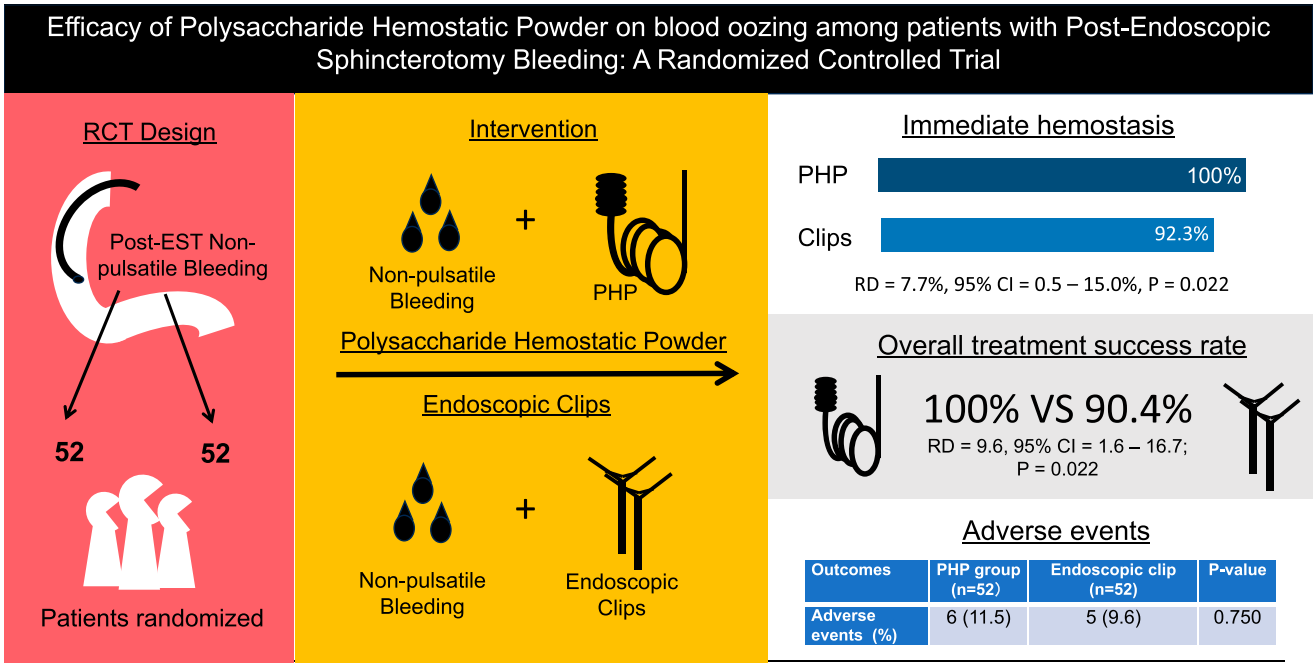
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Efficacy of Polysaccharide Hemostatic Powder on Blood Oozing Among Patients With Postendoscopic Sphincterotomy Bleeding: A Randomized Controlled Trial

Hengcun Li, PhD[1,*], Jiaxuan Zuo, MM[1,*], Wenhai Wang, PhD[1], Shanshan Wu, PhD[1], Yu Zhao, PhD[1], Yongqiu Wei, PhD[1], Jiugang Song, PhD[1], Zheng Zhang, PhD[1], Weilong Yao, PhD[1], Junxiong Wang, PhD[1], Chuntao Liu, PhD[1], Hongtao Wei, PhD[1], Zheng Liang, MM[1], Xiaohan Yang, MM[1], Kaiqi Yang, MM[1], Fujing Lv, PhD[1], Yongjun Wang, PhD[1], Peng Li, PhD[1] and Shutian Zhang, PhD[1]

INTRODUCTION: **Postendoscopic sphincterotomy (EST) bleeding presents challenges for endoscopists using side-viewing duodenoscopes. Recently, polysaccharide hemostatic powder (PHP) has shown promising results in managing gastrointestinal hemorrhage. Given the established efficacy of endoscopic clips in addressing post-EST bleeding, we aim to evaluate the efficacy of PHP and its noninferiority to endoscopic clips in patients with nonpulsatile post-EST bleeding.**

METHODS: **Patients with nonpulsatile post-EST bleeding were randomized to receive either PHP or endoscopic clips. The primary end point was the immediate hemostasis rate, with secondary end points including delayed bleeding rate, overall treatment success rate, mean hemostasis time, and other major complications.**



