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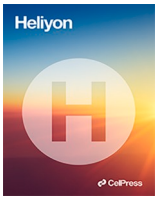

Research article

Preclinical evaluation of a novel endovascular thrombectomy device in a modified swine model for iliac vein thrombosis

Qiu Zeng, Zheng Chen, Biyun Teng, Fenghe Li, Yu Zhao *

Department of Vascular Surgery, the First Affiliated Hospital of Chongqing Medical University, Chongqing, PR China

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ABSTRACT

Objective: To evaluate the safety and efficacy of a novel endovascular thrombectomy device in a modified swine model of iliac vein thrombosis.

Methods: A modified swine model for iliac vein thrombosis was created using proximal–distal balloon occlusion combined with autologous venous thrombus and thrombin injections. The safety and efficacy of the newly developed Zylox endovascular thrombectomy system were evaluated in this animal model and its performance was compared with that of the AcoStream aspiration thrombectomy device.

Results: Bilateral iliac vein thrombosis models were successfully created in 12 swine, with 23 iliac veins used for device testing and one for anatomical observation. The thrombus length in the Zylox group was greater than in the AcoStream group (98.42 ± 17.56 mm vs. 84.12 ± 13.30 mm), while thrombus scores were not significantly different between the two groups. Although Grade I thrombus clearance was achieved in all iliac veins in both groups, blood loss in the Zylox group was significantly less than in the AcoStream group (81.09 ± 27.26 ml vs. 162.50 ± 61.96 ml, $P < 0.001$). Three swine (6 iliac veins) in each group underwent repeat venography evaluations 28 days postthrombectomy, showing that all the veins were patent without any rethrombosis. Histopathologic evaluation immediately and 28 days postthrombectomy revealed no differences between the two groups. No complications or deaths occurred in the swine during the entire process.

Conclusion: The current modified swine model is stable, reproducible, and appropriate for testing endovascular devices. This study preliminarily verified the safety and efficacy of the Zylox thrombectomy system for thrombus removal in this animal model and demonstrated its advantage in controlling blood loss. Future randomized controlled trials in humans are needed to further verify the safety and efficacy of the device.

1. Introduction

Deep venous thrombosis (DVT) is a highly prevalent disease, with an annual incidence of 50–100 cases per 100,000 adults [1]. If left untreated, lower extremity DVT can gradually worsen, resulting in further complications such as pulmonary embolism (PE) and postthrombotic syndrome (PTS) [2]. Even with standard anticoagulant treatment approximately 20 % of lower extremity DVT patients

* Corresponding author. Department of Vascular Surgery, the First Affiliated Hospital of Chongqing Medical University, Yuanjiagang Youyi Road No.1, Chongqing, 400042, PR China.
E-mail address: zhaoyu201514@gmail.com (Y. Zhao).

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still progress to PTS annually [3]. Catheter-directed intervention techniques, including catheter-directed thrombolysis (CDT), percutaneous mechanical thrombectomy (PMT) and pharmacomechanical CDT (PCDT), have been used as adjunctive strategies for systemic anticoagulation for DVT treatment. These techniques allow for a reduction in the thrombus burden in the affected veins within a short period, thereby providing rapid symptom relief and decreasing the future occurrence of PTS [4].

Over the past decade, there have been significant advancements in catheter-directed intervention devices for acute DVT treatment. These include mechanical thrombectomy catheters [5,6], vacuum-assisted thrombectomy devices [7,8], and pharmacomechanical thrombectomy devices [9]. The AngioJet catheter is the most widely used thrombectomy device based on the PCDT technique, but it presents some issues that cannot be ignored. For example, the lytic agent cannot be sufficiently retained because venous blood returns towards the heart, thereby reducing thrombolytic effectiveness. It has limited efficacy in removing subchronic and chronic thrombi, more prevalent in acute DVT than previously anticipated [10]. Our research shows that the AngioJet catheter cannot remove organized thrombus components, often necessitating additional methods [11]. Furthermore, there are reports of potential risks such as haemoglobinuria, acute kidney injury (AKI), and bradycardia resulting from high-pressure saline injections [12–14]. A recent meta-analysis has suggested that AngioJet thrombectomy does not significantly improve symptoms or reduce serious complications compared with traditional CDT [12]. Vacuum-assisted aspiration thrombectomy is another widely used modality because of its potential to quickly suction and remove thrombi. However, vacuum-assisted aspiration usually results in significant blood loss [15]. Although computer-aided mechanical aspiration has been designed to mitigate this issue, blood loss often still exceeds 150 ml [16].

