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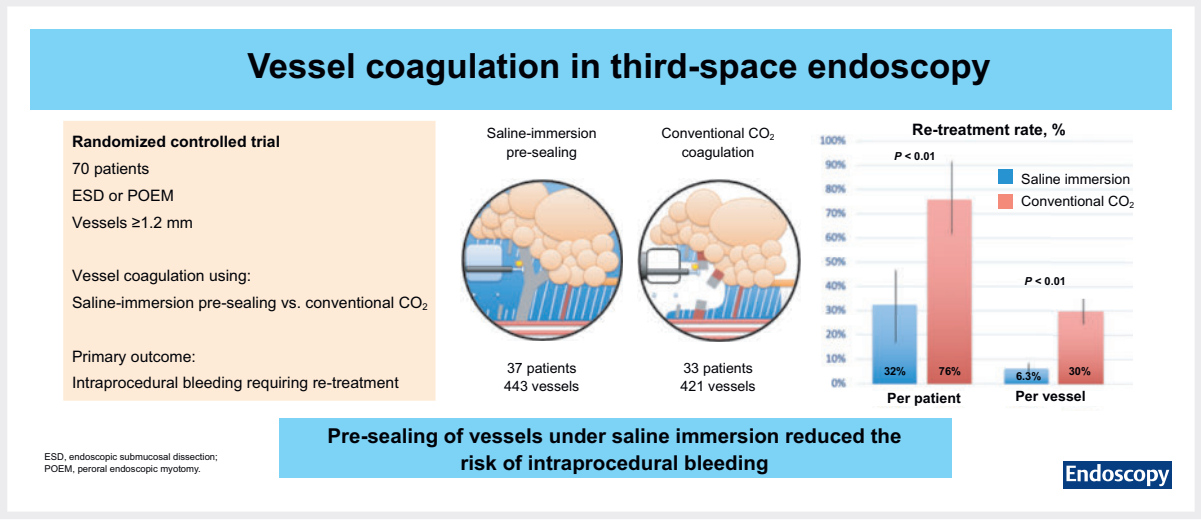
Vessel coagulation in third-space endoscopy: a randomized controlled trial

GRAPHICAL ABSTRACT



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ABSTRACT

Background Third-space endoscopy is standard practice for neoplastic and motility disorders; however, it carries a high risk of intraprocedural bleeding. Such risk may be reduced by prophylactic coagulation of submucosal vessels, but this requires instrument exchange. A new approach involves pre-sealing submucosal vessels under saline immersion using standard electrocautery settings and the same knife.

Methods Patients undergoing third-space procedures (endoscopic submucosal dissection or peroral endoscopic myotomy) were randomized to receive either targeted saline-immersion pre-sealing (intervention group) or conventional coagulation (carbon dioxide insufflation, control group) for prophylactic management of vessels ≥1.2 mm. Dissection settings were identical. Rate of per-patient intraprocedural bleeding requiring re-treatment for vessels ≥1.2 mm was the main outcome. Per-vessel analyses were also performed. The use of an adjunctive device and coagulation time were also assessed.

Results 70 patients (37 immersion, 33 control) with 864 ≥1.2-mm vessels were included. Saline-immersion pre-sealing significantly reduced bleeding rates: per patient (32.4% vs. 75.8%; relative risk [RR] 0.43, 95%CI 0.26–0.71; number needed to treat [NNT] 2.3; P<0.01); per vessel (6.3% vs. 29.9%; RR 0.21, 95%CI 0.14–0.31; NNT 4.2; P<0.01). Use of coagulation forceps for bleeding treatment also decreased (0% vs. 24.2% and 0% vs. 8.3%; P<0.01). A significant reduction in mean (SD) coagulation time was reported in the saline-immersion group (22.7 [26.4] vs. 29.6 [49.8] seconds; P<0.01).

Conclusions A substantial reduction in the risk of intraprocedural bleeding was achieved by saline-immersion pre-sealing in per-patient and per-vessel analyses, prompting its implementation in clinical practice.

Introduction

Third-space endoscopy is recommended for the management of gastrointestinal (GI) motility disorders, such as achalasia and gastroparesis, as well as for the resection of early cancers and precancerous lesions within both the upper and lower GI tract [1, 2, 3, 4].

