat ERCP is often intentionally scheduled for stent exchange, progressive dilation, or stent removal [6]. Therefore, planned repeat ERCP should not automatically be interpreted as treatment failure. By contrast, unplanned repeat ERCP is more clinically concerning because it usually indicates recurrent obstruction, infection, stent dysfunction, or biliary stone-related events. Earlier studies evaluating early repeat ERCP after liver transplantation suggested that early reintervention may reflect clinically meaningful biliary events rather than routine staged therapy [13]. Another analysis of repeat ERCP in liver transplant recipients identified clinical and procedural factors that may influence the need for repeat intervention [14]. Our study expands this concept by separating planned-only, unplanned-only, and combined planned plus unplanned patterns. This classification may better reflect real-world treatment burden and differentiate expected staged management from unexpected biliary deterioration.

The reasons for unplanned repeat ERCP in our cohort were clinically intuitive. Stent dysfunction was the most frequent trigger, followed by cholangitis, de novo biliary stones, and recurrent jaundice. These findings are consistent with the known limitations of plastic biliary stents. Plastic stents are easy to place and remove, but their limited internal diameter makes them vulnerable to sludge accumulation and occlusion over time [7]. Biofilm formation and bacterial colonization may further contribute to loss of stent patency and infectious complications [8]. Plastic-stent efficacy may also vary according to stricture characteristics and the selected treatment strategy [17]. These limitations may be particularly relevant after liver transplantation, where anastomotic narrowing, duct angulation, ischemic susceptibility, and biliary stasis may further predispose patients to stent occlusion and infection.

Biliary stones and sludge were also important triggers for unplanned repeat ERCP. Biliary stasis proximal to an anastomotic stricture may promote stone or sludge formation, especially in the presence of an indwelling stent. Guidelines for common bile duct stones support ERCP as the primary therapeutic approach for duct clearance in appropriate patients [18]. ERCP-related guidance also emphasizes that complete drainage and management of obstruction are central to preventing recurrent biliary events [15]. In transplant recipients, the coexistence of a stricture and stones may increase procedural complexity and may explain why some patients require unplanned repeat intervention despite scheduled follow-up.

The optimal stent strategy for post-transplant anastomotic biliary strictures remains debated. Multiple plastic stents have long been used because they permit gradual dilation and individualized treatment across repeated sessions [4]. Fully covered self-expandable metal stents may reduce the number of scheduled procedures by providing a larger effective diameter, but pooled comparisons have shown

mixed results regarding resolution and recurrence [11]. Stent migration and adverse events remain important concerns when metal stents are used for benign biliary strictures [19]. An updated meta-analysis of randomized trials continued to show broadly comparable efficacy between fully covered metal stents and multiple plastic stents [20]. A separate systematic review likewise emphasized that differences in procedure burden must be balanced against device-specific adverse events [21]. In the present cohort, all biliary stents were plastic stents, reflecting the practice pattern at our center. Accordingly, our findings are most applicable to centers using plastic-stent-based management and highlight the importance of scheduled surveillance and timely exchange.

The final endoscopic outcomes require careful interpretation. Documented stent-free resolution was confirmed in 43.8% of patients, and only a small proportion required PTBD or surgical revision. Long-term studies have shown that endoscopic treatment can provide durable resolution in a substantial proportion of patients [22]. Structured endoscopic treatment protocols also underscore the need for continued follow-up until treatment completion [23]. Additional long-term evidence indicates that final outcome assessment should account for both confirmed resolution and the completeness of follow-up documentation [24]. Outcome-oriented classification has been proposed to improve standardization of post-transplant biliary-stricture assessment [25]. In our cohort, 22.5% of patients died before resolution could be confirmed, 17.5% had indeterminate final endoscopic status, and 1.2% were lost to follow-up. Therefore, the observed 43.8% should not be interpreted as the biological resolution rate for the entire cohort; it represents documented stent-free resolution within the available records.