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[1]Department of Gastroenterology, Beijing Friendship Hospital, Capital Medical University, National Clinical Research Center for Digestive Diseases, State Key Laboratory of Digestive Health, Beijing Digestive Disease Center, Beijing Key Laboratory for Precancerous Lesion of Digestive Disease, Beijing, China.
Correspondence: Shutian Zhang, PhD, MD. E-mail: zhangshutian@ccmu.edu.cn. Peng Li, PhD. E-mail: lipeng@ccmu.edu.cn.
*Hengcun Li and Jiaxuan Zuo contributed equally to this article.
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RESULTS: **A total of 104 patients with nonpulsatile post-EST bleeding were included. Immediate hemostasis was achieved in 100% of the PHP group and 92.3% in the endoscopic clip group (risk difference, 7.7%, 95% confidence interval (CI) = 0.5%–15.0%, $P = 0.022$). Four patients in the endoscopic clip group experienced immediate hemostasis failure. Hemostasis time was shorter in the PHP group (50.77 vs 62.81 seconds, $P = 0.011$). One delayed bleeding case (2.1%) occurred in the clip group, whereas none were observed in the PHP group. The overall treatment success rate was higher in the PHP group compared with the endoscopic clip group (100% vs 90.4%; $P = 0.022$). No differences were observed in adverse events.**

DISCUSSION: **PHP is not inferior to endoscopic clip and could be of use in immediate hemostasis for nonpulsatile post-EST bleeding, with the added advantage of ease of use. Further research is needed to assess its efficacy in preventing delayed bleeding (chictr.org.cn, ChiCTR2400092280).**

KEYWORDS: polysaccharide hemostatic powder; post-EST bleeding; endoscopic clip; endoscopic retrograde cholangiopancreatography

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/D632

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INTRODUCTION

Post-EST bleeding is a common complication after EST, occurring either intraoperatively or several days post-EST, ranging from insignificant to life-threatening (1). According to the definition applied, immediate post-EST bleeding occurs in 1%–12.1% of cases, whereas delayed bleeding affects 1%–10.3% (2–5).

Multiple therapeutic options are available for managing post-EST bleeding. Endoscopic clips are recommended by guidelines as salvage therapy when standard hemostatic strategies fail (6). Studies show clips have excellent efficacy in refractory, immediate, and delayed post-EST bleeding cases, with success rates of 100% (53 cases), 88.9% (9 cases), and 100% (14 cases), respectively (7–9) However, using side-viewing duodenoscopes poses challenges in targeting the bleeding site because of limited space and acute angulation.

Recent studies have explored new hemostatic methods, including hemostatic powder, which offers advantages such as noncontact application and easily applied treatment (10). Polysaccharide hemostatic powder (PHP) is a kind of organic, absorbable powder. It rapidly absorbs water, causing dehydration and concentrating clotting components to form an "instant gel" that acts as a barrier and accelerates coagulation. PHP has demonstrated remarkable efficacy in the management of ulcer-related and tumor-related bleeding (11), which is easy to use and makes up for the disadvantage of the limited hemostatic range of endoscopic hemostatic clips. Few studies have assessed other hemostatic agents sharing a similar hemostatic mechanism such as PHP, showing promising results for immediate hemostasis (88.4%–100%) and delayed bleeding (2.4%–15.3%) in post-EST bleeding (12–15). Unfortunately, since its launch, it is still an off-label drug in endoscopic retrograde cholangiopancreatography (ERCP) operations.

To our best knowledge, the clinical efficacy of PHP has not been explored in post-EST bleeding. The aim of this study was to compare PHP with traditional clips for managing post-EST bleeding in a single-center randomized controlled trial (RCT). Based on the proven effectiveness of endoscopic clips, we hypothesized that PHP could be noninferior to clips, exploring its potential as a reliable alternative.

PATIENTS AND METHODS

Study design

This is a patient-blinded and outcome assessor-blinded, randomized clinical trial in Beijing Friendship Hospital, conducted between September 2023 and August 2024. The procedure was performed by experienced endoscopists with over 2,500 ERCPs. The study protocol was approved by the institutional Ethics Committee of Beijing Friendship Hospital (2023-P2-206-02). This study was registered with the China Clinical Trial Registry (ChiCTR2400092280).

Outcomes and definitions

The primary outcome was immediate hemostasis rate, defined as percentage of patients with none active oozing bleeding persisting 3 minutes after the immediate hemostatic procedure, according to the intention-to-treat analysis, regardless of any subsequent switches or interventions. Secondary outcomes included delayed bleeding rate, overall treatment success rate, hemostasis time, and the incidence rate of advert events. Immediate bleeding was defined as active oozing bleeding persisting more than 3 minutes after the completion of all therapeutic ERCP procedures. Delayed bleeding was defined as the simultaneous fulfillment of both (a) hematemesis, melena, hematochezia, or fresh blood in the endoscopic nasobiliary drainage (ENBD) tube, accompanied by either (i) hemoglobin drop ≥20 g/L and/or transfusion requirement or (ii) hemodynamic instability or hemorrhagic shock, and (b) active bleeding at the papilla confirmed by direct visualization during emergent endoscopy. Overall treatment success was defined as immediate hemostasis with no delayed bleeding. Hemostasis time was the duration from the entry of the hemostatic device into the biopsy channel to the observation of bleeding cessation. Catheter occlusion refers to blockage of the hemostatic powder delivery catheter during application. Clip slippage refers to the failure of the endoscopic clip to securely anchor at the target site, including cases of misplacement or dislodgement.