In third-space endoscopy, clear visualization of the submucosal area to be dissected is essential, particularly to avoid inadvertent injury to the underlying muscle layer [5]. However, optimal visualization is often compromised by intraprocedural bleeding owing to the abundance of vessels of varying calibers within the submucosal layer [6]. Such bleeding substantially slows third-space endoscopy by requiring frequent aspiration and instrument changes within a limited operative channel, leading to incomplete resection. In addition, bleeding events may obscure the operative field, further compromising safety by increasing the risk of mucosal injury during peroral endoscopic myotomy (POEM) and muscularis propria damage during endoscopic submucosal dissection (ESD) [7, 8].

Pre-sealing of vessels prior to dissection, which involves coagulation of the entire vessel wall prior to incision, is an effective strategy for preventing intraprocedural bleeding [7, 8]. Typically, this pre-sealing is achieved using dedicated hemostatic instruments such as coagulation forceps; however, frequent device changes required during the procedure can negatively impact the efficiency of the dissection.

One potential alternative method of achieving a pre-sealing effect involves the use of the same electrosurgical knife employed for submucosal dissection without modifying the current itself. Instead, the procedural environment is altered by replacing the standard insufflation medium (e. g. carbon dioxide [CO_2]) with isotonic saline, as described in recent reports on third-space endoscopy [7, 8, 9, 10]. This change fundamentally modifies the electrical circuit: saline immersion markedly reduces impedance, which in turn lowers the peak voltage required for current delivery and enhances ionic conduction at the tissue interface [11, 12]. These conditions promote coagulation prior to cutting, effectively mimicking a pre-sealing effect. Clinical adoption of this technique has been associated with reduced intraprocedural bleeding in retrospective cohort analyses [7, 13]. While other techniques for achieving pre-sealing in CO_2 have been described, none of them has been validated in strictly controlled settings.

The aim of this randomized trial was to further assess the efficacy of saline-immersion pre-sealing in the prevention of intraprocedural bleeding and the overall efficiency of third-space endoscopy.

Methods

A single-center, randomized, non-profit prospective trial was conducted at Humanitas Research Hospital, Rozzano, Italy. Patients undergoing ESD or POEM were randomized to either conventional CO_2-based coagulation or saline-immersion coagulation. The study is reported according to Consolidated Standards of Reporting Trials (CONSORT) guidelines (see the online-only **Supplementary Material** for the CONSORT checklist and the study protocol).

