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Pure Cut or Endocut for Biliary Sphincterotomy? A Multicenter Randomized Clinical Trial

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INTRODUCTION: **Adverse events (AE) after endoscopic retrograde cholangiopancreatography (ERCP) are not uncommon and post-ERCP acute pancreatitis (PEP) is the most important one. Thermal injury from biliary sphincterotomy may play an important role and trigger PEP or bleeding. Therefore, this study evaluated the outcomes of 2 electric current modes used during biliary sphincterotomy.**

METHODS: **From October 2019 to August 2021, consecutive patients with native papilla undergoing ERCP with biliary sphincterotomy were randomized to either the pure cut or endocut after cannulation. The primary outcome was PEP incidence. Secondary outcomes included intraprocedural and delayed bleeding, infection, and perforation.**

RESULTS: **A total of 550 patients were randomized (272 pure cut and 278 endocut). The overall PEP rate was 4.0% and significantly higher in the endocut group (5.8% vs 2.2%, $P = 0.034$). Univariate analysis revealed >5 attempts ($P = 0.004$) and endocut mode ($P = 0.034$) as risk factors for PEP. Multivariate analysis revealed >5 attempts ($P = 0.005$) and a trend for endocut mode as risk factors for PEP ($P = 0.052$). Intraprocedural bleeding occurred more often with pure cut ($P = 0.018$), but all cases were controlled endoscopically during the ERCP. Delayed bleeding was more frequent with endocut ($P = 0.047$). There was no difference in perforation ($P = 1.0$) or infection ($P = 0.4999$) between the groups.**

DISCUSSION: **Endocut mode may increase thermal injury leading to higher rates of PEP and delayed bleeding, whereas pure cut is associated with increased intraprocedural bleeding without clinical repercussion. The electric current mode is not related to perforation or infection. Further RCT assessing the impact of electric current on AE with overlapping preventive measures such as rectal nonsteroidal anti-inflammatory drugs and hyperhydration are needed. The study was submitted to the Brazilian Clinical Trials Platform (http://www.ensaiosclinicos.gov.br) under the registry number RBR-5d27tn.**

KEYWORDS: ERCP; electric current; endocut; pancreatitis/PEP; pure cut

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/D13

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is a widely performed procedure; however, it is associated with a nonnegligible rate of adverse events (AE) (4%–9.8%) (1–5). The main AE are post-ERCP acute pancreatitis (PEP), bleeding, infection, and perforation. Of those, the most feared is PEP because of its incidence (1.4%–5.4%) and potential severity (2–4,6,7).

The pathophysiology of PEP is not fully understood. However, data suggest that patient characteristics and procedure events, such as main pancreatic duct (PD) catheterization and contrast injection, and cannulation trauma play central roles as risk factors (6,8,9). Recent guidelines highlight the importance of considering it during the procedure and recommend several measures to avoid PEP, such as guidewire use, early advanced cannulation

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strategies (precut, fistulotomy, double guidewire, and transpancreatic sphincterotomy), nonsteroidal anti-inflammatory drugs (NSAID), pancreatic stenting, and hyperhydration (8–10).

Furthermore, several studies have addressed the influence of the electric current mode used during biliary sphincterotomy on post-ERCP AE, including PEP (11–18). Presumably, pure cut causes less thermal injury around the PD when compared with mixed currents (endocut and blend). However, the available literature does not prove whether pure cut is effective in preventing PEP or whether it increases clinically significant bleeding due to its lower coagulation effect (5).

Therefore, to better understand the effect of the electric current mode on PEP and other ERCP-related AE, we conducted this multicentric randomized clinical trial (RCT) comparing the use of pure cut and endocut during biliary sphincterotomy of native papilla.

METHODS

Study population

This RCT was conducted according to the Consolidated Standards of Reporting Trials (CONSORT) statements in 2 Brazilian tertiary referral centers (Hospital das Clínicas da Faculdade de Medicina de São Paulo [HCFMUSP] and Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto [HCFMRP]). The protocol was registered in the Brazilian Clinical Trials Protocol under the registry number RBR-5d27tn and was approved by the internal review board of both institutions. Consecutive patients undergoing ERCP were assessed for recruitment. Only biliary sphincterotomy was considered because it is more frequently performed worldwide and because the included centers have a relatively smaller proportion of pancreatic interventions when compared with centers in the United States and Europe.