Given the inherent limitations of existing widely used thrombectomy devices, we have developed an innovative thrombectomy system. This system enables simultaneous thrombolysis and thrombus fragmentation under balloon occlusion, introducing a novel pharmacomechanical thrombectomy approach. Following initial debulking the residual thrombus is manually aspirated through the catheter, thereby reducing overall blood loss. In this study, a modified swine model of iliac vein thrombosis was established using a

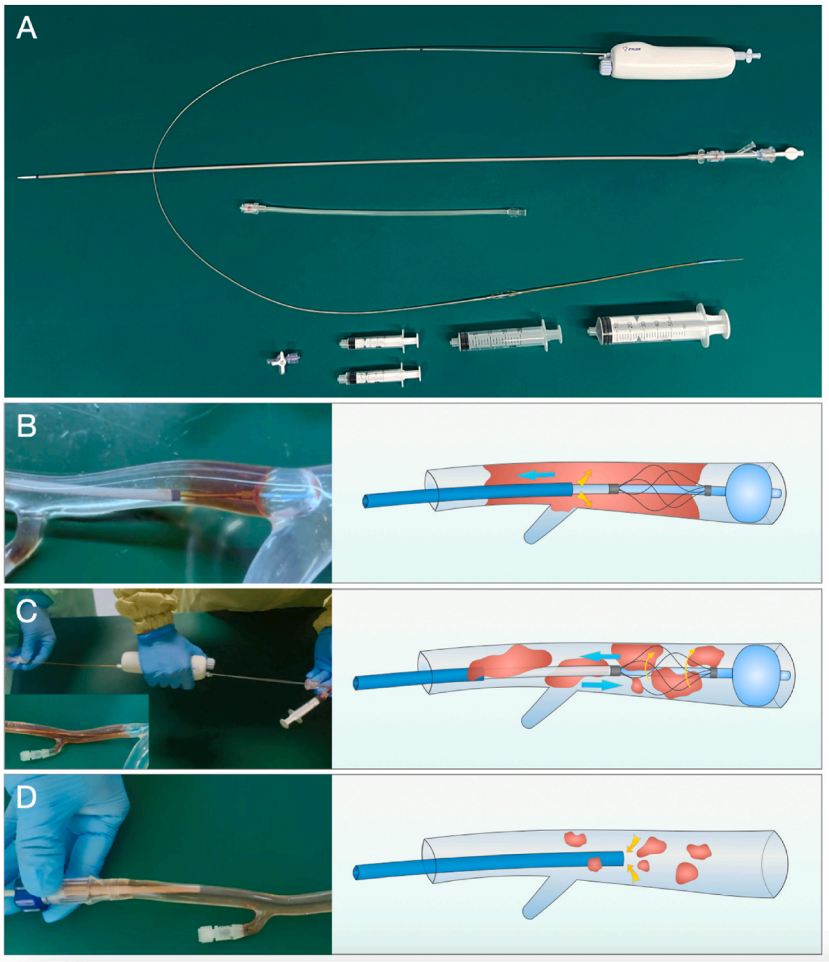

Fig. 1. Appearance and crucial operational steps of the Zylox thrombectomy system. (A) Display of the Zylox device along with essential accessories. (B–D) In vitro simulation and schematic diagrams illustrating crucial operational steps, which include: (B) retraction catheter and lytic agent application during balloon occlusion, (C) securing the occlusion balloon while maintaining basket rotation and controlling the handle to perform thrombus fragmentation, and (D) removal of the balloon and basket, followed by aspiration of residual thrombus using the catheter.