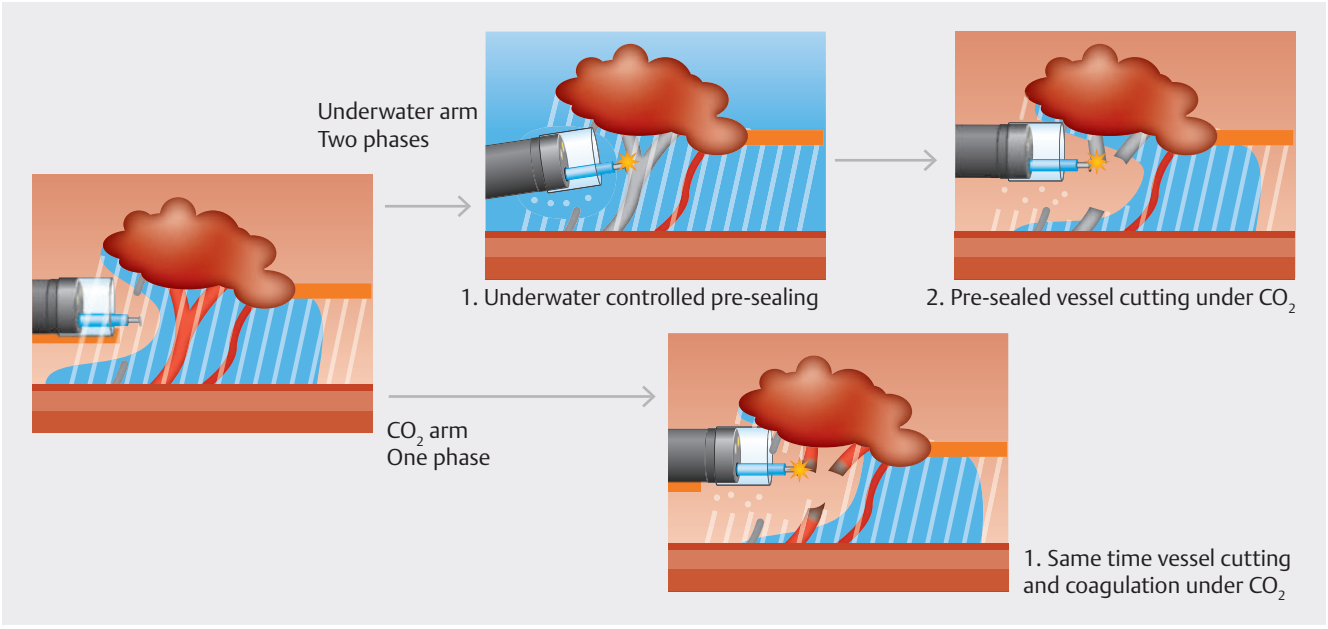
Study population

Consecutive patients aged ≥18 years who were referred for ESD for superficial GI neoplastic lesions in the upper or lower GI tract or POEM for esophageal achalasia were considered for enrollment. Exclusion criteria were patients with ongoing antithrombotic/anticoagulant therapy or with bleeding disorders, and those with esophageal and/or gastric varices. Patients who had been previously treated with either POEM for achalasia or ESD for GI neoplastic lesions were excluded.

Procedures

Endoscopist expertise was defined according to official recommendations: for POEM, endoscopists who had performed ≥100 unsupervised procedures, including complex cases, were considered experts [14]; for ESD, those who maintained an annual volume of ≥25 procedures were considered experts [15]. Non-experts were those who did not match these thresholds.

All procedures (POEM and ESD) were performed in accordance with the established protocol of our unit, as detailed in the **Supplementary Material**. A single type of knife that had al-



▶ **Fig. 1** Schematic representation of submucosal vessel pre-sealing performed in an saline-immersion environment. The diagram emphasizes dynamic management by the operator, highlighting the differences in vessel treatment compared with standard carbon dioxide-based settings.

ready been validated for vessel pre-sealing [8] was adopted with the same electrosurgical settings to minimize the variability between the two groups (HybridKnife; Swift-Coag E3; VIO 3; ERBE Elektromedizin GmbH, Tübingen, Germany).

All procedures were performed in a CO_2 setting to exclude unintentional vessel pre-sealing in the control group (see below). Thus, the switch from CO_2 to the saline-immersion setting was allowed only in the intervention group with the specific purpose of achieving pre-sealing of the vessels (▶ **Fig. 1**).

Submucosal vessel classification

Each vessel encountered in the submucosal layer was classified by a physician assistant (see the case report form template in the **Supplementary Material**). All vessels detected in the submucosal dissection phase were considered, while those identified in other phases (i. e. myotomy and incision) were excluded due to the use of different electrosurgical settings. Study vessels were divided into ≥1.2 mm or <1.2 mm compared with the bottom width of the HybridKnife tip (1.2 mm). Because of the very low risk of intraprocedural bleeding, vessels <1.2 mm were not considered for the purposes of the study (i. e. all these vessels were treated with conventional coagulation, irrespective of the randomization group). Vessels ≥1.2 mm were included in the study and were further divided into medium (1.2–2.1 mm) and large (≥2.2 mm) using the top of the knife, measuring 2.1 mm, as the reference standard.

Study intervention: vessel pre-sealing and re-treatment after bleeding

In patients who were randomized to receive the intervention, vessels measuring ≥1.2 mm were treated with vessel pre-sealing/coagulation in a saline-immersion setting. In summary, upon the detection of a vessel measuring ≥1.2 mm within the intervention group, the endoscopist was instructed to replace the submucosal CO_2 with saline solution and to pre-seal the vessel. Pre-coagulation of the vessel wall before cutting was achieved by placing the knife tip adjacent to the vessel wall and applying a high-voltage coagulation current (Swift-Coag E3 for POEM and Swift-Coag E4 for ESD). The pre-sealing effect, which involved pre-coagulation of the vessel wall prior to cutting, is demonstrated in ▶ **Video 1**.

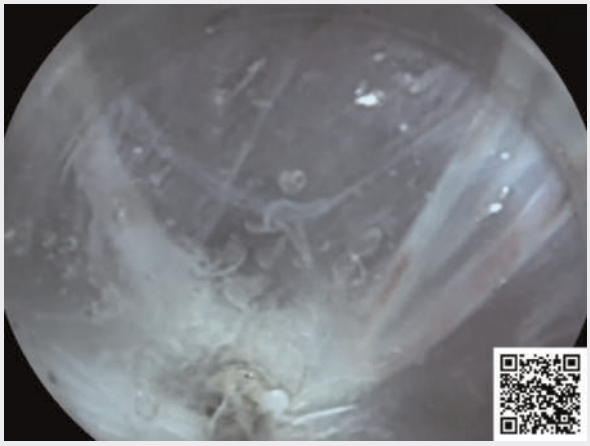
Furthermore, in the active intervention group, the same setting used for pre-sealing was employed for hemostasis of bleeding vessels (i. e. re-treatment). Hemostasis was defined as cessation of visible bleeding with no further requirement for additional coagulative intervention.