Study population

Patients requiring elective ERCP and expected to undergo EST were screened for eligibility. Patients with immediate post-EST bleeding were included. The exclusion criteria were as follows: (i) age below 18 or above 80 years, (ii) without immediate bleeding

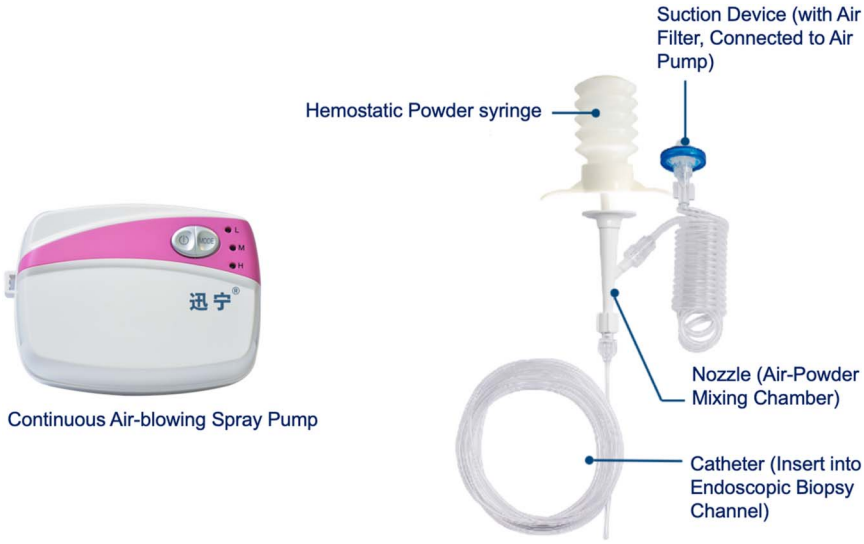


Figure 1. PHP delivery system, including a suction device, nozzle, catheter, continuous air-blowing spray pump, and syringe with PHP powder. PHP, polysaccharide hemostatic powder.

after EST, (iii) pulsatile bleeding after EST, (iv) without native papilla, (v) failure to access to Vater ampulla, (vi) with coagulation disorders or thrombocytopenia (platelet count $<100 \times 10^9$/L, activated partial thromboplastin time $>$ 1.5$\times$ normal value, or international normalized ratio $>$ 2.5), (vii) unable to discontinue antiplatelet or anticoagulant agents (except acetylsalicylic acid), and (viii) pregnancy or lactation.

Random allocation and intervention

A trial nurse generated the randomization sequence using Microsoft Excel. Treatment assignments were concealed in ordered, sealed envelopes that were later opened by an endoscopy nurse. Patients met the inclusion criteria were enrolled and randomized 1:1 using a simple randomization approach into the PHP or the endoscopic clip group using the technique of random numbers in sealed envelopes.

ERCP with EST was performed using a standard side-viewing duodenoscope (TJF-260v; Olympus, Tokyo, Japan). The sphincterotomy was made in a stepwise manner toward the 11–12 o'clock direction using a triple-lumen sphincterotome (DSP-25A-AC-Y-Y-X-B-3; Nanjing Micro-Tech Medical, Nanjing, Jiangsu, China). The small EST was made from the papilla orifice proximally, not extending beyond the horizontal fold or the transverse fold of the papilla, whereas the large EST extended from the papillary orifice to between the proximal hooding fold and the major horizontal fold.

The PHP (XunNing®; Lianbai Bochao Medical Equipment, Chongqing, China) is composed of cross-linked potato starch and sodium carboxymethyl starch. It consists of a disposable delivery system (including a Suction Device, Nozzle, and Catheter), a continuous air-blowing spray pump, and a syringe containing 1 g of PHP powder (Figure 1). Spray bursts were applied to the bleeding site under direct vision, positioning the catheter tip 1–2 cm from the lesion, and repeating bursts until a stable barrier covered the site.

The endoscopic clip (Sure Clip®, ROCC-D-26-195-C; Nanjing Micro-Tech Medical, China) has a prong length of 9.8 mm (retained in the body) and an opening size of 12 mm (see Supplementary Figure 1, http://links.lww.com/AJG/D632). The endoscopic clips were advanced through the biopsy channel, pushed to the second part of the duodenum, and placed on the bleeding point until the bleeding site was securely grasped.

If immediate hemostasis failed with the assigned treatment, the choice of hemostasis method was left to the physician's discretion. If further hemostasis still failed, biliary stent placement, interventional, or surgical treatment was applied when necessary. Subjects with successful immediate hemostasis were observed for 3 days to detect delayed bleeding or AEs. Delayed bleeding triggered immediate endoscopy. The choice of hemostatic modality was at the endoscopist's discretion, typically managed with clips and epinephrine injection. Refractory cases received stent placement, interventional, or surgical treatment.