"sandwich" method involving proximal–distal balloon occlusion combined with autologous venous thrombus and thrombin injections. The thrombus removal efficacy, blood loss, and the laboratory and histopathological outcomes of this novel device were evaluated and compared with those of the AcoStream device (Acotec Scientific, Beijing, China). The aim of this study was to assess the efficacy and safety of a newly developed thrombectomy device in a modified swine model.

2. Methods

2.1. Zylox thrombectomy system description

The Zylox thrombectomy system (Zylox-Tonbridge Medical, Hangzhou China) consists of two main components (Fig. 1A): the first is a handheld motor drive that rotates a nitinol basket equipped with a compliant balloon at the proximal end to occlude the vessel. The second is a 10 F catheter with a dilator designed for delivering lytic agent (Fig. 1B) and manually aspirating the thrombus. The primary feature of this device is its ability to simultaneously fragment and dissolve thrombi while occluding the outflow vein. The operator can manipulate the handle back and forth to control the basket's movement, facilitating thrombus fragmentation (Fig. 1C). After this process, any residual thrombus can be manually aspirated through the 10 F catheter without the need for a vacuum source (Fig. 1D). This design introduces a new pharmacomechanical approach that enhances thrombectomy efficiency and prevents thrombus segments from escaping to distal vessels.

2.2. Experimental animals

Domestic experimental white swine were chosen because their size, vascular anatomy, and coagulation properties are comparable