Study control: vessel coagulation and re-treatment after bleeding

In patients assigned to the control group, coagulation of vessels measuring ≥1.2 mm was accomplished by positioning the knife tip adjacent to the vessels in a CO_2 setting and employing the same high-voltage current utilized in the intervention group (Swift-Coag E3 for POEM and Swift-Coag E4 for ESD). In the CO_2 setting, this approach led to concurrent coagulation and vessel incision. In cases of rebleeding, a previously employed coagulation approach was reinstituted.

Re-treatment and pre-sealing with coagulation forceps

In both randomized groups, vessel re-treatment following initial failure of knife-tip coagulation was performed using coagulation forceps (Soft Coag E5.5 – FD-410LR; Olympus Corp., Tokyo, Japan). Furthermore, at the discretion of the endoscopist,



Video 1 Pre-sealing of submucosal vessels ≥1.2 mm under saline immersion, followed by cutting under carbon dioxide insufflation.
Online content viewable at:
https://doi.org/10.1055/a-2780-5445

pre-sealing with coagulation forceps was permitted in both groups, as it was deemed a safer alternative to either pre-sealing or direct treatment with the knife. In general, vessels ≥2.1 mm, pulsating, and arising from the muscle layer were considered to be at very high risk. The use of coagulation forceps was documented as two instances of device exchange, defined as the removal of the knife and subsequent insertion of the forceps, followed by removal of the forceps and insertion of the knife.

Time for pre-sealing and coagulation

For each ≥1.2-mm vessel identified during submucosal dissection, an endoscopist's assistant started a digital timer at the beginning of pre-sealing/coagulation, including vessel isolation and time spent on device exchange, and recorded the time required to achieve complete pre-sealing or hemostasis.

Study end points and statistical analysis

The primary outcome of the study was the proportion of patients who experienced at least one episode of intraprocedural bleeding from vessels ≥1.2 mm that required additional hemostatic intervention (i. e. re-treatment).

The main secondary end points in the per-patient analysis were rate of intraprocedural bleeding requiring coagulation forceps and adverse events, including intraprocedural (perforation) and postprocedural events. Delayed bleeding was defined as any clinical sign of bleeding, such as hematemesis, melena, hematochezia, or a drop in hemoglobin level >2 g/dL, which required blood transfusion or repeated endoscopic intervention within 30 days of hospital discharge.

The main secondary end points in the per-vessel analysis were rate of intraprocedural bleeding per vessel requiring re-treatment with either the knife tip or coagulation forceps, and coagulation time, defined as the mean time required to achieve effective pre-sealing or hemostasis for each bleeding vessel, providing a metric for technical performance.

Additional end points are reported in the **Supplementary Material**.

Randomization

The trial adopted a fully automated randomization technology and systematic data collection to maximize participant inclusion and minimize the trial burden. Study randomization was performed using the RedCap program based on predefined block randomization, with sizes varying from 4 to 8. No individual had access to the random assignment sequence.

The endoscopists were aware of each patient's randomization group; however, patients and data analysts were blinded to group allocation.

Statistical analysis

We considered the intention-to-treat (ITT) population as the total of all patients randomized, the modified ITT (mITT) population as the total of all randomized patients in whom the third-space procedure was at least started, and the per-protocol analysis as those in the mITT population who had at least one ≥1.2-mm vessel treated.

Continuous variables were reported as mean (SD) or median (range). Numbers and percentages were used for categorical variables. Baseline clinical and procedural features were compared using the chi-squared test or Fisher exact test for the categorical variables and the two-tailed *t* test for the continuous variables.

Relative risks (RRs) with 95%CIs were calculated for bleeding events requiring re-treatment or the use of coagulation forceps, according to Altman (1991) [16]. The number needed to treat (NNT) [17] was also determined for significant outcomes.

The main secondary outcomes at the patient level were also estimated, and RR and 95%CI were calculated.

The Mann–Whitney *U* test was used to compare non-normally distributed continuous variables between the groups.