The following eligibility criteria were applied:

Inclusion criteria: patients submitted for ERCP with native papilla undergoing biliary sphincterotomy after transpapillary cannulation.

Exclusion criteria: younger than 18 years, previous biliary sphincterotomy, pancreatic sphincterotomy, coagulopathy, use of antiaggregation/anticoagulation, biliary primary access by alternative techniques (precut, fistulotomy, and transpancreatic sphincterotomy), surgically altered anatomy (Roux-en-Y anastomosis or Billroth II gastrectomy), periampullary lesions, and unavailable contact for follow-up.

Randomization and allocation

The randomization was balanced between groups (1:1) and in blocks of 8. A researcher not involved in the study created the randomization list using electronic online software (random.org). The full list was generated before the first enrollment and was independent for each of the participating centers. The allocation concealment was secured by numbered opaque envelopes that were opened only after transpapillary selective biliary cannulation in patients fulfilling all eligibility criteria.

ERCP procedure and follow-up

All ERCP procedures were performed according to the standard routine of each center. The type of sedation (monitored anesthetic care or general anesthesia), patient positioning, and measures to prevent PEP were at the discretion of the attending endoscopists. Fellows participated in all cases but were thoroughly monitored by expert endoscopists with >1,000 ERCP, who would take over accordingly. A protocol member masked to the electric current mode used during biliary sphincterotomy followed all patients after the procedure at 24 hours, 48 hours, and 7 days. For inpatient procedures, laboratory tests, including serum amylase and lipase, were requested on the first postprocedural day. For outpatient procedures, follow-up was performed through phone calls at those same time end points. If any AE was detected, patients were assessed and managed accordingly. Antibiotics were prescribed based on typical indications (19), including cholangitis, previous liver transplant, primary sclerosing cholangitis, cholangioscopy, and inadequate biliary drainage. Biliary sphincterotomy was oriented to the 10–11-o'clock position. If indicated, further procedures, such as papillary balloon dilation, stent placement, stone removal, and cholangioscopy, were performed.

Rectal NSAID were not used to prevent PEP because they were unavailable in both centers during the recruitment. High-risk patients for PEP (defined according to the ESGE ERCP-related AE Guideline) without contraindications received lactated Ringer solution hyperhydration (8,9). Pancreatic stents were used according to the center's availability and indication by international guidelines (8).

Electrosurgical unit settings

The electric current settings were standardized as follows:

1. Pure cut: WEM SS-200E pure cut 30–50 W (WEM/Medtronic, Minneapolis, MN) in both institutions and ERBE ICC 200 (ERBE Elektromedizin, Tübingen, Germany) AUTO CUT effect 3, 30–50 W in HCFMUSP.
2. Endocut: ERBE VIO 300 in HCFMUSP and ERBE VIO 3 in HCFMRP—Endocut I, effect 2, cutting duration 3, cutting interval 3 (per manufacturer's guidelines).

Outcome measures and definitions

The primary outcome was PEP incidence. Secondary outcomes were bleeding (immediate and delayed), infection (cholangitis and cholecystitis), and perforation.

PEP and bleeding were defined and graded according to the Cotton criteria (see Supplementary Material, Supplementary Digital Content 1, http://links.lww.com/AJG/D13) (20). Immediate bleeding was graded as self-limited or requiring endoscopic intervention. Perforation was classified according to the Stapfer classification (21). Cholangitis was defined as a new onset temperature ≥38 °C for ≥24 hours with cholestasis (22). Cholecystitis diagnosis was based on localized pain and systemic signs of inflammation with consistent imaging findings (23). Cannulation time was defined as the time between the first touch of the sphincterotome on the papilla and the selective biliary cannulation confirmed with fluoroscopy.

A recent RCT demonstrated that the early double guidewire technique defined as after only a single unintentional PD cannulation does not increase PEP incidence (24). Our local experience corroborates this finding. Therefore, patients requiring the double guidewire technique with up to 1 PD guidewire pass were grouped with those with no PD cannulation for baseline and logistic regression analyses.