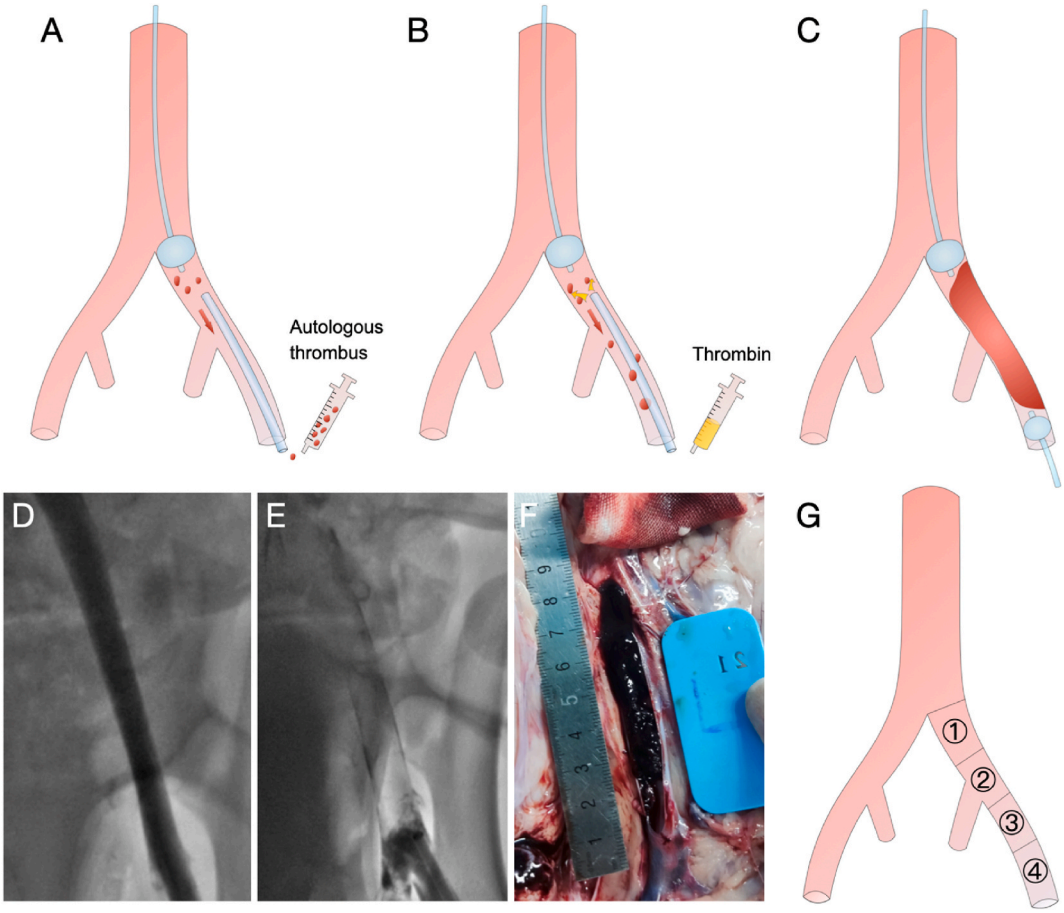

Fig. 2. Creation and evaluation of the swine model for acute iliac venous thrombosis. (A–C) Schematic diagrams of animal model creation using proximal-distal balloons occlusion combined autologous thrombus and thrombin injections. (D) Angiography of left iliac vein before model creation. (E) Angiography after model creation shows a large clot and complete occlusion of the left iliac vein lumen. (F) Anatomy of the left iliac vein, highlighting thrombus formation. (G) Schematic diagram shows a venography-based four-segment scale method utilized to evaluate iliac vein occlusion.

to those of adult humans and they are relatively easy to obtain [17]. Twelve swine were divided into two groups to evaluate the devices (Zylox group, n = 6; AcoStream group, n = 6). In the Zylox group, one iliac vein was used solely for anatomical observation of thrombus formation and not for device assessment (Fig. 2F). Consequently, a total of 23 iliac veins (Zylox group, n = 11, AcoStream group, n = 12) were used for device assessment in this study. Angiography was performed again 28 days postthrombectomy on 3 swine (6 iliac veins) in each group, followed by dissection of the iliac veins, pulmonary arteries, and major organs. All 6 animals were administered an antibiotic (ceftriaxone, 2.0 g/day, intramuscular) for 3 days postoperatively and given anticoagulation therapy (rivaroxaban, 40 mg/day for 20 days and 20 mg/day for 7 days, orally).

2.3. Thrombus induction procedure

The method of proximal–distal balloon occlusion combined with autologous thrombus and thrombin injection was used to create the animal model as previously described with modifications [18,19]. Briefly, to prepare the autologous thrombus 120 ml of blood was collected via the femoral vein then mixed with 3000 U thrombin (Yuanye Bio-Technology, Shanghai, China) for 20 min until it turned into a fresh and soft thrombus. The thrombus was cut and placed in 20 ml syringes separately for subsequent direct injection.

Venous access was then established in the bilateral jugular and bilateral femoral veins using a micro-puncture set (COOK, Bloomington, IN, USA). The jugular vein access was upsized to an 8 F introducer sheath and the femoral veins were upsized to 11 F. A 6 F Forgarty occlusion balloon (Edwards Lifesciences, Irvine, California) was inserted through the jugular vein and occluded at the proximal iliac vein near the inferior vena cava (IVC). Venography was repeated to confirm the arrest of blood flow in the target vessel. An 8 F guiding catheter (Vista Brite, Cordis, Miami, USA) was introduced through femoral vein access to a position near the occlusion balloon. The prepared thrombus was then injected while retracting the catheter to ensure good dispersion of the thrombus (Fig. 2A), with a total injection volume of approximately 40 ml. The 8F guiding catheter was reinserted, and 4000 U thrombin was slowly injected while retracting the catheter(Fig. 2B). Finally, another Forgarty occlusion balloon was inserted into the distal iliac vein for occlusion (Fig. 2C). The same method was used to establish the model in the contralateral iliac vein. After 2 h, all the balloons in the bilateral iliac veins were deflated and removed and angiography was repeated to evaluate thrombus formation (Fig. 2D and E).

2.4. Thrombectomy procedures

Zylox thrombectomy system protocol **(Supplemental Video. 1)**: A 10 F introducer catheter along with a dilator was inserted through a vascular sheath from femoral vein access, guided by a 0.035″ guidewire, to completely cross the thrombus. After the dilator was withdrawn and the 10 F catheter was in place, an integrated occlusion balloon and rotating basket were inserted through the catheter until the balloon was fully deployed. The balloon was then inflated and the 10 F catheter was gradually retracted while urokinase (Humanwell Pharmaceutical, Wuhan, China) was continuously injected to ensure good dispersion (Fig. 3A and B). The balloon position was secured and the rotating basket was spun by the rotator unit. The operator could manipulate the handle back and forth to control the basket's movement (Fig. 3C). After 5–10 min the balloon and basket were removed and the residual thrombus was manually aspirated through the 10 F catheter (Fig. 3D).