Post-ERCP pancreatitis occurred in 12.5% of patients, post-ERCP cholangitis in 1.2%, and no bleeding or perforation was observed. A transplant-specific meta-analysis found that ERCP-related complications are clinically relevant but generally manageable in experienced centers [26]. A large inpatient database analysis similarly supports risk-aware procedural planning for liver transplant recipients undergoing ERCP [27]. Contemporary evidence also confirms that adverse events remain an important consideration across ERCP indications [28]. In our study, post-ERCP pancreatitis was analyzed as a binary event because severity grading was not systematically recorded. Transplant-specific data support considering PEP a clinically relevant post-procedural outcome in this population [29], while broader literature highlights its multifactorial nature [30]. In the plastic-stent subgroup, PEP and biliary stones at index ERCP were associated with a higher hazard of repeat ERCP. These findings are hypothesis-generating and require validation in larger cohorts.

Maximum plastic stent diameter was not significantly associated with repeat ERCP in the plastic-stent subgroup. This result should not be interpreted as evidence that stent caliber is irrelevant. In our cohort, stent diameter showed limited variability, with most patients receiving 8.5-Fr plastic stents, which reduced power to detect a dose-response association. Stent patency is also influenced by sludge accumulation, biofilm formation, indwelling time, stricture morphology, duct angulation, drainage completeness, and local exchange protocols [7]. Repeat ERCP is therefore multifactorial and should not be attributed to a single procedural parameter.

This study has several limitations. First, it was a single-center retrospective study, and treatment strategies reflected local practice patterns. Second, the sample size was modest, particularly for unplanned repeat ERCP, which occurred in only 12 patients. Therefore, risk factor analyses were exploratory, and models containing sparse categories may be unstable. Third, all stents in this cohort were plastic stents; thus, the results cannot be directly generalized to centers using fully covered metal stents as the primary strategy. Fourth, final stricture resolution could not be confirmed in a substantial proportion of patients because of death before resolution, loss to follow-up, or insufficient documentation. Fifth, post-ERCP pancreatitis severity, detailed cannulation parameters, prophylactic measures, and some transplant-related variables were not systematically available. Despite these limitations, the study provides a clinically practical description of repeat ERCP burden, planned versus unplanned intervention patterns, unplanned triggers, and final endoscopic outcomes in a real-world post-transplant cohort.

## Conclusions

In conclusion, repeat ERCP was frequently required after initial endoscopic therapy for post-liver transplantation anastomotic biliary strictures. Planned repeat ERCP accounted for most repeat procedures, whereas unplanned repeat ERCP occurred in 15.0% of patients and was mainly triggered by stent dysfunction, cholangitis, and biliary stones. Endoscopic therapy achieved documented stent-free resolution in a substantial subset of patients, with low rates of PTBD, surgical revision, and retransplantation. Distinguishing planned from unplanned repeat ERCP may provide a more clinically meaningful framework for evaluating endoscopic treatment burden and outcomes in post-transplant anastomotic biliary strictures.

## Abbreviations

ABS
anastomotic biliary stricture
ALP
alkaline phosphatase
ALT
alanine aminotransferase
ASGE
American Society for Gastrointestinal Endoscopy
AST
aspartate aminotransferase
CI
confidence interval
ENBD
endoscopic nasobiliary drainage
ERCP

endoscopic retrograde cholangiopancreatography
GGT
gamma-glutamyl transferase
HR
hazard ratio
IQR
interquartile range
PEP
post-ERCP pancreatitis
PTBD
percutaneous transhepatic biliary drainage
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology
WBC
white blood cell count.

# Declarations

### Ethics approval

The study protocol was approved by the Ethics Committee of the Second Affiliated Hospital of Guangxi Medical University (approval No. 2018-KYL [003]).

### Consent to participate

The requirement for written informed consent was waived by the Ethics Committee of the Second Affiliated Hospital of Guangxi Medical University because of the retrospective nature of the study.

### Consent for publication

Not applicable.

# Competing interests

The authors declare that they have no competing interests.

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The authors received no specific funding for this work.

# Author Contribution

MQ conceived and designed the study. HW, GL, JQ, FQ, JW, SL, and JH acquired and curated the data. HW and GL performed the statistical analyses and prepared the tables and figures. MQ supervised the study and verified the clinical data and statistical outputs. HW drafted the manuscript. MQ critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.


# Acknowledgements

Not applicable.


# Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available because they contain potentially identifiable clinical information and are subject to institutional and ethical restrictions, but are available from the corresponding author on reasonable request and with appropriate institutional approval.