Sample size calculation

The sample size was calculated based on the latest systematic review and meta-analysis (evidence 1A) on this topic, which included all published RCT comparing endocut and pure cut and

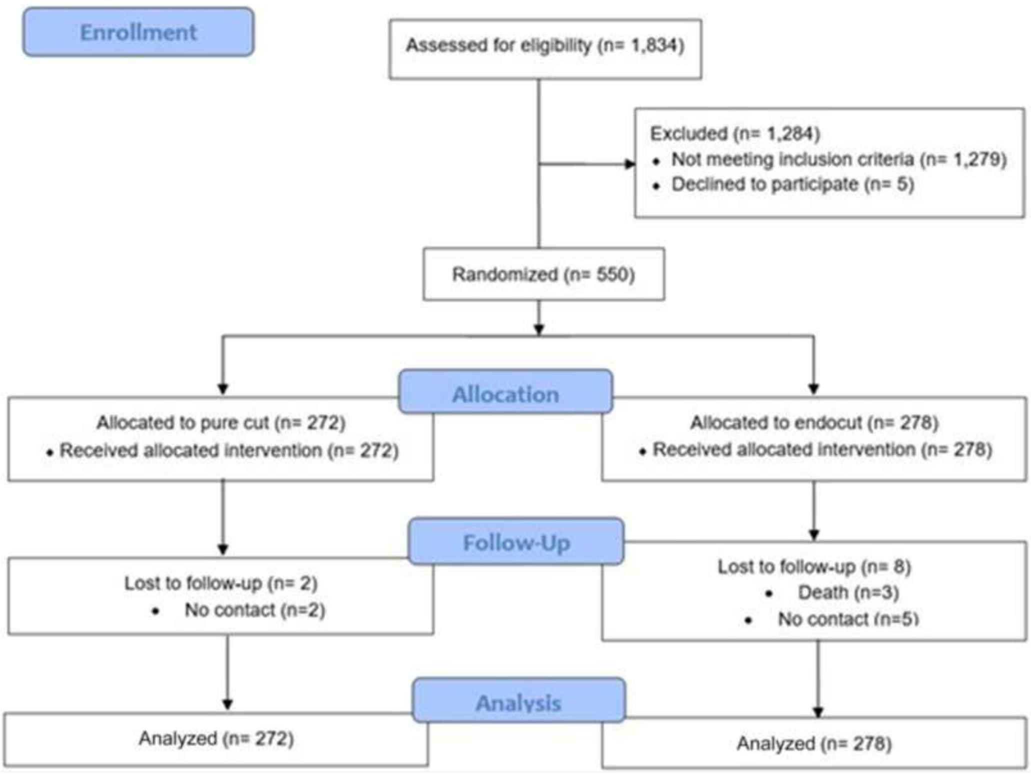

Figure 1. Consolidated Standards of Reporting Trials flow diagram.

revealed PEP rates of 5.2% and 0.9%, respectively (5). Based on such a difference, considering a power of 80%, 95% confidence interval (CI), and significance level of 0.05, 500 patients were needed. With an estimated 10% loss of follow-up, 550 individuals were necessary to test the null hypothesis. Calculation was performed using BioEstat 3.0 software (Marimauá Institute, Tefé, Amazonas, Brazil).

Statistical analysis

All analyses were run using SPSS 17.0 software (IBM, Armonk, NY) for Windows. Subanalyses and logistic regression were performed on intention-to-treat basis. Continuous variables were described using the minimal and maximum values, mean, SD, and median. Categorical variables were reported using absolute and relative (percentage) frequencies.

Means were compared using the Student *t* test and the nonparametric Mann-Whitney test. Homogeneity among groups was tested with χ^2 and Fisher exact tests. We considered a 95% CI and a significance level of 0.05.

Primary and secondary outcomes and the odds ratio (OR) were calculated with the multivariate logistic regression model. Initially, variables with $P < 0.05$ in the univariate analysis were selected. Then, the stepwise process in the multivariate logistic regression model was used.

RESULTS

From October 2019 to August 2021, 1,834 ERCP were performed in both centers (Figure 1). We enrolled 550 patients from both F1 institutions, with 272 cases in the pure cut arm and 278 in the endocut arm. Of those, 544 completed 24 hours and 48 hours, and 540 completed the 1-week follow-up. Both arms' baseline clinical (Table 1) and laboratory characteristics were homogeneous. The ERCP characteristics were also similar among the groups T1 (Table 2). T2

Post-ERCP acute pancreatitis

The overall PEP rate was 4.0% (22/550), and all cases were mild or moderate. The PEP rate was significantly higher in the endocut arm (5.8% × 2.2%, $P = 0.034$) (Table 3).