Per-vessel analysis was also performed allowing for a comprehensive assessment of the effect of the intervention on intraprocedural bleeding and procedural efficiency. Vessel re-treatment at the per-vessel level was compared by using a mixed effect logistic regression model to control for multiple vessels per patient. The mixed effects model was fitted with a random intercept for effects of clusters (i. e. multiple vessels per patient) and study group as a fixed effect. Data were presented as odds ratios (ORs) with 95%CIs. In addition, to give a complete picture of the effect and its implication, the predicted probabilities (95%CI) of intraprocedural bleeding from the model for both study groups were reported.

Finally, using a (quasi) Poisson regression, we compared the mean number of vessels requiring re-treatment per patient. A *P* value of <0.05 was considered statistically significant. All statistical analyses were performed using R software version 4.0.2 (2020–10–10; R Foundation for Statistical Computing, Vienna, Austria).

Sample size

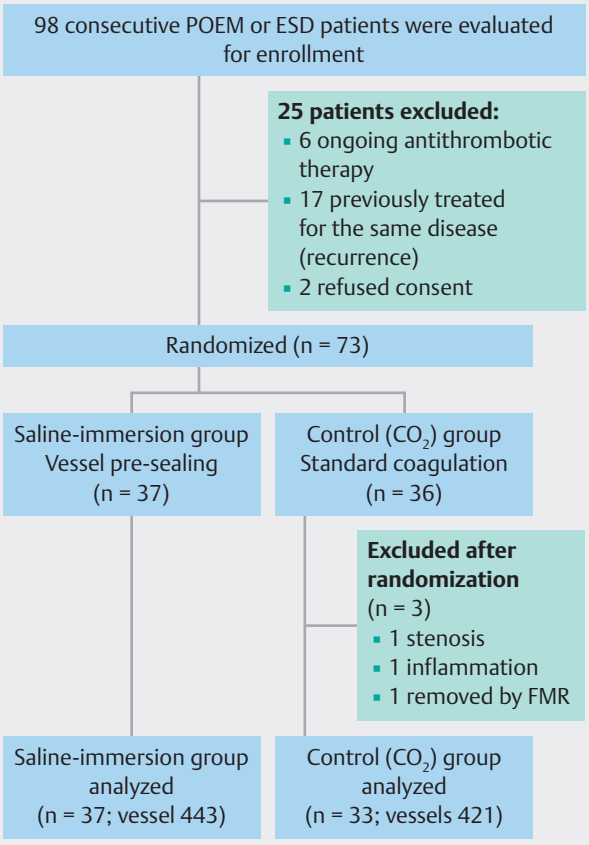
The hypothesis was based on previously published data, in which standard coagulation resulted in 36% of patients requiring adjunctive hemostasis, while saline-immersion pre-sealing showed a reduced rate of 6% [8]. These estimates informed our power calculation, assuming a 4:1 ratio of treated vessels to patient vessels. Considering a mean number of treated vessels of 4 per patient, with the standard technique we expected that 36% of patients would have at least one bleeding vessel requiring adjunctive hemostasis compared with 6% of patients with the saline-immersion pre-sealing technique. With an alpha error of 5% and power of 80%, we needed a total of 70 patients (35 in each group) to detect this difference.

Results

Study population

During the study period (April 2024 – March 2025), 98 patients were evaluated for enrollment. As outlined in the study flow chart (▶ **Fig. 2**), 25 patients were excluded. Therefore, 73 patients were included in the study. The main demographic and clinical characteristics of the patients are shown in ▶ **Table 1**. Patients were divided into two groups: saline-immersion group (37 patients) and CO_2 group (36 patients). This approach reflects the ITT the population. Of the patients who were randomized, three were excluded from the study because third-space endoscopy was not considered feasible at the time of the procedure. Consequently, 37 in the saline-immersion group and 33 patients in the control group were included in the mITT analysis (▶ **Table 1, Fig. 2**).

A total of 864 vessels with a diameter of ≥1.2 mm were treated in 70 patients, including 305 vessels in the large/medium category and 559 vessels in the small category (▶ **Table 1**).



▶ **Fig. 2** Patient flow diagram illustrating the selection process for the patients included in the trial. EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; POEM, peroral endoscopic myotomy.

Per-patient analysis

Among the 70 patients, 12 of 37 patients (32.4%) in the saline-immersion group and 25 of 33 patients (75.8%) in the control group had at least one instance of intraprocedural vessel bleeding that necessitated further hemostatic treatment (RR 0.43, 95%CI 0.26–0.71; NNT 2.3; P<0.01) (▶ **Table 2, Fig. 3**). Coagulation forceps were used in the control group for 8/33 patients (24.2%) but were not required in any patient in the saline immersion group (RR 0.05, 95%CI 0.00–0.88; NNT 4.2; P<0.01). Consequently, there were additional hemostatic instrument exchanges (mean 1.8 [SD 6.8] per procedure in the control group), in contrast to the absence of such exchanges in the saline-immersion group (P>0.99). Analyses of additional treatment of submucosal vessels for POEM and colorectal ESD and laboratory findings are summarized in **Tables 1s**, **2s**, and **Table 3s**.

