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Endoscopic papillary balloon dilation decreases the risk of bleeding in cirrhotic patients compared with endoscopic biliary sphincterotomy

A national population-based study

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Abstract

Although endoscopic papillary balloon dilation (EPBD) seems to cause fewer instances of bleeding, there are insufficient data to determine the optimal methods for decreasing the risk of bleeding in cirrhotic patients.

In this study, we compared the bleeding risks following endoscopic biliary sphincterotomy (EST) vs EPBD in cirrhotic patients and identified clinical factors associated with bleeding and 30-day mortality.

Taiwan's National Health Insurance Database was used to identify 3201 cirrhotic patients who underwent EST or EPBD between January 1, 2010, and December 31, 2013.

We enrolled 2620 patients receiving EST and 581 patients receiving EPBD. The mean age was 63.1 ± 13.9 years, and 70.4% (2252/3201) were men. The incidence of post-endoscopic retrograde cholangiopancreatography (ERCP) bleeding was higher among patients treated with EST than those treated with EPBD (EST vs EPBD: 3.5% vs 1.9%). Independent predisposing factors for bleeding included EST, renal function impairment, and antiplatelet or anticoagulant therapy. The overall 30-day mortality was 4.0% (127/3201). Older age, renal function impairment, hepatic encephalopathy, bleeding esophageal varices, ascites, hepatocellular carcinoma, biliary malignancy, and pancreatic malignancy were associated with higher risks for 30-day mortality.

To decrease post-ERCP hemorrhage, EPBD is the preferred method in patients with cirrhosis, especially for those who have renal function impairment or are receiving antiplatelet or anticoagulant therapy.

Abbreviations: BTI = biliary tract infection, CI = confidence interval, EPBD = endoscopic papillary balloon dilation, ERCP = endoscopic retrograde cholangiopancreatography, EST = endoscopic sphincterotomy, EVB = esophageal variceal bleeding, HCC = hepatocellular carcinoma, HE = hepatic encephalopathy, HR = hazard ratio, MELD = model for end-stage liver disease, NHIB = National Health Insurance Bureau, NHRI = National Health Research Institute, RFI = renal functional impairment.

Keywords: EPBD, ERCP, EST, hemorrhage, liver cirrhosis

1. Introduction

During therapeutic endoscopic retrograde cholangiopancreatography (ERCP), a wide opening of the ampulla of Vater is crucial for a successful endoscopic treatment. Endoscopic sphincterotomy (EST) and endoscopic papillary balloon dilation (EPBD) are common techniques used to open the sphincter. EST is safe and effective but still has an associated complication rate of approximately 5% and a mortality rate of <1%.[1,2] Post-EST bleeding is a common complication and is associated with elevated morbidity and mortality, especially among cirrhotic patients.[3] A landmark prospective study of 2347 patients undergoing EST reported that clinically significant post-EST bleeding occurred in 2% of patients (n = 48), and 21 patients (0.89%) underwent ≥1 subsequent endoscopic procedures to control bleeding.[1] Death related to delayed bleeding occurred in 2 patients with Child–Pugh class C cirrhosis despite appropriate endoscopic and radiologic interventions.

EPBD is the other main procedure to open the sphincter.[4–6] The advantage of EPBD is the lower risk of hemorrhage and biliary sphincter damage compared with EST.[7–9] A meta-analysis that included 12 trials demonstrated the lower occurrence of major bleeding in patients treated with EPBD compared with EST (0.1% vs 4.8%).[9] Because EPBD causes

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fewer cases of hemorrhaging, EPBD is the recommended procedure in patients with an underlying coagulopathy or the need for anticoagulation following ERCP.[3,10,11] The risks of hemorrhage with EST or EPBD are associated with underlying conditions such as coagulopathy, use of antithrombotic and antiplatelet medications, cirrhosis, thrombocytopenia, and chronic renal failure.[1,11–14] The risk of complications is high among cirrhotic patients, especially those with liver decompensation.[15–17] The only retrospective study that investigated coagulopathy in cirrhotic patients directly compared the risk of hemorrhage between treatment with EPBD vs EST and showed that the bleeding rate following EPBD was lower than that following EST (0% vs 30%, respectively), and higher rates of bleeding were associated with poor liver preservation.[12] To our knowledge, the risks of hemorrhage associated with these two methods have not been well evaluated or extensively discussed with respect to cirrhotic patients.

To understand the risk of hemorrhage and identify the risk factors between EST and EPBD in cirrhotic patients, we used Taiwan's nationwide population-based database, and we also attempted to identify the clinical factors associated with 30-day mortality.