Univariate analysis identified the number of attempts >5 ($P =$ T3 0.004) and endocut ($P = 0.034$) as statistically significant risk factors (Table 4).

Multivariate analysis embracing the 2 abovementioned vari- T4 ables revealed >5 attempts as statistically significant (OR 4.3; 95% CI 1.57–11.77; $P = 0.005$) and a border value ($P = 0.052$) (backward analysis) for endocut as a risk factor for PEP (Table 5). T5

Bleeding

The immediate bleeding rate was 18% (9% self-limited and 9% with the need for intervention). The latest was more frequent in the pure cut arm ($P = 0.018$) (Table 6). All cases were controlled endoscopically (coagulation with the sphincterotome, hemoclips, T6 adrenalin and/or saline injection therapy, and balloon compression). None of the cases required metallic stents to control the bleeding.

Univariate analysis revealed age (each year old adds 1% risk of bleeding: OR 1.013; 95% CI 1.000–1.025; $P = 0.046$), supine position (OR 2.454; 95% CI 1.416–4.253; $P = 0.001$), PD contrast injection (OR 2.287; 95% CI 1.010–5.177; $P = 0.047$), papillary hydrostatic balloon dilation (OR 2.120; 95% CI 1.275–3.524; $P = 0.004$), and pure cut (OR 2.554; 95% CI 1.594–4.093; $P < 0.001$) as

Table 1. Patient baseline clinical characteristics

	Sample (n = 550)	Group		*P* value
		Pure cut (n = 272)	Endocut (n = 278)	
Age (yr), mean (SD)	52.84 + 18.66	52.08 + 18.86	53.58 + 18.48	0.348[a]
Sex, n (%)				0.565[b]
Female	331 (60.2)	167 (61.4)	164 (59.0)	
Male	219 (39.8)	105 (38.6)	114 (41.0)	
Diagnosis, n (%)				
Choledocolithiasis	423 (76.9)	215 (79.0)	208 (74.8)	0.240[b]
Cancer (malignant stricture)	85 (15.5)	37 (13.6)	48 (17.3)	0.235[b]
Fistula	19 (3.5)	10 (3.7)	9 (3.2)	0.778[b]
Benign stricture	18 (3.3)	5 (1.8)	13 (4.7)	0.061[b]
Others	14 (2.6)	8 (2.9)	6 (2.2)	0.560[b]
Suspected sphincter of Oddi dysfunction, n (%)	10 (1.8)	6 (2.2)	4 (1.4)	0.541[c]
Previous acute pancreatitis, n (%)	64 (11.7)	30 (11.0)	34 (12.0)	0.638[b]
Chronic pancreatitis, n (%)	2 (0.4)	0 (0.0)	2 (0.7)	0.499[c]
Comorbidities, n (%)				
Arterial hypertension	191 (34.7)	95 (34.9)	96 (34.5)	0.923[b]
Diabetes	92 (16.7)	49 (18.0)	43 (15.5)	0.424[b]
Obesity	72 (13.1)	37 (13.6)	35 (12.6)	0.725[b]
Cardiovascular disease	20 (3.6)	7 (2.6)	13 (4.7)	0.188[b]
COPD/smoking	18 (3.3)	6 (2.2)	12 (4.3)	0.164[b]
Chronic liver disease	18 (3.3)	10 (3.7)	8 (2.9)	0.599[b]
Cancer	9 (1.6)	2 (0.7)	7 (2.5)	0.176[c]
No comorbidities	226 (41.1)	112 (41.2)	114 (41.0)	0.968[b]

COPD, chronic obstructive pulmonary disease.
[a]Student *t* test.
[b]Qui-square test.
[c]Fisher exact test.

risk factors. In the multivariate analysis, all variables were significantly associated with intraprocedural bleeding (Table 7).

Delayed bleeding occurred in 2.9% and was more frequent in the endocut group ($P = 0.047$) (Table 3).