AcoStream aspiration system protocol: the device includes a vacuum aspiration pump and an aspiration catheter. Initially, a 4 F catheter (Tempo, Cordis, Miami, USA) was advanced to the proximal end of the thrombus. Urokinase was intermittently injected through the catheter while retracting it to allow the lytic agent to fully disperse. After 15 min, an 8 F AcoStream aspiration catheter was connected to a disposable connecting tube, a waste collection tank, and an aspiration pump, which was then activated and maintained in a ready state. The AcoStream aspiration catheter was inserted and advanced to the distal end of the thrombus. Upon opening the

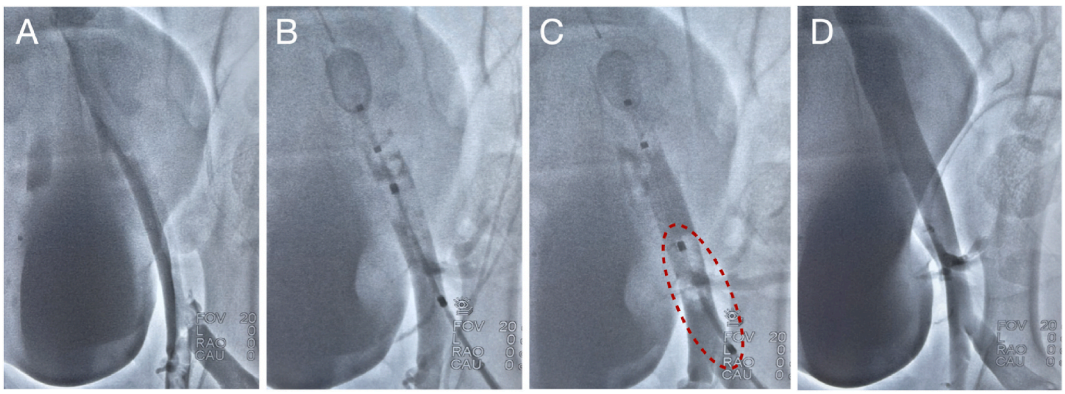

Fig. 3. Venographic confirmation from the thrombectomy procedures of Zylox thrombectomy system. (A) Venography showing thrombus formation in the left common iliac, internal iliac, and external iliac veins. (B, C) After proximal occlusion of iliac vein, thrombolysis and thrombus fragmentation were performed simultaneously, angiography shows partial dissolution and fragmentation of the thrombus, resulting in a significant reduction in thrombus volume. The area marked with a red dashed line indicates the position of the basket. (D) Post-thrombectomy angiography shows no residual thrombus.

valve on the connecting tube the process of venous thrombus aspiration began. If there was no thrombus or blood backflow for an extended period, the catheter could be retracted to a position with blood flow to continue generating effective negative pressure. If an aspiration remains unsuccessful, the catheter should be retracted and flushed. To avoid PE, an IVC filter (Zylox-Tonbridge medical, Hangzhou, China) was placed in the IVC through jugular vein access before the thrombectomy procedure in each animal in both groups.

2.5. Angiographic evaluation

The effect of thrombus removal was observed using venography. The thrombus score and lysis grade according to a previous study with little modification were used [20]. The thrombus segment is evenly divided into four segments labelled 1–4, as shown in Fig. 2G. Each segment of the vein was scored before and after thrombectomy using the following criteria: 0 points for no occlusion (0 %), 1 point for partial occlusion (<50 %), 2 points for substantial occlusion (50%–99 %), and 3 points for complete occlusion (100 %). Thrombus removal rate = (prethrombectomy score - postthrombectomy score)/prethrombectomy score * 100 %). The thrombus removal grade was classified as follows: 100 % thrombus clearance (grade I); 50%–99 % thrombus clearance (grade II); and <50 % thrombus clearance (grade III).