Statistical analysis

We hypothesized that PHP's immediate hemostasis rate would be noninferior to endoscopic clips. Literature reports show success rates for the clip group ranging from 81.3% to 100% (12,13), and we assumed a rate of 93% for the control group. A 10% noninferiority margin was chosen, meaning PHP would be considered efficacious with an immediate hemostasis success rate of $\geq$83%. This margin aligns with similar studies using 10%–15% margins (16–18). Clinically, a 10% difference in immediate hemostasis success is acceptable for oozing bleeding after EST, as it is unlikely to significantly affect patient outcomes or necessitate additional interventions. Based on the primary end point, a minimum of 52 patients were required in each group (α = 0.025 [one-tailed]; 1 $-$ β = 0.8). The grouping was conducted intraoperatively, with no dropouts during the study.

We performed an intention-to-treat analysis with no missing data. Baseline data were reported as means and SDs for continuous variables and percentages and frequencies for categorical variables. Continuous variables were compared using the Student *t* test, and categorical variables were analyzed using the χ^2 test.

Risk differences (RDs) were used to evaluate the immediate hemostasis rate, delayed bleeding rate, and overall treatment success rate. The primary outcome was assessed using a one-sided *P* value, whereas the secondary outcomes were analyzed using 2-sided *P* values.

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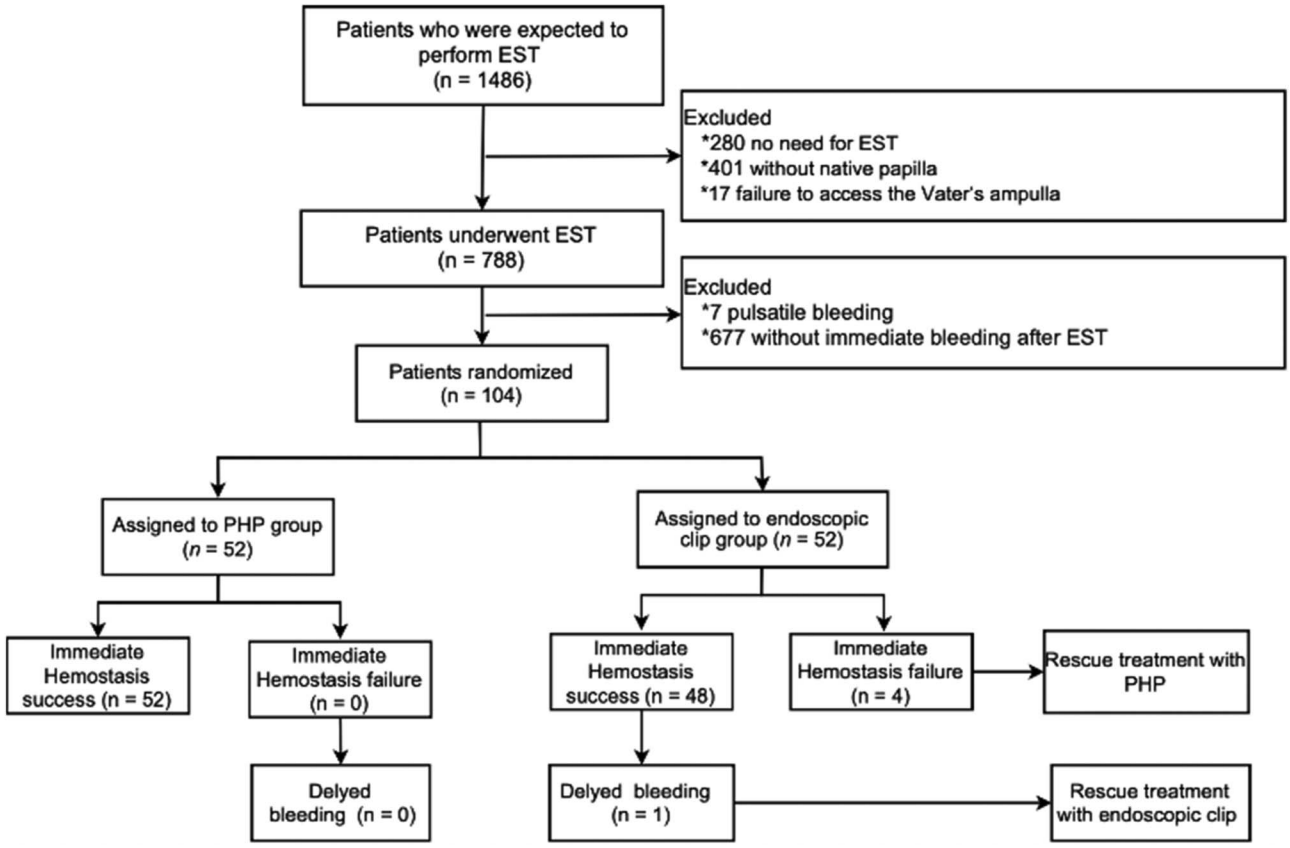


Figure 2. Flow chart of patient enrollment. EST, postendoscopic sphincterotomy; PHP, polysaccharide hemostatic powder.