Intraprocedural and other AE

Intraprocedural AE are summarized in Table 6. There was 1 case of uncontrolled biliary sphincterotomy (zipper) in the endocut arm. There was 1 perforation case unrelated to the sphincterotomy (ductal injury during a biopsy of a suspected malignant biliary stricture, Stapfer type III).

Postprocedural abdominal pain was similar between the 2 groups. Other AE included basket impaction in the common bile duct (treated with surgery) and persistent nausea and vomiting after ERCP without PEP (managed with symptomatic drugs), both in the endocut arm ($P = 0.499$). There were no cases of cholecystitis.

Three deaths occurred, all in the endocut group, because of postprocedural cholangitis (Klatskin tumor), delayed bleeding, and baseline disease complications (unrelated to the procedure). The delayed bleeding death occurred in a patient who left the hospital against medical advice. After follow-up contact, she described hypotension and melena, and was oriented to go to the nearest emergency center immediately. However, shortly after admission, she died of a hypovolemic shock, with no time for endoscopic treatment, embolization, or surgery.

DISCUSSION

Many studies have been dedicated to better understand the electric current influence on ERCP-related AE, especially PEP (11–18). If an electric current mode and/or setting was effective to avoid PEP, it would be a very simple way to lower such an inconvenient AE. Despite previous publications, whether a lower coagulation effect would increase significant bleeding or affect other AE remains a concern.

Three systematic reviews and meta-analyses from RCT comparing the electric current mode used during sphincterotomy have been published. The first one, from Verma et al (11), assembles endocut and blend in the same group (mixed-current group). This affects their results once these modes perform differently. None of the included studies used modern electrosurgical units (ESU), such as VIO 300 and VIO 3, which hold the

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Table 2. ERCP characteristics

	Sample (n = 550)	Group		P value
		Pure cut (n = 272)	Endocut (n = 278)	
Anesthesia, n (%)				0.464[a]
General	81 (14.7)	35 (12.9)	46 (16.6)	
Sedation by anesthesiologist	93 (16.9)	48 (17.6)	45 (16.2)	
Sedation by endoscopist	376 (68.4)	189 (69.5)	187 (67.3)	
ASGE complexity level (25), n (%)				0.749[b]
2	399 (72.5)	199 (73.2)	200 (71.9)	
3	151 (27.5)	73 (26.8)	78 (28.1)	
Patient position, n (%)				0.697[a]
Prone	463 (85.0)	231 (85.6)	232 (84.4)	
Supine	82 (15.0)	39 (14.4)	43 (15.6)	
Cannulation time (min), mean (SD)	6.92 + 6.11 (0.00; 33.00)	6.61 + 6.09 (0.00; 33.00)	7.22 + 6.12 (1.00; 29.00)	0.174[c]
No. of cannulation attempts, mean (SD)	3.30 + 2.23 (1.00; 10.00)	3.21 + 2.17 (1.00; 10.00)	3.40 + 2.28 (1.00; 10.00)	0.353[c]
PD cannulation, n (%)	183 (33.3)	83 (30.5)	100 (36.0)	0.175[a]
PD contrast injection, n (%)	33 (6.0)	14 (5.2)	19 (6.8)	0.405[a]
Pancreatic stenting, n (%)	4 (0.7)	1 (0.4)	3 (1.1)	0.624[b]
Periampullary diverticulum, n (%)	63 (11.5)	34 (12.5)	29 (10.4)	0.614[a]
Papillary balloon dilation, n (%)	109 (19.8)	51 (18.8)	58 (20.9)	0.534[a]
Double guidewire, n (%)	32 (5.8)	11 (4.0)	21 (7.5)	0.079[a]

ASGE, American Society for Gastrointestinal Endoscopy; ERCP, endoscopic retrograde cholangiopancreatography; PD, pancreatic duct.
[a]Student *t* test.
[b]Qui-square test.
[c]Nonparametric Mann-Whitney test.

endocut settings currently used worldwide. In addition, blend is not the usual choice to improve coagulation in centers where endocut is available. The second one, from Li et al (26), compares blend and endocut, which brings us useful information; however, it does not focus on the idea of less coagulation power (both arms include mixed currents) to decrease PEP. In addition, their analysis included a nonrandomized trial among RCT, which limits the results (15). Our group published the most recent one

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Table 3. Delayed adverse events