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# Figures

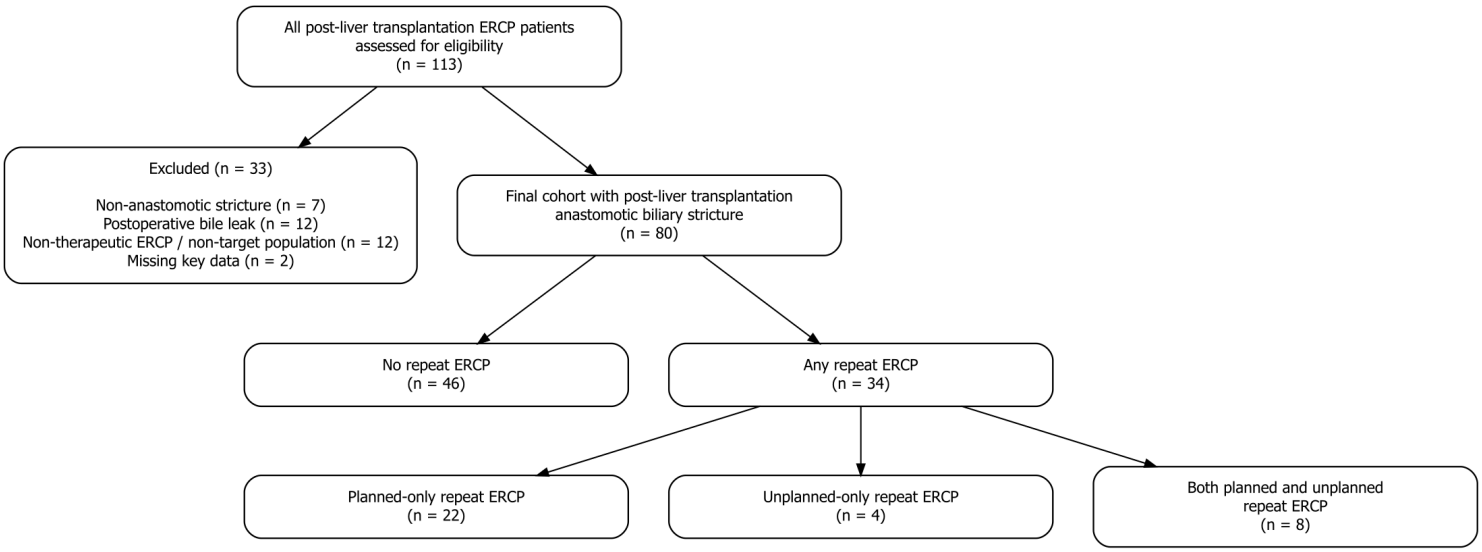



**Figure 1**

**Study flow and repeat ERCP classification.** Among 113 post-liver transplantation patients who underwent ERCP, 33 were excluded, including 7 with non-anastomotic stricture, 12 with postoperative bile leak, 12 who underwent non-therapeutic ERCP or did not meet the target population criteria, and 2 with missing key data. The final cohort included 80 patients with post-liver transplantation anastomotic biliary stricture. Of these, 46 had no repeat ERCP and 34 underwent repeat ERCP, including 22 with planned-only repeat ERCP, 4 with unplanned-only repeat ERCP, and 8 with both planned and unplanned repeat ERCP.