Statistical significance was defined as a P of < 0.05. All analyses were performed using SPSS version 26 (IBM SPSS Statistics for Mac; IBM, Armonk, NY) and SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Study population

A total of 1,486 patients expected to undergo EST provided informed consent. Of these, 788 patients with native papilla received EST. Six hundred eighty-four without immediate bleeding after EST (677 patients) or pulsatile bleeding (7 patients) were excluded. Finally, 104 patients were randomized equally into the PHP group (n = 52) and the endoscopic clip group (n = 52) (Figure 2). Full baseline characteristics and endoscopic operations were presented in Table 1.

Immediate hemostasis rate

Immediate hemostasis was achieved in all 52 patients (100%) in the PHP group, compared with 48 of 52 patients (92.3%) in the endoscopic clip group (RD, 7.7%, 95% confidence interval = 0.5%–15.0%, $P = 0.022$). The lower limit of the CI for the treatment difference (0.5%) did not extend beyond the noninferiority margin of 10%, indicating that PHP is not inferior to endoscopic clips in achieving immediate hemostasis.

The mean time to achieve hemostasis was significantly shorter in the PHP group relative to the endoscopic clip group (50.77 vs 62.81 seconds; $P = 0.011$) (Table 2).

In the endoscopic clip group, 4 cases failed to achieve immediate hemostasis. In 2 cases, persistent bleeding was observed after 3 minutes despite the application of clips. In the remaining 2 cases, the duodenal papilla was located within a diverticulum. Despite repeated attempts to deploy the endoscopic clip, the procedure was unsuccessful. All operators chose to perform PHP as salvage therapy, achieving hemostasis in all 4 patients.

Delayed bleeding rate

Delayed bleeding occurred in 1 patient (2.1%) in the endoscopic clip group vs none (0%) in the PHP group (RD = −2.1%, 95% CI: −6.0 to 1.8; $P = 0.480$). The affected patient developed tachycardia (114 bpm), hyperactive bowel sounds, melena, and fresh ENBD tube bleeding 12 hours post-ERCP, with hemoglobin levels declining from 115 g/L (pre-ERCP) to 78 g/L. Emergent endoscopy revealed adherent clots and persistent exudative bleeding near the pancreatic duct orifice. The operator then chose epinephrine injection combined with endoscopic clip as a rescue treatment, achieving hemostasis. We demonstrate the representative cases in Figure 3.

Overall treatment success rate

The overall treatment success rate was significantly higher in the PHP group compared with that in the endoscopic clip group (100% vs 90.4%; RD = 9.6, 95% CI = 1.6–16.7; $P = 0.022$).

Adverse events

In the PHP group, adverse events occurred in 11.5% of patients, compared with 9.6% in the endoscopic clip group. Catheter occlusion was noted in 5.8% among the PHP group. In the

Table 1. Baseline information and endoscopic operations of patients

Variable	PHP group (n = 52)	Endoscopic clip group (n = 52)
Age (mean ± SD), yrs	65.4 ± 10.03	65.3 ± 10.66
Sex, n (%)		
Male	24 (46.2)	34 (65.4)
Female	28 (53.8)	18 (34.6)
Laboratory tests, (median ± SD)		
INR	1.12 ± 0.01	1.13 ± 0.02
Platelets, 10^9/L	208.8 ± 53.26	207.46 ± 65.53
Hemoglobin, g/L	126.04 ± 17.59	129.35 ± 16.58
Creatinine, μmol/L	76.04 ± 43.90	76.40 ± 32.01
ALT, μ/L	73.04 ± 91.85	103.54 ± 134.05
AMY, μ/L	73.41 ± 81.51	60.33 ± 30.16
LPS, μ/L	93.55 ± 168.64	61.46 ± 64.02
Charlson Comorbidity Index (mean ± SD)	2.87 ± 1.65	2.52 ± 1.37
Performance status (%)		
ECOG score 0	33 (63.5)	29 (55.8)
ECOG score 1	12 (23.1)	15 (28.8)
ECOG score 2	7 (13.5)	8 (15.4)
Drugs, n (%)		
Antiplatelets	9 (17.3)	6 (11.5)
Anticoagulants (bridge)	1 (1.9)	3 (5.8)
Both antiplatelets/anticoagulants	0 (0)	1 (1.9)
Indication for procedure		
CBD stone	52 (100)	52 (100)
CBD stone with biliary obstruction	6 (11.5)	2 (3.8)
Procedure, n (%)		
EPBD	33 (63.5)	38 (73.1)
Biliary biopsy	6 (11.5)	2 (3.8)
ERPD	6 (11.5)	5 (9.6)
IDUS	7 (13.5)	3 (5.8)
Incision size of EST, n (%)		
Large	10 (19.2)	12 (23.5)
Small	42 (80.8)	39 (76.5)

ALT, alanine aminotransferase; AMY, amylase; CBD, common bile duct; ECOG, eastern cooperative oncology group; EPBD, endoscopic papillary balloon dilation; ERPD, endoscopic retrograde pancreatic drainage; EST, endoscopic sphincterotomy; IDUS, intraductal ultrasound; INR, international normalized ratio; IQR, interquartile range; LPS, lipase; PHP, polysaccharide hemostatic powder.

endoscopic clip group, 4 patients (7.7%) experienced clip slippage during the procedure. Post-ERCP pancreatitis was not statistically significant between the 2 groups. No perforations occurred in either group. No other serious adverse events or mortalities were observed in either group (Table 3).