The saline-immersion group did not demonstrate any adverse events, whereas the control group exhibited three (0/37 vs. 3/33; P=0.1): one intraprocedural perforation, one delayed bleeding, and one post-polypectomy syndrome.

Per-vessel analysis

In the 37 and 33 patients in the intervention and control groups, 443 and 421 vessels, respectively, were found. There were no differences in the mean number of vessels between study groups: saline-immersion group 10 (IQR 6–15) vs. control group 10 (IQR 8–14).

Re-treatment due to intraprocedural bleeding for ≥1.2-mm vessels was required in 28/443 vessels (crude proportion, 6.3%) in the saline-immersion group compared with 126/421 (crude proportion, 29.9%) in the conventional group (RR 0.21, 95%CI 0.14–0.31; NNT 4.2; P<0.01) (▶ **Table 2, Fig. 3**).

Results from a mixed effects logistic regression model showed that the risk of re-treatment was significantly lower in the saline-immersion group than in the control group (OR 0.10, 95%CI 0.04–0.26; P<0.001). Accordingly, the mean probabilities of vessel re-treatment were estimated to be 4.0% (95%CI 2.2–7.2) and 19.8% (95%CI 13.0–30.1) in the saline-immersion and control groups, respectively. Finally, (quasi) Poisson regression showed that the mean number of vessels requiring re-treatment per patient was 0.76 (95%CI 0.52–1.10) for patients in the saline-immersion group compared with 3.8 (95%CI 3.2–

▶ **Table 1** Baseline patient demographics and procedural characteristics for both study groups (saline-immersion and conventional carbon dioxide [CO_2] coagulation) in the modified intention-to-treat analysis.[1]

	Saline immersion	Conventional
Patients, n	37	33
▪ Age, mean (SD), years	63.3 (15.5)	62.8 (17.5)
▪ Sex, male, n (%)	21 (56.8)	19 (57.6)
▪ Antiplatelet, n (%)	3 (8.1)	5 (15.2)
▪ Anticoagulant, n (%)	4 (10.8)	5 (15.2)
▪ POEM, n (%)	22 (59.5)	20 (60.6)
▪ ESD, n (%)	15 (40.5)	13 (39.4)
▪ Upper	7 (18.9)	8 (24.2)
▪ Lower	8 (21.6)	5 (15.2)
Vessels ≥1.2 mm, n	443	421
▪ 1.2 mm–2.1 mm, n (%)	290 (65.5)	269 (63.9)
▪ POEM	155 (35)	161 (38.2)
▪ ESD	135 (30.5)	108 (25,7)
▪ >2.1 mm, n (%)	153 (34.5)	152 (36.1)
▪ POEM	87 (19.6)	103 (24.5)
▪ ESD	66 (14.9)	49 (11.6)

ESD, endoscopic submucosal dissection; POEM, peroral endoscopic myotomy.
[1]Modified intention-to-treat population included all randomized patients in whom the third-space procedure was at least started.

▶ **Table 2** Per-patient and per-vessel analyses summarizing key outcomes of intraprocedural bleeding events and additional hemostatic interventions required (e. g. use of coagulation forceps).

	Saline immersion	Conventional	*P* value
Per-patient analysis			
▪ Patients, n	37	33	
▪ Vessels ≥1.2 mm requiring additional hemostasis, n (%)	12 (32.4)	25 (75.8)	<0.01
▪ Vessels ≥1.2 mm requiring coagulation forceps, n (%)	0 (0)	8 (24.2)	<0.01
Per-vessel analysis			
▪ Vessels, n	443	421	
▪ Vessels ≥1.2 mm requiring additional hemostasis, n (%)	28 (6.3)	126 (29.9)	<0.01
▪ Vessels ≥1.2 mm requiring coagulation forceps, n (%)	0 (0.0)	35 (8.3)	<0.01
▪ Coagulation time, mean (SD), seconds	22.7 (26.4)	29.6 (49.8)	<0.01

4.6) for those receiving the conventional procedure (incidence rate ratio 0.20, 95%CI 0.07–0.47; $P = 0.001$).