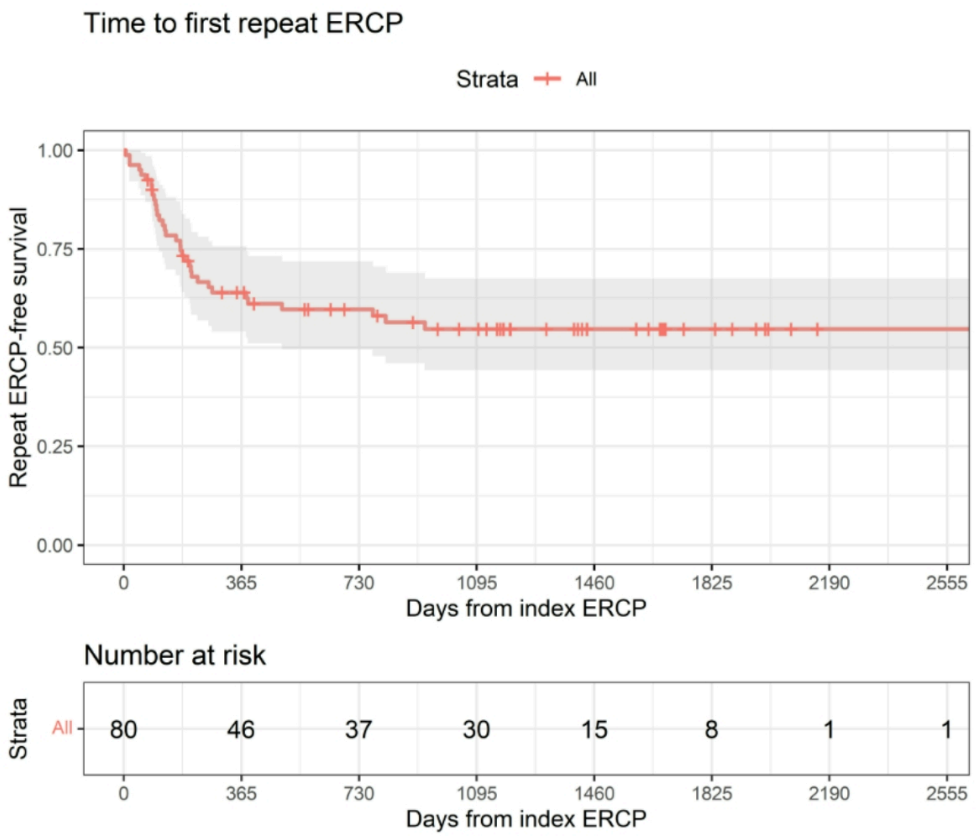



**Figure 2**

**Time to first repeat ERCP after index ERCP.** Kaplan-Meier curve showing repeat ERCP-free survival after index ERCP. Time was measured from index ERCP to the first repeat ERCP. Patients without repeat ERCP were censored at the last available follow-up. ERCP, endoscopic retrograde cholangiopancreatography.