2. Materials and methods

2.1. Database

The secondary database used in our study was derived from the National Health Insurance research database in Taiwan, using deidentified patients. The database was established and is maintained by the Taiwan National Health Insurance Bureau (NHIB) and the National Health Research Institute (NHRI). In 1995, Taiwan rolled out the National Health Insurance program that currently covers >99% of the population in Taiwan. For medical payment, all medical records from all contracted medical institutions are required by the NHIB. This dataset includes all diagnostic coding information for hospitalized patients in Taiwan. All investigators using this database are required to undergo an evaluation by the NHRI. This study was approved by the NHRI (application and agreement number 104359). The identities of patients and health care providers and other personal information were protected.

This study was initiated with the approval of the Institutional Review Board of the Buddhist Dalin Tzu Chi Hospital, Chiayi, Taiwan (IRB B10403026). The review board waived the requirement for written informed consent from all patients because all identifying personal information was removed from the secondary files prior to analysis.

2.2. Study sample

This retrospective study included patients who were discharged with a diagnosis of cirrhosis according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM, codes 571.5, or 571.2) and who received ERCP with EST or EPBD, between January 1, 2010, and December 31, 2013. In cases of multiple hospitalizations, only the first episode was included. Each patient was followed individually from the time of first hospitalization until December 31, 2013. A total of 3201 cirrhotic patients were included in the analyses. Of these, 2620 patients received EST, and 581 patients received EPBD for biliary assessment.

The diagnostic accuracy of records indicating ERCP treatment by EST, EPBD, or endoscopic hemostatic treatment was also confirmed by the payment records. Information regarding insurance-paid endoscopic treatment was reliable because every treatment is strictly regulated by the NHIB. The choice of either EST or EPBD depended on preferences of the treating physicians. Post-ERCP hemorrhage was defined as an endoscopic hemostatic treatment post-ERCP.

To analyze the effects of EST or EPBD on the endoscopic hemostatic treatment of cirrhotic patients, we selected comorbid medical factors, including alcoholism (ICD-9-CM codes 291, 303, 305.00–305.03, 571.0–571.3), esophageal variceal bleeding (EVB) (ICD-9-CM codes 456.0, 456.20), hepatic encephalopathy (HE) (ICD-9-CM code 572.2), hepatocellular carcinoma (HCC) (ICD-9-CM code 155.0), and renal function impairment (RFI) (ICD-9-CM codes 584, 585, 586, 572.4, or other procedure codes related to renal failure).[18]

2.3. Statistical analyses

SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA) was used to perform the analyses in this study. The mean and standard deviation (SD) for continuous variables and values for demographic and baseline clinical features are presented for all included patients. The chi-square test or Fisher's exact test was used to compare categorical variables. Student's *t* test was used to compare continuous variables with normal distributions, and the Mann–Whitney *U*-test was used for continuous variables with nonnormal distributions.

The basic comparisons of demographics and baseline clinical features between the patients with and without endoscopic hemostasis (i.e., EST and EPBD) were performed with logistic regression analyses. When we compared these two groups, a P value $< .05$ was considered statistically significant.

The starting point for evaluating the 30-day mortalities in the EST and EPBD groups was the date of the patient's admission. Calculation and comparison of cumulative incidences of 30-day mortality between the two groups were conducted using the Kaplan–Meier method. Differences were tested in the full time-to-event distributions between the study groups using the log-rank test. In order to identify risk factors for mortality, the proportional hazards Cox regression model was used to control possible confounding factors. We calculated hazard ratios (HRs) with 95% CIs for the 30-day mortality, and the significance level (P value) was set as .05.

3. Results

3.1. Baseline demographics and clinical characteristics

A total of 3201 cirrhotic patients received EST or EPBD (70.4% male; mean age = 63.1 ± 13.9 years) were included in the analyses. Of these, 2620 patients received EST, and 581 patients received EPBD for biliary assessment. One hundred and three patients (3.2%; 103/3201) developed post-ERCP bleeding that required endoscopic hemostasis treatment. Demographic characteristics of patients treated with EST compared with those treated with EPBD are showed in Table 1. No statistically significant differences were noted between these two groups regarding age, alcoholism, antiplatelet or anticoagulant therapy, and endoscopic hemostasis treatment. Patients who received EPBD were younger and presented with a greater number of

Table 1

Demographic characteristics of patients who received EST compared with those treated with EPBD.