Variable	Sample (n = 550)	Group		P value
		Pure cut (n = 272)	Endocut (n = 278)	
Delayed bleeding, n (%)				0.047[a]
No	534 (97.1)	268 (98.5)	266 (95.7)	
Yes	16 (2.9)	4 (1.5)	12 (4.3)	
Hyperamylasemia (n = 45), n (%)	27 (60.0)	11 (57.9)	16 (61.5)	0.805[b]
Cholangitis, n (%)	2 (0.4)	0 (0.0)	2 (0.4)	0.499[c]
PEP, n (%)				0.034[b]
No	528 (96)	266 (97.8)	262 (94.2)	
Yes	22 (4)	6 (2.2)	16 (5.8)	
PEP severity, n (%)				—
Mild	12 (75.0)	3 (75.0)	9 (75.0)	
Moderate	4 (25.0)	1 (25.0)	3 (25.0)	
Severe	0 (0.0)	0 (0.0)	0 (0.0)	

PEP, post-endoscopic retrograde cholangiopancreatography acute pancreatitis.

Table 4. Univariate analysis for PEP

Variable	PEP		P value
	No	Yes	
Anesthesia, n (%)			0.171[a]
General anesthesia	76 (14.4)	5 (22.7)	
Sedation by anesthesiologist	92 (17.4)	1 (4.6)	
Sedation by endoscopist	360 (68.2)	16 (727)	
Patient position, n (%)			0.355[a]
Prone	446 (85.3)	17 (77.3)	
Supine	77 (14.7)	5 (22.7)	
Cannulation time, n (%)			0.404[a]
<5 min	237 (45.4)	8 (36.4)	
≥5 min	285 (54.6)	14 (63.6)	
No. of cannulation attempts, n (%)			0.004[a]
<5	407 (77.1)	11 (50.0)	
≥5	121 (22.9)	11 (50.0)	
PD cannulation, n (%)	172 (32.6)	11 (50.0)	0.089[a]
PD contrast injection, n (%)	30 (5.7)	3 (13.6)	0.139[a]
Pancreatic stent, n (%)	4 (0.8)	0 (0.0)	1.000[a]
Periampullary diverticulum, n (%)	62 (11.6)	1 (6.2)	1.000[a]
Papillary balloon dilation, n (%)	103 (19.5)	6 (27.3)	0.411[a]
Double guidewire, n (%)			0.371[a]
No	498 (94.3)	20 (90.9)	
Yes	30 (5.7)	2 (9.15)	
Electric current mode, n (%)			0.034[b]
Pure cut	266 (50.4)	6 (27.3)	
Endocut	262 (49.6)	16 (77.3)	

PEP, post-endoscopic retrograde cholangiopancreatography acute pancreatitis; PD, pancreatic duct.

revealing no significant difference regarding PEP rates or clinically significant bleeding. Although only RCT (evidence 1A) were included, the low quality of these studies and inclusion of abstracts limit the conclusions (5).

In the current study, PEP was more frequent with endocut (16/278, 5.8%) than with pure cut (6/272, 2.2%). Univariate analysis identified ≥5 cannulation attempts ($P = 0.005$) and endocut ($P = 0.034$) as risk factors. However, in the multivariate analysis, ≥5 cannulation attempts were shown to be the most important risk factor (OR 4.3; 95% CI 1.57–11.77; $P = 0.005$), whereas endocut presented a borderline value ($P = 0.052$). All previous RCT comparing endocut and pure cut have shown similar results (respectively): Ellahi et al 5 of 55 (9.1%) vs 0 of 31 (0%); Kida et al 4 of 41 (9.8%) vs 1 of 43 (2.3%); Norton et al 3 of 133 (2.3%) vs 1 of 134 (0.75%) (27–29) (see Supplementary Material, Supplementary Digital Content 1, http://links.lww.com/AJG/D13). Such results did not reach statistical significance when pooled in a meta-analysis (5). Still, adding the results from our study to new a meta-analysis would probably be enough to show a statistical difference.