DISCUSSION

In this trial, we established the noninferiority of PHP vs endoscopic clip in the post-EST oozing bleeding. To our best knowledge, this is the first sufficiently powered RCT comparing PHP with the endoscopic clip, offering an effective and safe hemostatic approach for post-EST bleeding while addressing the limitations of existing methods.

The commonly used endoscopic hemostatic methods for post-EST bleeding include epinephrine injection, argon plasma coagulation, fully covered metal stents, and endoscopic clips. Previous studies reviewed that argon plasma coagulation can lead to adverse events such as necrosis, acute pancreatitis, and perforation, with a rebleeding rate of up to 25% (8). Fully covered metal stents are expensive and require a second procedure for removal (8). Endoscopic clips, recommended as salvage therapy by guidelines, have shown higher efficacy than epinephrine injection (85.4%–95%) and was widely applied in our center over the past

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Table 2. Study outcomes and procedure-related feature

Outcomes	PHP group, n (%)	Endoscopic clip group, n (%)	Risk difference (95% CI, %)	*P* value[a,b]
Total patients	52 (100)	52 (100)		
Immediate hemostasis	52 (100)	52 (100)		
Success	52 (100)	48 (92.3)	7.7 (0.5 to 15.0)	0.022[a]
Failure	0 (0)	4 (7.7)		
Delayed bleeding	52 (100)	48 (100)		
3-d rebleeding (%)	0 (0)	1 (2.1)	−2.1 (−6.0 to 1.8)	0.480[b]
14-d rebleeding (%)	0 (0)	0 (0)		
Overall treatment success	52 (100)	52 (100)		
Yes	52 (100)	47 (90.4)	9.6 (1.6 to 16.7)	0.022[b]
No	0 (0)	5 (9.6)		
Mean hemostasis time (s)	52 (100)	48 (92.3)		
	50.77 ± 28.15	62.81 ± 16.54	NA	0.011[b]

NA, not applicable; PHP, polysaccharide hemostatic powder.
[a]Single-sided *P* value for immediate hemostasis.
[b]Two-sided *P* value for delayed bleeding, overall treatment success, and mean hemostasis time.

decade (13,19,20). Given the high efficacy and safety of endoscopic clips, we considered them a suitable control group to demonstrate the noninferiority of PHP.

In this trial, PHP demonstrated noninferior immediate hemostasis (100% [52/52] vs 92.3% [48/52]; RD 7.7%, 95% CI 0.5–15.0), with the lower confidence limit (0.5%) within the prespecified 10% margin. Furthermore, PHP resulted in a shorter hemostasis time (50.77 vs 62.81 seconds; $P = 0.011$), higher overall treatment success rate (100% vs 90.4%; $P = 0.022$), with no delayed bleeding events, whereas one case (2.1%) was observed in the clip group. Adverse event rates were similar between the groups (11.5% vs 9.6%; $P = 0.750$). These findings support the