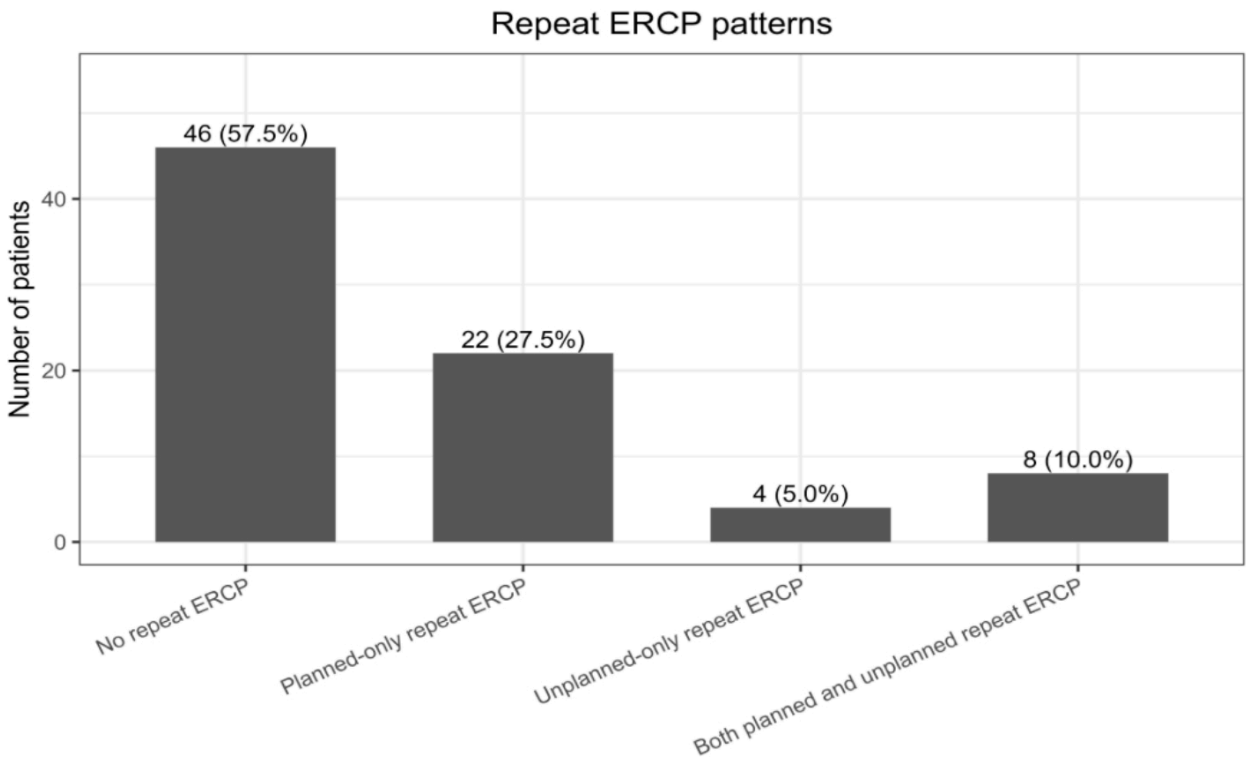



**Figure 3**

**Repeat ERCP patterns after index ERCP.** Distribution of repeat ERCP patterns among the 80 included patients. Forty-six patients had no repeat ERCP, 22 underwent planned-only repeat ERCP, 4 underwent unplanned-only repeat ERCP, and 8 underwent both planned and unplanned repeat ERCP. ERCP, endoscopic retrograde cholangiopancreatography.

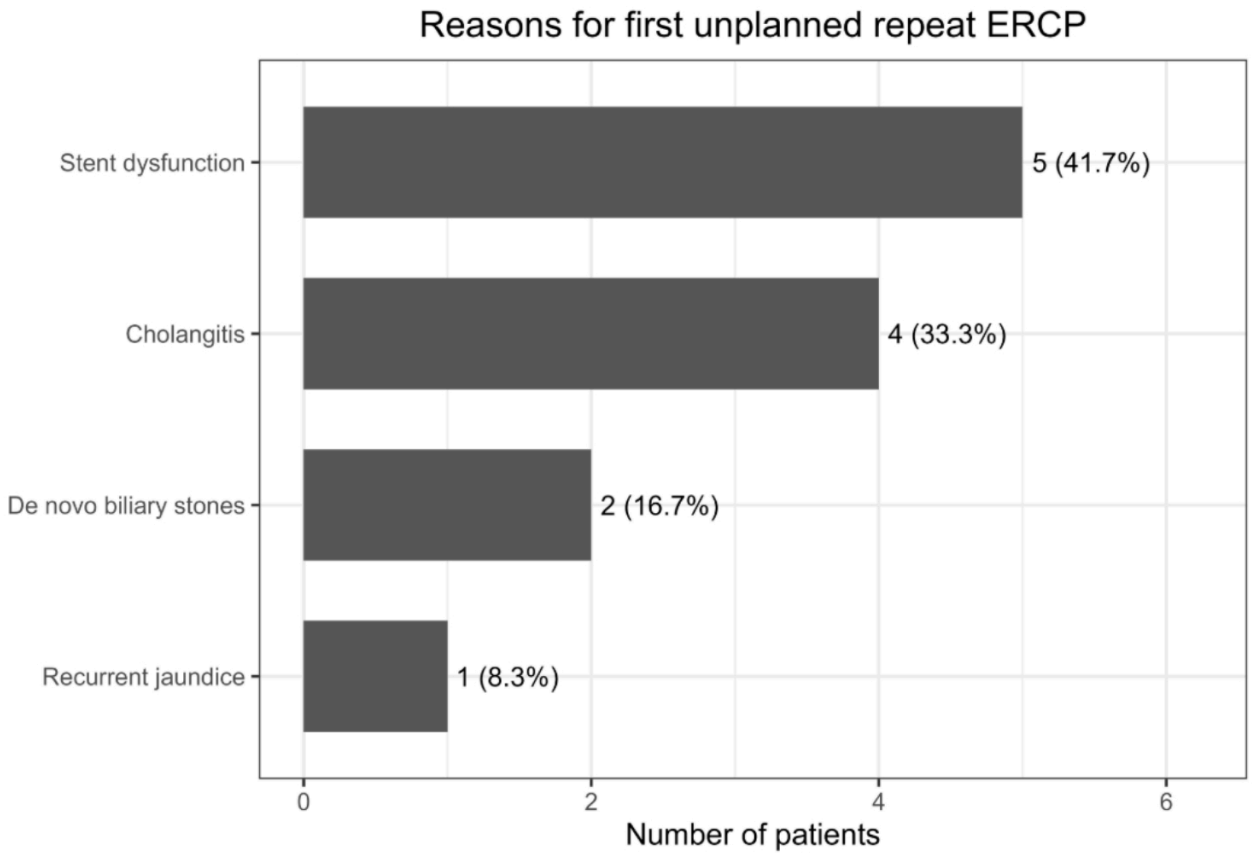



**Figure 4**

**Reasons for first unplanned repeat ERCP.** Dominant clinical triggers for the first unplanned repeat ERCP among 12 patients. Stent dysfunction occurred in 5 patients, cholangitis in 4, de novo biliary stones in 2, and recurrent jaundice in 1. ERCP, endoscopic retrograde cholangiopancreatography.