There are no available data comparing less coagulation (pure cut) to conventional measures, such as NSAID, hyperhydration, and pancreatic stenting, to prevent PEP. Therefore, it is not

Table 5. Backward analysis in the multivariate assessment for PEP

Step	Excluded variable	P value
1	PD cannulation	0.346
2	Endocut	0.052

PEP, post-endoscopic retrograde cholangiopancreatography acute pancreatitis; PD, pancreatic duct.

known whether using pure cut would remain a preventive measure against PEP and whether these other methods were implemented. AU3 This rationale goes both ways: whether well-established measures will remain significant ones once pure cut is routinely adopted remains to be determined. Interestingly, Thanage et al (30) recently published an RCT assessing the impact of overlapping measures in preventing PEP. When both NSAID and hyperhydration were implemented, there was no statistical difference between combined and single-therapy groups regarding PEP. Thus, studies with a similar design including the electric current mode as a preventive measure are warranted.

One concern when using less coagulation is sphincterotomy-related bleeding. Previous studies and guidelines recommend mixed currents over pure cuts to prevent such AE (8,11,26,31). It is important to note that such recommendations are mostly based on intraprocedural bleeding without clinical significance (5). Our results confirm increased intraprocedural bleeding with pure cut ($P = 0.018$), yet all cases were controlled with relatively simple measures, such as hemoclips, coagulation, balloon compression, and injection therapy (with and without adrenaline). Univariate and multivariate analyses confirmed age (1% increased risk per year old), supine position, PD contrast injection, papillary balloon dilation, and pure cut as risk factors (Table 5). However, none of the cases required surgery, packed red blood cell transfusion, or interventional radiology management. In summary, the exposed risk factors were associated with endoscopically controllable intraprocedural bleeding with no clinical repercussions after ERCP. Such conditions might be considered to select an electric current mode with improved coagulation.

Delayed bleeding was more frequent in the endocut group ($P = 0.047$). However, previous studies have pointed to intraprocedural bleeding as a risk factor for delayed bleeding, which is not a consensual finding (1,3,5,27). A theory for endocut not to decrease (and perhaps to increase) postprocedural hemorrhage is that its coagulation effect would not be sufficient to coagulate a thicker vessel once thermal injury progresses. Greater thermal injury (coagulation) may also reach thicker vessels more often, which might explain our results. A parallel may be made with recent publications that demonstrate less delayed bleeding and postpolypectomy coagulation syndrome with cold snare when compared with hot snare endoscopic mucosal resection for colonic sessile or flat lesions (32,33).

Previous studies with large casuistries have shown similar mortality rates for severe cases of PEP and bleeding (2–4,7). As PEP occurs more often, strategies to avoid such AE without higher rates of bleeding might decrease overall mortality. In our case of 3 deaths (all in the endocut arm), only 1 might be related to the electric current mode: delayed bleeding.

Considering the exposed discussion over PEP, intraprocedural, and delayed bleeding, further investigation might confirm the benefit of using pure cut routinely. It is also important

Table 6. Intraprocedural adverse events

	Sample (n = 550)	Group: Pure cut (n = 272)	Group: Endocut (n = 278)	P value
Bleeding, n (%)				0.018[a]
Self-limited	50 (49.5)	27 (40.9)	23 (65.7)	
Need for endoscopic intervention	51 (50.5)	39 (59.1)	12 (34.3)	
Perforation (Stapfer classification), n (%)				1.000[b]
Type II (periampullary)	0 (0.0)	0 (0.0)	0 (0.0)	
Type III (ductal injury)	1 (0.2)	0 (0.0)	1 (0.4)	
Uncontrolled sphincterotomy (zipper), n (%)	1 (0.2)	0 (0.0)	1 (0.4)	1.000[b]
Other adverse event, n (%)	2 (0.4)	0 (0.0)	2 (0.7)	0.499[b]

[a]Qui-square test.
[b]Fisher exact test.
AU7 [c]Nonparametric Mann-Whitney test.

Table 7. Multivariate analysis for intraprocedural bleeding

Variable	Odds ratio	95% CI: Inferior limit	95% CI: Superior limit	P value
Age	1.013	1.000	1.025	0.046
Position				0.001
Prone	1.000			
Supine	2.454	1.416	4.253	
PD contrast injection				0.047
No	1.000			
Yes	2.287	1.010	5.177	
Papillary balloon dilation				0.004
No	1.000			
Yes	2.120	1.275	3.524	
Electric current mode				<0.001
Endocut	1.000			
Pure cut	2.554	1.594	4.093	

CI, confidence interval; PD, pancreatic duct.

to note the possibility of intensifying coagulation in modern ESU with pure cut as the effect increases. For endoscopists more fa- AU4 miliarized with endocut, we emphasize that the *effect one* does not coagulate between the cutting cycles, providing a programed and controlled pure cut (see Figure in Supplementary Material, Supplementary Digital Content 1, http://links.lww.com/AJG/D13). Thus, the endocut effect one is an alternative to using pure cut without the coagulation effect present in higher effects.