No use of coagulation forceps, for active bleeding or prophylactic purposes, was recorded in any vessel in the saline-immersion group. Conversely, coagulation forceps were employed in 35/421 vessels (8.3%) for re-treatment in the conventional group and in 34/421 vessels (8.1%) for prophylactic interventions (RR 0.01, 95%CI 0.00–0.22; NNT 12.4; $P<0.01$). The mean time to achieve hemostasis for each bleeding vessel was 26.1 (SD 39.7) seconds. No differences in mean total procedure time were recorded between the two groups: However, a coagulation time of 22.7 (SD 26.4) seconds in the saline-immersion group and 29.6 (SD 49.8) seconds in the control group was reported ($P<0.01$) (▶ **Table 2**).

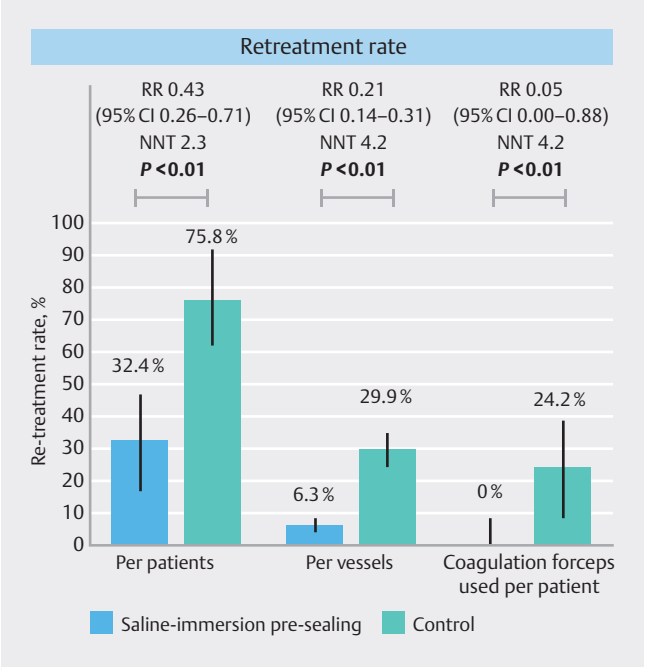
Discussion

According to our study, the adoption of saline-immersion pre-sealing using the Swift-Coag setting in third-space endoscopy reduced the risk of intraprocedural bleeding requiring re-treatment by 57% and 79% in per-patient and per-vessel analyses, respectively, converting what was previously regarded as a procedure at high risk of intraprocedural bleeding into one with limited, if not negligible, bleeding risk.

The corresponding NNTs to prevent clinically relevant intraprocedural bleeding at per-patient and per-vessel analyses (2.3 and 4.2, respectively) showed the efficiency of this intervention in preventing bleeding risk in third-space endoscopy. In addition, saline-immersion coagulation in the intervention group also proved to be an effective rescue hemostatic procedure in a few cases where initial pre-sealing was not effective. The combination of these two factors eliminated the need for coagulation forceps.

In the control group, conventional coagulation was confirmed to be an inefficient procedure. Three-quarters of the patients experienced at least one intraprocedural bleeding event that required re-treatment. This was due to a combination of a mean of 12 vessels per patient and a roughly 30% risk of bleeding per treated vessel. The fact that three-quarters of patients were affected by intraprocedural bleeding is technically relevant. Intraprocedural bleeding in the dissection phase results in immediate effusion of blood into the submucosal space due to lack of a barrier preventing blood spreading. This is only partially compensated for by clot suction, as residual blood continues to blur the submucosal layer, preventing adequate vessel and layer recognition. This is likely to affect the efficiency and safety of third-space endoscopy.

The 79% efficacy for prevention of intraprocedural bleeding requiring re-treatment at per-vessel analysis (from 29.9% to 6.3%) is in line with our previous evidence of a 69% decrease (from 26.7% to 8.2%) in intraprocedural bleeding shown in a retrospective series of 43 patients treated with the same pre-sealing intervention compared with standard coagulation [8].



▶ **Fig. 3** Comparison of re-treatment rates (with 95%CIs) for bleeding between the saline-immersion and conventional coagulation groups. Left column: per-patient analysis (% of patients requiring re-treatment). Center column: per-vessel analysis (% of vessels requiring re-treatment). Right column: use of coagulation forceps (% of vessels treated with forceps for active bleeding or prophylactic purposes).NNT, number needed to treat; RR, relative risk.