2.6. Histopathology

Histopathologic evaluations were performed immediately postoperation or at 28 days postoperation to determine the degree of damage to the vessel caused by the device. To assess the degree of arterial injury, ordinal data were collected for multiple parameters including inflammation, vessel injury, endothelialization, fibrosis, and intimal thickening, using the semiquantitative scoring system of previous studies [21,22]. The degrees of endothelialization and fibrosis were classified as “no change”, “change <25 %“, “change between 25 % and 50 %“, “change between 51 % and 75 %” and “change >75 %“. The degrees of inflammation and intimal thickening were classified as “normal”, “mild”, “moderate”, “moderate to severe” or “severe”. The degree of vessel injury was classified as “normal”, “disruption between the intima and the internal elastic lamina”, “disruption between the internal and external elastic laminae”, “disruption between the external elastic lamina and the adventitia” or “disruption of the adventitia”.

2.7. Statistical analysis

Data analysis was performed using SPSS for Mac (Version 20; IBM Corporation, Armonk, NY, USA). Parametric data are presented as means ± standard deviations for normally distributed data or medians (ranges) for nonnormally distributed data. Categorical data are presented as n (%). Student’s *t*-test was used for normally distributed continuous variables. The Mann−Whitney *U* test or rank-sum test was used for nonnormally distributed continuous variables depending on whether the data were independent or paired. Fisher’s exact test was used to compare categorical variables. The results were considered significant at $P < 0.05$.

3. Results

A total of 12 swine were used in the study. Venography of the iliac vein was performed before the procedure to confirm vessel patency and establish the baseline vessel diameter. There was no significant difference in the iliac vein diameter between the Zylox

Table 1
Comparison of baseline characteristics, thrombosis induction, and thrombectomy outcome between the Zylox group and AcoStream group.

	Zylox	AcoStream	P value
Female (n = 8)	4 (60 %)	4 (60 %)	1.00
Animal weight (n = 12)	64.5 ± 3.85	63.05 ± 2.08	0.44
Iliac vein diameter, mm (n = 23)	9.24 ± 0.87	9.03 ± 0.90	0.59
Thrombus length, mm (n = 23)	98.42 ± 17.56	84.12 ± 13.30	0.038
Thrombus score (n = 23)	10 (8–12)	10.5 (9–12)	0.40
Blood loss, ml (n = 23)	81.09 ± 27.26	162.50 ± 61.96	<0.001
Thrombectomy time, min (n = 23)	26.73 ± 4.58	27.33 ± 4.25	0.75
Thrombus clearance grade (n = 23)			
Grade I (100 %)	11 (100 %)	12 (100 %)	
Grade II (50%–99 %)	0	0	
Grade III (<50 %)	0	0	1.00
Filter captured thrombus (n = 12)	3 (50 %)	3 (50 %)	1.00
Complications (n = 12)			
Perforation	0	0	NA
PE	0	0	NA
Death	0	0	NA

Parametric data are presented as mean ± standard deviation for normally distributed data, or median (range) for non-normally distributed data. Categorical data are presented as n (%).
$P < 0.05$ was considered statistically significant.
PE = pulmonary embolism; NA = not available.

group and the AcoStream group, with values of 9.24 ± 0.87 mm and 9.03 ± 0.90 mm, respectively (P = 0.59). Thrombus induction was successfully achieved in all patients as verified by venography. The mean thrombus length in the Zylox group was 98.42 ± 17.56 mm, which was significantly greater than that in the AcoStream group (84.12 ± 13.30 mm) (P = 0.038). The median (range) thrombus scores in the two groups were 10 (8–12) and 10.5 (9–12), respectively, showing no statistically significant difference (P = 0.40) (Table 1).