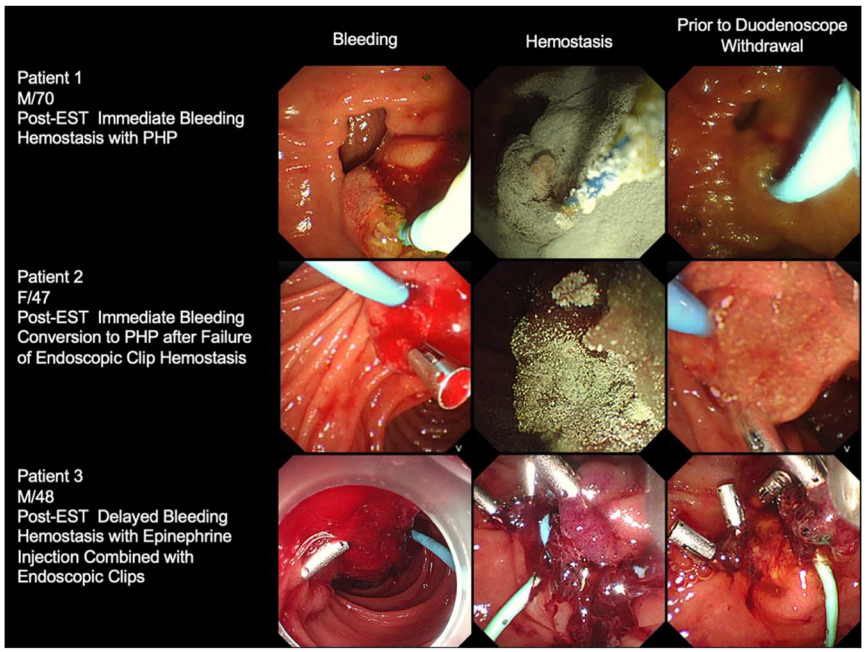


Figure 3. Hemostasis of post-EST bleeding with PHP or endoscopic clip. Patient 1 (Top row): A 70-year-old man who underwent a large incision of EST for CBD stone extraction. Immediate post-EST bleeding was effectively controlled using PHP. Patient 2 (Middle row): A 47-year-old woman who experienced immediate bleeding after EST for CBD stone extraction. Initial hemostasis with endoscopic clips was unsuccessful, leading to conversion to PHP, which successfully achieved hemostasis. Patient 3 (Bottom row): A 48-year-old man who developed delayed bleeding 12 hours post-EST for CBD stone extraction. Initial hemostasis with endoscopic clips was followed by delayed bleeding, which was successfully managed using epinephrine injection and additional endoscopic clips. CBD, common bile duct; EST, postendoscopic sphincterotomy; PHP, polysaccharide hemostatic powder.

Table 3. Adverse events suspected to be associated with procedure

Outcomes	PHP group (n = 52)	Endoscopic clip group (n = 52)	*P* value
Adverse events (%)	6 (11.5)	5 (9.6)	0.750
Catheter occlusion	3 (5.8)	NA	
Clip slippage	NA	4 (7.7)	
Perforation	0 (0)	0 (0)	
Post-ERCP pancreatitis	3 (5.8)	5 (9.6)	0.713
Amylase (U/L)	122.67 ± 242.72	174.50 ± 274.39	0.310
Lipase (U/L)	146.58 ± 414.96	173.95 ± 356.58	0.719

ERCP, endoscopic retrograde cholangiopancreatography; NA, not applicable; PHP, polysaccharide hemostatic powder.

clinical efficacy of PHP as a noninferior alternative to endoscopic clips, with potential practical advantages in procedural efficiency.

Transient biliary obstruction has been reported after using hemostatic powders in post-EST bleeding, typically resolved with irrigation and papillotomy orifice dilation using a sphincterotome tip (21). In our study, no such events or other severe adverse events occurred in the PHP group. All 3 cases of catheter occlusion, a commonly reported issue (22), caused by the catheter tip contacting the duodenal wall resulting in gel blockage, were successfully resolved by catheter replacement.

In clinical practice, we observed that the use of endoscopic clips poses technical challenges, particularly during closure with a duodenoscope when the elevator is fully elevated. This difficulty arises from the tension applied to the clipping device, especially when the endoscope is positioned in a short-route configuration (23). Meanwhile, clip slippage during ERCP, particularly when using endoscopic clips to manage bleeding in challenging anatomical areas such as duodenal diverticula or stricture, presents a significant concern (24). Four patients in our study experienced clip slippage during deployment. Although the clips were successfully reapplied, this prolonged the procedure and increased treatment costs.

By contrast, the catheter blockage issue with hemostatic powder is relatively easy to address. We recommend lubricating the catheter tip with petroleum jelly, clearing the channel with air, and avoiding contact with the lesion during application. In addition, no catheter kinking occurred, likely due to the PHP catheter's hydrophilic coating and reinforced distal tip, which reduce friction and resist deformation. We also used techniques to prevent the catheter tip from forming acute angles when using the elevator, such as increasing the distance between the catheter tip and the lesion; partially releasing the elevator; and adjusting the catheter orientation using the knobs to minimize elevator usage.

In our procedures, PHP demonstrated notable advantages when the bleeding site could not be identified because of poor visibility (25). Although the 10-second reduction in hemostasis time (50.77 vs 62.81 seconds; $P = 0.011$) may not directly reduce intraprocedural blood loss or shorten total ERCP duration, it represents a 15%–25% improvement in hemostasis time, reflecting the technical simplicity of PHP application—requiring no precise lesion targeting and lowering the procedural skill threshold. These advantages may facilitate a shorter learning curve compared with other hemostatic devices.

Another key advantage of PHP is its low cost. In China, PHP costs 113 RMB (≈16 USD) per application prereimbursement, significantly lower than clips at 260 RMB (≈37 USD). In addition, as a class A reimbursable drug, PHP entails a lower patient copayment ratio compared with clips, which are categorized under Class B reimbursement. This cost advantage enhances the accessibility of PHP, particularly in resource-limited settings, helping it become a practical first-line option.

In this study, only 1 patient (1%) in the endoscopic clip group experienced delayed bleeding, consistent with previous reports (2%) (3) Notably, none of the patients in the PHP group developed delayed bleeding. Previous studies on PHP for gastrointestinal bleeding also suggest a potential for reduced rebleeding (26). A vitro study shows the gel formed after PHP application has strong adhesive properties and allow it to remain on the wound, sealing it, promoting mucosal healing, and therefore reducing delayed bleeding.