Variable	EST (n = 2620)	EPBD (n = 581)	*P* value*
Male, n (%)	1840 (70.2)	412 (70.9)	.744
Age, years†	63.6 ± 14.0	61.1 ± 13.5	<.001
Alcoholism, n (%)	267 (10.2)	80 (13.8)	.012
RFI, n (%)	158 (6.0)	41 (7.1)	.354
Antiplatelet or anticoagulant therapy, n (%)	177 (6.8)	59 (10.2)	.005
HCC, n (%)	500 (19.1)	102 (17.6)	.394
HE, n (%)	66 (2.5)	19 (3.3)	.308
Ascites, n (%)	229 (8.7)	63 (10.8)	.111
EVB, n (%)	23 (0.9)	8 (1.4)	.266
Biliary tract infection, n (%)	1248 (47.6)	301 (51.8)	.063
Acute pancreatitis, n (%)	295 (11.3)	61 (10.5)	.662
Biliary malignancy, n (%)	133 (5.1)	23 (4.0)	.288
Pancreatic malignancy, n (%)	28 (1.0)	6 (1.1)	1.000
ERBD, n (%)	780 (29.8)	166 (28.6)	.581
ENBD, n (%)	134 (5.1)	39 (6.7)	.128
Endoscopic hemostasis treatment, n (%)	92 (3.5)	11 (1.9)	.05

ENBD = Endoscopic nasobiliary drainage, EPBD = endoscopic papillary balloon dilation, ERBD = endoscopic retrograde biliary drainage, EST = endoscopic sphincterotomy, EVB = esophageal variceal bleeding, HCC = hepatocellular carcinoma, HE = hepatic encephalopathy, RFI = renal function impairment.

* Performed using the chi-square test and the Mann–Whitney *U*-test.

† Data are expressed as means ± standard deviations.

histories of alcoholism and use of antiplatelet or anticoagulant therapy compared with those who received EST. More patients treated with EST developed post-ERCP hemorrhage and required endoscopic hemostasis treatment (EST vs EPBD: 3.5%, n = 92/2620 vs 1.9%, n = 11/581).

3.2. Demographics and baseline clinical features predisposing to post-ERCP hemorrhage

In univariate analysis, renal function impairment, antiplatelet or anticoagulant therapy, and EST were all found to be significantly different between the groups of patients with and without endoscopic hemostasis treatment (Table 2). Table 3 shows the results of multivariate logistic regression analysis, adjusted by age, sex, HCC, EVB, HE, ascites, alcoholism, biliary malignancy, pancreatic malignancy, biliary tract infection, antiplatelet or anticoagulant therapy, and acute pancreatitis to determine the ORs for requiring endoscopic hemostasis among cirrhotic patients post-ERCP. Renal function impairment (OR, 2.197; 95% CI, 1.201–4.021; $P = .011$), antiplatelet or anticoagulant therapy (OR, 1.840; 95% CI, 1.007–3.362; $P = .047$), and EST (OR, 1.961; 95% CI, 1.041–3.696; $P = .037$) were significant predisposing factors for patients who required endoscopic hemostasis (Table 3).

Table 3

Multivariate analysis of clinical characteristics of cirrhotic patients who received endoscopic hemostasis treatment†.

	Odds Ratio	95% CI	*P* value*
RFI	2.197	1.201–4.021	.011
Antiplatelet or anticoagulant therapy	1.840	1.007–3.362	.047
EST vs. EPBD	1.961	1.041–3.696	.037

EPBD = endoscopic papillary balloon dilation, EST = endoscopic sphincterotomy, RFI = renal function impairment.

* Performed using multivariate logistic regression.

† Adjusted for age, sex, hepatocellular carcinoma, esophageal variceal bleeding, hepatic encephalopathy, ascites, alcoholism, biliary malignancy, pancreatic malignancy, biliary tract infection and acute pancreatitis.

3.3. Clinical features associated with 30-day mortality in cirrhotic patients receiving EST or EPBD

The overall 30-day mortality was 4.0% (127/3201). The 30-day mortality for patients treated with EST vs EPBD was 4.1% (n = 108/2620) vs 3.3% (n = 19/581), respectively, showing no statistically significant differences between the two groups (log-rank test: $P = .341$). Table 4 shows the results of Cox proportional regression model analysis adjusted by age, sex, and other comorbid disorders, including HCC, EVB, HE, ascites, alcoholism, biliary malignancy, acute pancreatitis, pancreatic malignancy, biliary tract infection, EST vs EPBD, endoscopic

Table 2

Univariate analysis of clinical characteristics among cirrhotic patients who received endoscopic hemostasis treatment (n = 103).