Perforation is another relevant AE. It has been proposed that an automatically controlled cut (endocut) could avoid uncontrolled sphincterotomy (zipper) and periampullary perforation (Stapfer type II) (16,27,34). As in ours, several other studies do not point to any electric current mode or zipper as a risk factor for biliary sphincterotomy-related perforation (4,23,35–37). In 550 cases, there was only 1 case of uncontrolled sphincterotomy in the endocut group, which did not result in perforation. Regardless, it is important to state that pure cut requires expertise and great caution during sphincterotomy.

Post-ERCP infection has well-determined risk factors such as impaired biliary drainage, immunosuppression (e.g., liver transplant), and combined percutaneous drainage (6,8). In pathophysiology, the electric current mode used during biliary sphincterotomy has no influence on either biliary drainage or the patient's immunological status. Therefore, it is unlikely that an electric current mode could lead to infection, which was reinforced in the exposed results.

Although this RCT is the largest available data to date, our study has some limitations. As previously exposed, our data do not clarify whether pure cut can decrease PEP rates when compared to established measures and whether its association would bring additional benefit. The lack of rectal NSAID use is a limitation that elicits such uncertainty. In addition, owing to its little availability, there was a lack of significant PD stenting, which might influence the results. We also have the participation of fellows, which has been shown to increase the rate of AE in a few trials (38). However, all fellows were thoroughly assisted by experts, who would take over whenever necessary, respecting the time and number of attempts as international guidelines' recommendations (39). Moreover, our PEP rate (4.0%) was comparable to other series (2–4,6,7). All cases were from reference high-volume centers, which makes it uncertain to apply the results to centers with less complex cases and fewer experienced professionals. The ESU was different for endocut and pure cut between the centers, albeit endocut was used according to the manufacturer's recommendations and as used in reference centers worldwide. Cotton criteria were used to grade PEP given that the study was designed before the international recommendation to use the revised Atlanta classification (9,40). In addition, our registry is based on primary transpapillary biliary cannulation in patients without an increased risk for bleeding, which is considerably common in clinical practice. Thus, it is not certain that our results can be applied to patients with an increased risk for bleeding. Despite important limitations, this new finding's importance is that it points for further studies to better understand an area with little available data.

This RCT indicates that endocut might be associated with increased thermal injury, leading to higher rates of PEP and delayed bleeding, whereas pure cut is associated with increased intraprocedural bleeding without clinical repercussions. The electric current mode is not related to perforation or infection. Further RCT assessing the impact of electric current on AE with overlapping preventive measures such as rectal NSAID and hyperhydration are needed.

CONFLICTS OF INTEREST

Guarantor of the article: Mateus Pereira Funari, MD, MSc, PhD.
Specific author contributions: All authors performed the conception and design of the work. M.P.F., V.O.B., D.T.H.d.M., and E.G.H.d.M. drafted the manuscript. I.M.P., P.V.A.G., L.T.A.G., and Y.Z.V. contributed to the patients follow-up. All authors contributed

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to the ERCP performance. All authors contributed to the approval of the version to be published, have participated in conceptualizing the research or content of the manuscript, in writing or critically editing the manuscript, and/or in analysis of data presented in the manuscript. Consent to submit has been received from all co-authors.

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Study Highlights

WHAT IS KNOWN

- ✓ Endoscopic retrograde cholangiopancreatography (ERCP) is a widely performed procedure and has a significant adverse event rate.
- ✓ Thermal injury from biliary sphincterotomy may play an important role and trigger post-ERCP acute pancreatitis (PEP) or bleeding.

WHAT IS NEW HERE

- ✓ Less coagulation (pure cut) might decrease PEP rates with no increase in clinically significant bleeding.
- ✓ New studies are warranted to assess the impact of electric current on adverse events with overlapping preventive measures such as rectal nonsteroidal anti-inflammatory drugs and hyperhydration.

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