To date, several hemostatic powders, including Nexpowder®, Hemospray®, EndoClot®, and CGGEL® (detailed in Supplementary Digital Content, see Supplementary Table 1, http://links.lww.com/AJG/D632), have been reported for managing gastrointestinal bleeding from various causes. However, studies on hemostatic agents for post-EST bleeding are limited, with small sample sizes and varied inclusion criteria. In Choi RCT, post-EST bleeding was defined as persistent bleeding beyond 3 minutes after EST, involving 37 cases treated with CGGEL® (a novel hemostatic gel), achieving a 100% immediate hemostasis rate with one case of delayed bleeding (13). Uba et al (12) included patients with oozing (21/26) and pulsatile (5/26) post-EST bleeding in a retrospective study using PuraStat® (a novel self-assembling peptide hemostatic gel), reporting an 88.4% success rate with 7.7% rebleeding. Sulz et al (27) evaluated 16 cases of upper gastrointestinal bleeding, including 2 post-EST cases, where hemostasis was successfully achieved using Hemospray® (an inorganic hemostatic powder) without complications. Two additional case reports also documented the application of Hemospray® for delayed post-EST bleeding (14,21). Compared with the existing studies, our study used a strict classification of post-EST bleeding types and enough cases to validate its efficacy.

This trial has several limitations. First, the 3-minute cutoff for immediate hemostasis may need further discussing, and future studies should extend the cutoff to assess its impact on hemostasis rates. In addition, as the delayed bleeding rate may better reflect

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the efficacy in clinical outcomes, future studies may set it as the primary outcome and dig deeper into this area. Second, we initially included only oozing bleeding cases because of the rarity (11), high mortality of post-EST pulsatile bleeding, and limited evidence on hemostatic powders for upper gastrointestinal pulsatile hemorrhage (18,26). Although this enhances safety monitoring, it may limit generalizability to high-risk scenarios. Future trials should evaluate PHP in pulsatile bleeding and explore its role as a second-line therapy after epinephrine failure, thereby investigating its efficacy in refractory bleeding scenarios while preserving the mechanical advantages of clips for vessel coaptation. Third, despite broad inclusion criteria, our cohort comprised only common bile duct stone patients because of their predominance at our center and the absence of immediate bleeding in nonstone cases (e.g., diagnosis or management of strictures or obstructions requiring precutting). Larger studies with more diverse patient populations are needed to improve generalizability. Fourth, this study did not use operator-reported scales to quantify procedural difficulty. Although the observed time reduction suggests the operational convenience of PHP, future studies should incorporate subjective assessments to evaluate device usability. Finally, the 10% noninferiority margin and limited sample size may increase the risk of Type 2 error and limit our ability to assess PHP's efficacy in preventing delayed bleeding after EST. Larger-scale studies are needed to strengthen the evidence.

In conclusion, PHP is a promising tool for managing post-EST bleeding. It can be considered not only as an alternative to current treatment modalities but also as a salvage therapy when standard approaches fail. PHP is safe for patients and easy for clinicians to use. Its noncontact nature is particularly advantageous in cases with complex anatomy or unclear visual fields that may not be suitable for standard targeted therapies. However, larger-scale studies are needed to validate its effectiveness across diverse ERCP indications and in preventing delayed bleeding after EST.

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CONFLICTS OF INTEREST

Guarantors of the article: Shutian Zhang Ph.D., Peng Li Ph.D.

Specific author contributions: Conceptualization: S.Z., P.L., W.W., H.L., J.Z.; Writing - original draft: J.Z., H.L.; Formal analysis: J.Z., S.W.; Investigation: H.L., J.Z., W.W., S.W., Y.Z., Y.W., J.S., Z.Z., W.Y., J.W., C.L., H.W., Z.L., X.Y., K.Y., F.L., Y.W., P.L., S.Z.; Data Collection: W.W., Y.Z., Y.W., J.S., P.L., J.W., F.L., Y.W.; Writing - review: S.W., H.L., P.L., J.Z.; Supervision: S.Z., P.L., H.L.; Funding acquisition: S.Z., P.L.

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Potential competing interests: None to report.

Trial registry and the registration number: chictr.org.cn, ChiCTR2400092280.

Data transparency statement: Data will be managed using the ResMan electronic data capture (EDC) system. For more details, please visit http://www.medresman.org.cn/login.aspx. Raw data are expected to be uploaded within 1 year of the end of the study.

Study Highlights

WHAT IS KNOWN

- ✓ Postendoscopic sphincterotomy bleeding is a challenge for endoscopists.
- ✓ Polysaccharide hemostatic powder (PHP) has shown promise in controlling gastrointestinal hemorrhage.

WHAT IS NEW HERE

- ✓ PHP is noninferior to endoscopic clips in achieving immediate hemostasis for nonpulsatile postendoscopic sphincterotomy bleeding.
- ✓ PHP achieved a higher overall treatment success rate and no delayed blleding events. PHP has a shorter hemostasis time and easier application.
- ✓ PHP can be considered as an alternative to current treatment modalities or a salvage therapy when standard approaches fail.

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