Variable		Odds Ratio	95% CI	*P* value*
Male, n (%)	69 (67.0)	1.176	0.774–1.785	.448
Age, years†	64.1 ± 13.1	1.005	0.991–1.019	.487
Alcoholism, n (%)	14 (13.6)	1.306	0.735–2.321	.363
RFI, n (%)	13 (12.6)	2.261	1.241–4.121	.008
Antiplatelet or anticoagulant therapy, n (%)	28 (27.2)	1.862	1.025–3.384	.041
HE, n (%)	3 (2.9)	1.103	0.343–3.552	.869
Ascites, n (%)	11 (10.7)	1.199	0.634–2.267	.577
EVB, n (%)	1 (1.0)	1.003	0.135–7.424	.998
HCC, n (%)	13 (12.6)	0.615	0.432–1.108	.106
Biliary malignancy, n (%)	3 (2.9)	0.577	0.181–1.842	.353
Pancreatic malignancy, n (%)	1 (1.0)	0.911	0.123–6.723	.927
Biliary tract infection, n (%)	42 (40.8)	0.727	0.488–1.084	.117
Acute pancreatitis, n (%)	8 (7.8)	1.503	0.724–3.119	.274
EST, n (%)	92 (89.3)	1.886	1.002–3.547	.049

EST = endoscopic sphincterotomy, EVB = esophageal variceal bleeding, HCC = hepatocellular carcinoma, HE = hepatic encephalopathy, RFI = renal function impairment.

* Performed using logistic regression.

† Data are expressed as mean ± standard deviation.

Table 4

Adjusted hazard ratios for 30-day mortality in cirrhotic patients receiving EST or EPBD†.

Variable	Hazard Ratio	95% CI	*P* value*
Age	1.023	1.008–1.039	.003
RFI	3.396	2.120–5.439	<0.001
Ascites	3.094	2.080–4.602	<0.001
HE	2.923	1.562–5.469	.001
EVB	2.232	0.871–5.724	.095
HCC	3.633	2.487–5.308	<.001
Biliary malignancy	2.983	1.686–5.277	<.001
Pancreatic malignancy	5.974	2.837–12.582	<.001
BTI	0.660	0.445–0.980	.039
Acute pancreatitis	0.246	0.078–0.776	.017
EST vs EPBD	0.967	0.589–1.589	.895

BTI = biliary tract infection, EPBD = endoscopic papillary balloon dilation, EST = endoscopic sphincterotomy, EVB = esophageal variceal bleeding, HCC = hepatocellular carcinoma, HE = hepatic encephalopathy, RFI = renal function impairment.

* Performed using Cox proportional regression model analysis.

† Adjusted for age, sex, and other comorbid disorders including HCC, EVB, HE, ascites, alcoholism, biliary malignancy, acute pancreatitis, pancreatic malignancy, biliary tract infection, EST vs. EPBD, endoscopic hemostasis treatment, and antiplatelet or anticoagulant therapy.

hemostasis treatment, and antiplatelet or anticoagulant therapy to determine the HRs for 30-day mortality. The choice of EST or EPBD was not associated with the 30-day mortality (HR 0.967; 95% CI 0.589–1.589; $P = .895$). Older age (HR 1.023; 95% CI 1.008–1.039; $P = .003$), HE (HR 2.923; 95% CI 1.562–5.469; $P = .001$), bleeding from esophageal varices (HR 2.232; 95% CI 0.871–5.724; $P = .095$), HCC (HR 3.633; 95% CI 2.487–5.308; $P < .001$), RFI (HR 3.396; 95% CI 2.120–5.439; $P < .001$), ascites (HR 3.094; 95% CI 2.080–4.602; $P < .001$), biliary malignancy (HR 2.983; 95% CI 1.686–5.277; $P < .001$), and pancreatic malignancy (HR 5.974; 95% CI 2.837–12.582; $P < .001$) were associated with higher risks for mortality in cirrhotic patients receiving EST or EPBD. Patients with biliary tract infection (HR 0.660; 95% CI 0.445–0.980; $P = .039$) or acute pancreatitis (HR 0.246; 95% CI 0.078–0.776; $P = .017$) presented lower 30-day mortality.