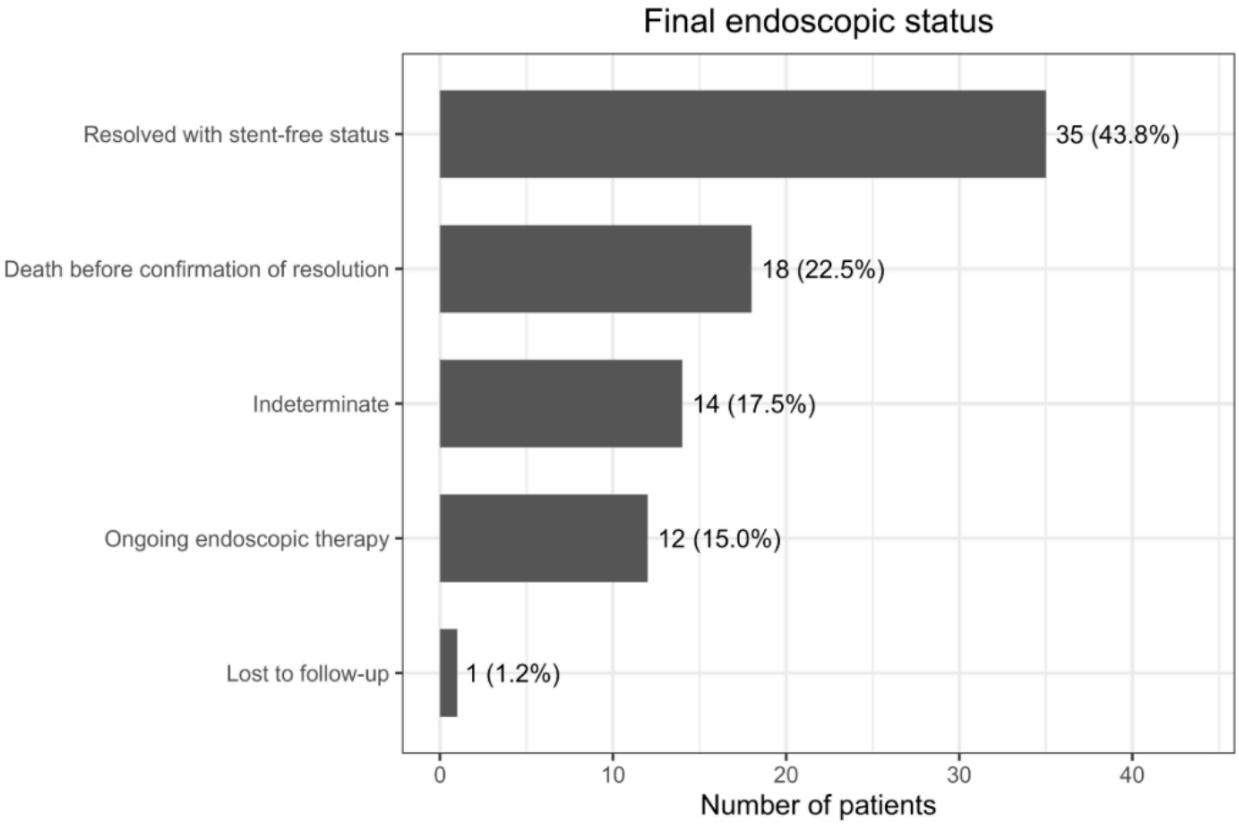



**Figure 5**

**Final endoscopic status at last follow-up.** Final endoscopic status at the last available follow-up. Documented stricture resolution with stent-free status was confirmed in 35 patients, 12 remained on ongoing endoscopic therapy, 18 died before confirmation of resolution, 14 had indeterminate status, and 1 was lost to follow-up.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- STROBEchecklistcohort.docx