The relevance of our study lies in the biological plausibility of the benefits of pre-sealing in an saline-immersion setting, as demonstrated in ex vivo studies, where conversion from CO_2 to underwater resulted in a 99% drop in the impedance of the current, converting a high-voltage current to low voltage [12]. Of note, this low-voltage effect has been beneficial both for the pre-sealing effect (vessel coagulation without cutting), and for the re-treatment of bleeding vessels, as the superficial coagulation of this current without cutting avoids coagulation-driven perforation. In addition, we included POEM and ESD in order to assure the generalizability of the procedure, and showed a similar effect in the two subgroups.

The main limitation of our study is the relatively small sample size (n = 70). Nonetheless, the large number of vessels analyzed (864, mean of 12 vessels per patient) provided a robust dataset for evaluating the study end points. Notably, the actual number of included vessels was threefold higher than that estimated in the sample size calculation based on previous unselected publications. This may be informative for future research on hemostatic interventions in third-space endoscopy. The second limitation is the lack of high-voltage low-effect coagulation (Forced Coag, E0.3) in the conventional group due to the lack of ex vivo and robust clinical validation; in this regard, future studies comparing our setting to such a setting may be informative. A third limitation is the lack of difference in resection speed between the two groups. This may be explained by the adoption of the saline-immersion setting exclusively for coagulation, rather than throughout the entire procedure. However, when the evaluation is limited to coagulation time, saline-immersion pre-sealing remains 23.3% faster than conventional coagulation, despite including the time for desufflation and CO_2–water exchange. Fourth, bleeding that occurred during accidental cutting of unrecognized vessels was excluded from the study in both groups. This condition can be avoided in the future by utilizing mechanisms of advanced technology to enhance vessel detection, such as digital chromoendoscopy or dedicated artificial intelligence. Fifth, for ethical reasons, the use of prophylactic coagulation forceps was allowed in very high-risk vessels; however, this technique was used only in the control group, representing the worst-case scenario of the study intervention. The lack of use in the intervention group may be justified by the psychological trust of the operator in the pre-sealing effect. However, the prophylactic use of coagulation forceps was an exploratory end point that did not affect primary end point estimation. Finally, ESD-specific studies are needed due to the different magnitude of adverse events compared with POEM.

In conclusion, in a controlled trial, saline-immersion pre-sealing dramatically reduced the risk of intraprocedural bleeding in both per-patient and per-vessel analyses. This technical modification is likely to improve the safety and efficiency of third-space endoscopy.

Contributors' Statement

Antonio Capogreco: Conceptualization, Data curation, Investigation, Methodology, Project administration, Supervision, Writing - original draft, Writing - review & editing. Roberta Maselli: Conceptualization, Methodology, Supervision. Davide Massimi: Conceptualization, Writing - original draft, Writing - review & editing. Ludovico Alfarone: Conceptualization, Writing - original draft, Writing - review & editing. Roberto De Sire: Conceptualization, Writing - original draft, Writing - review & editing. Emanuela Morenghi: Formal analysis. Loredana Correale: Formal analysis. Luca Brandaleone: Data curation, Investigation, Writing - review & editing. Elisabetta Mastrorocco: Data curation. Maritalia Simone: Data curation, Investigation. Chiara Morelli: Data curation, Investigation. Marco Spadaccini: Conceptualization, Methodology, Supervision. Markus Enderle: Resources. Nermin Salkic: Resources. Pradeep Bhandari: Supervision. Romain Legros: Supervision. Jeremie Jacques: Supervision, Validation. Cesare Hassan: Conceptualization, Methodology, Supervision. Alessandro Repici: Conceptualization, Methodology, Supervision.

Conflict of Interest

A. Capogreco is a consultant for ERBE. R. Maselli is a consultant for ERBE, Fujifilm, 3DMatrix, and Boston Scientific. M. Spadaccini is a consultant for Boston Scientific and Olympus. M. Enderle and N. Salkic are full-time employees of ERBE Elektromedizin GmbH. J. Jacques has received honoraria from ERBE for medical ESD training; has conducted training for Olympus (ESD), Fujifilm (ESD), Pentax Medical (ESD), and Boston Scientific (therapeutic EUS). C. Hassan is a consultant for Fujifilm, Medtronic, and Olympus. A. Repici is a consultant for Medtronic, ERBE, Fujifilm, and Olympus. The remaining authors declare that they have no conflict of interest.

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Clinical Trial

EU Clinical Trials Register (https://www.clinicaltrialsregister.eu) | Registration number (trial ID): NCT05804266 | Type of study: Randomized prospective single-center trial

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