4. Discussion

In this large national study, we demonstrate that performing EST in patients who have cirrhosis is an independent risk factor associated with post-ERCP bleeding. Our study provides evidence supporting the usefulness of EPBD in cirrhotic patients to reduce the bleeding risk. For cirrhotic patients with renal function impairment or accepting antiplatelet or anticoagulant therapy, the bleeding risk is also increased. We further observed that the 30-day mortality in those patients is not related to EST or EPBD. Advanced age, underlining disease (malignancy or RFI), and the complications of liver cirrhosis were the most important factors associated with increased 30-day mortality.

There is an overall higher rate of hemorrhage related to ERCP in patients with cirrhosis.[19] One meta-analysis showed the incidence of post-ERCP bleeding is 4.58% (95%CI: 2.77–6.75%, $I^2 = 85.9\%$).[19] The incidences vary from 1.1% to 25% in different reports.[1,15–17,20,21] The variations among these studies could arise because of differences in the patient populations, types of procedures and the definition of bleeding. For example, Adler et al[17] performed biliary sphincterotomy in only 15% of the procedures (82/538 procedures), and the bleeding rate was only 1.1%. A national database study by Navaneethan reported that 57.8% of 3228 patients underwent EST, and the reported bleeding rate was 2.1%.[15] The patients included in our study were cirrhotic patients who received EST or EPBD, the post-ERCP bleeding rate (overall 3.2%; 130/3201; EST vs EPBD: 3.5% vs 1.9%) was higher than rates seen in previous studies.[15,17] By using the necessary of endoscopic hemostasis, this study reports more significant bleeding events.

Several randomized, controlled trials have shown that EPBD may significantly reduce the risk of bleeding compared with EST.[7,9,22,23] A meta-analysis that included 12 trials reported about the occurrence of bleeding and found a significantly lower occurrence of major bleeding in patients treated with EPBD than in patients treated with EST (0.1% vs 4.8%) (relative risk 0.15, 95% CI 0.06–0.39 by the random-effects model).[9] All subgroups (except a dilation time < 45 s, anatomic variance) were associated with a significantly lower rate of major bleeding in patients treated with EPBD compared with those treated with EST. Using large-balloon dilatation for difficult stone removal may induce extensive tissue injury. However, the meta-analysis also showed a lower bleeding rate in EPBD compared with EST.[24,25] Although EPBD is suggested for patients with coagulopathy, the risks of hemorrhage associated with the two methods have not been extensively studied in cirrhotic patients. Only one retrospective study showed lower bleeding rates with EPBD compared with EST (0% vs 30%, respectively) in patients with cirrhosis and coagulopathy.[12] Because only 20 patients were included in that analysis, the study's power is weak.

The present national population-based study included a total of 3201 cirrhotic patients who received either EST or EPBD. The data confirmed the higher bleeding risk associated with EST in cirrhotic patients (EST vs EPBD: 3.5% [92/2620] vs 1.9% [11/581]). The multivariate analysis also demonstrated that EST is an independent predictor of post-ERCP bleeding compared with EPBD (OR, 1.961; 95% CI, 1.041–3.696; $P = .037$). These results increase the evidence supporting the EPBD treatment in patients with cirrhosis.

Our study highlights certain risk factors for cirrhotic patients who receive EST and EPBD. The risk factors associated with bleeding have been studied in cirrhotic patients, including therapeutic ERCPs, EST, antiplatelet or anticoagulant therapy, Model for End-stage Liver Disease (MELD) score, and the Child–Pugh classification.[12,15,17,20,26,27] Among these factors, EST is the only one identified by all reports, and renal function impairment has not been well studied. Except for EST, the bleeding risk is double in cirrhotic patient with RFI compared with those without RFI (OR, 2.197; 95% CI, 1.201–4.021; $P = .011$) in our study.

Although the effect seems marginal, our report also demonstrated that antiplatelet or anticoagulant therapy is associated with post-procedure bleeding (OR, 1.840; 95% CI, 1.007–3.362; $P = .047$). The data were compatible with those from a nationwide administrative database study from Japan (n = 61,002; EST vs EPBD = 54,493 vs 6,509), which investigated the association between oral administration of antithrombotic agents and clinically significant bleeding within 3 days after the procedure.[28] EPBD was performed more frequently than EST in patients with chronic renal failure or liver cirrhosis and in those receiving antithrombotic agents, but the rate of severe bleeding was similar in both groups (0.8%).[28] Severe bleeding after EST and EPBD was increased among patients who received anti-

coagulants but was not increased in those who received antiplatelet agents. Age (OR, 1.27; 95% CI, 1.05–1.54; $P = .012$), chronic renal failure (OR, 3.62; 95% CI, 2.53–5.18; $P < .001$), and liver cirrhosis (OR, 2.10; 95% CI 1.13–3.91; $P = .020$) were also important factors that predicted post-procedure bleeding.[28] Both the national databases from Japan and Taiwan showed similar conclusions: EPBD seems to be a reasonable choice for treating cirrhosis patients, especially patients who have RFI and receive anticoagulants.

Our study showed that liver decompensation (HE, EV bleeding, or ascites) and malignancy were not related to the bleeding risk but were associated with the 30-day mortality. Although some small series reported a high bleeding rate in patients with Child–Pugh class C,[12,20] most reports showed no differences among patients with different Child–Pugh classifications.[21,26,27] However, researchers also observed that decompensated liver cirrhosis is associated with an increased length of stay and greater hospitalization costs following ERCP.[15] The high rate of mortality among cirrhotic patients is well known and usually is due to patients' decompensated status and susceptibility to infectious diseases.[29,30] In our study, the 30-day mortality rates showed no statistically significant differences between EST and EPBD (4.1% vs 3.3%). Liver decompensation, including HE, BEV, and ascites, were predictive factors for 30-day mortality. Comorbidities including RFI and malignancy were also risk factors for mortality in those patients. Patients with decompensated status and higher comorbidities required surgeons to weigh the risks and benefits of the EST or EPBD procedure in the context of the elevated mortality.

To the best of our knowledge, this is the first population-based study that compares the differential risk of hemorrhage following EST and EPBD in cirrhotic patients. Nonetheless, certain limitations of our study should be addressed. First, the major limitation is that our national insurance-based databases lack detailed clinical data. Although the severity of liver cirrhosis was based on the Child–Pugh or MELD score, it was not possible, on the basis of ICD-9-CM coding numbers in this database, to obtain other laboratory data such as prothrombin time or albumin, bilirubin, or creatinine levels. The method of hemostasis, the size of biliary balloons, the size of stones, the degree of coagulopathy, platelet count, and the degree of hemorrhage were not available in the database. However, we did consider confounding factors and adjusted for them using multivariate logistic regression analysis. Although unmeasured confounders may still exist in the data, we believe the methodology used in the present study is solid and robust.

Second, the severity of post-ERCP bleeding is not reported here. The severity of post-ERCP bleeding is not reported in sufficient detail in the database according to the hemoglobin drop, blood transfusion amount, and hospital stay, all of which may relate to the complications of underlining end-stage liver diseases. By using the necessary of endoscopic hemostasis, this study reports the events with high severity. The large sample size provides the statistical power to detect differences in hemorrhage risk between EST and EPBD in cirrhotic patients and may provide useful information for clinical practice.

Third, this study was approved by the NHRI in 2015. According the agreement, the study period is limited from January 2010 to December 2013. The data of the patients in recent period was not included in this study. However, EPBD and EST were standard and mature techniques for biliary tract disease in Taiwan. We believe our results still have the clinical implication in this field. Fourth, this study did not analysis the indications of the two groups. Although the actual indications can't be identified by ICD coding, the baseline characters and procedures (ERBD and ENBD) between both groups (included biliary trace infection, pancreatic cancer, biliary cancer, pancreatitis, etc) were compatible (Table 1). The indication bios may be minimal. If the patient selectin bios existed, the EPBD may be a favor procedure in patients with altered anatomy and bleeding tendency. In those high-risk patients, the EPBD still need fewer endoscopic hemostasis. This result could support that EPBD is the preferred method in cirrhotic patients.

In conclusion, this nationwide population-based study showed that the risk of hemorrhage is higher in cirrhotic patients who have RFI and are receiving antiplatelet or anticoagulant therapy. In routine clinical practice, EPBD should be the most reasonable procedure in cirrhotic patients to reduce the post-ERCP bleeding. Liver decompensation (HE, EV bleeding, or presence of ascites) and malignancy were not related to the bleeding risk but were associated with the 30-day mortality.

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Author contributions

Tsung-Hsing Hung: material support, collected and analyzed the data, drafting of the manuscript.
Chih-Wei Tseng: contributed to the design of the study, material support, drafting of the manuscript, critical revision of the manuscript for important intellectual content.
Kuo-Chih Tseng: material support, critical revision of the manuscript for important intellectual content.
Yu-Hsi Hsieh: contributed to the design of the study, critical revision of the manuscript for important intellectual content.
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