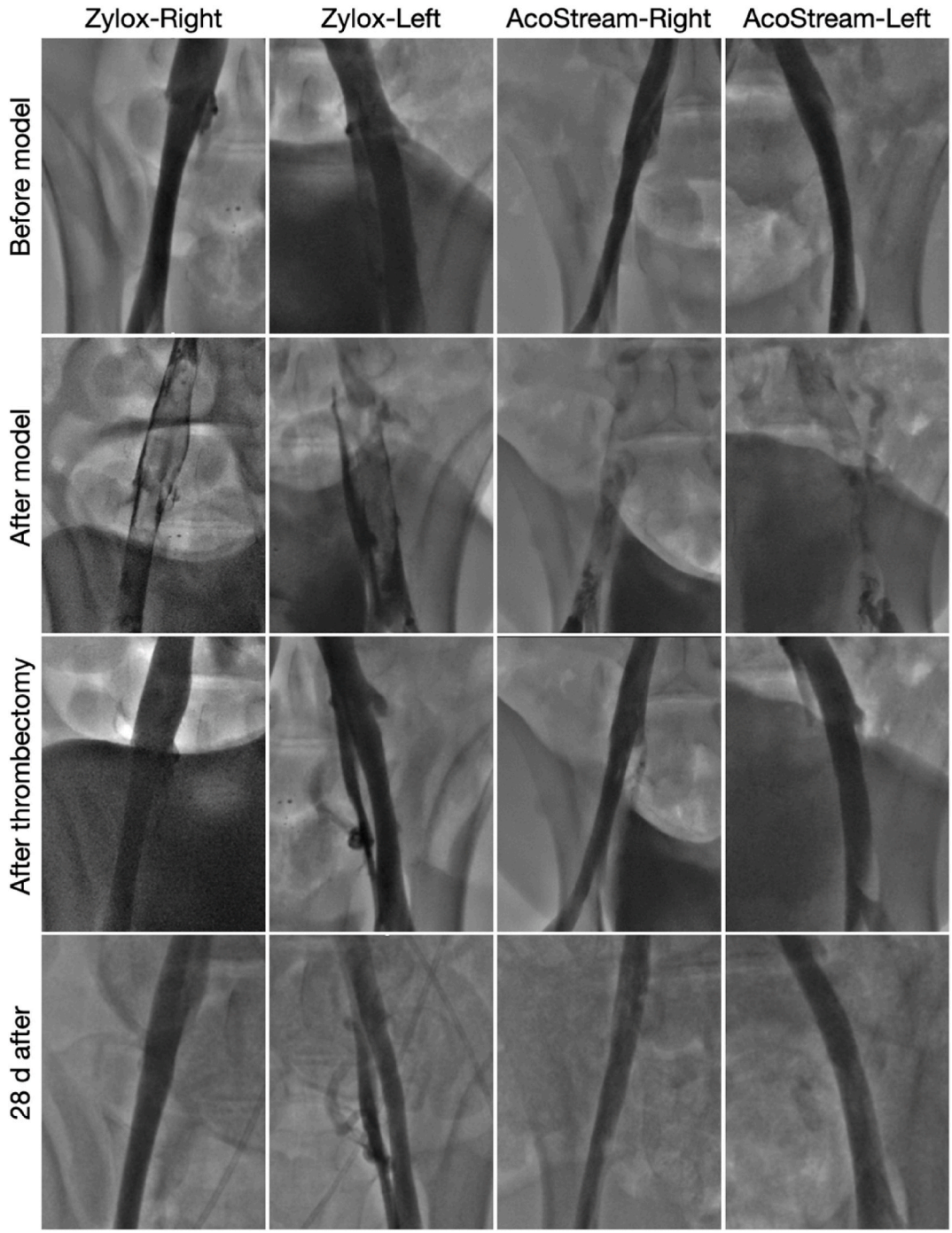

Fig. 4. Venography before and after thrombectomy using the Zylox system and AcoStream system. The left two columns present sequential venography images of the bilateral iliac veins in a single swine from the Zylox group, taken before model creation, after model creation, 0 day postthrombectomy, and 28 days postthrombectomy. Similarly, the right two columns display the venography results from a single swine in the AcoStream group.

Thrombectomy resulted in complete recanalization without residual thrombus in both groups, effectively achieving Grade I thrombus removal in all cases. Notably, the Zylox group experienced significantly less blood loss (81.09 ± 27.26 ml, compared to 162.50 ± 61.96 ml) ($P < 0.05$) (Table 1). There were 3 cases of filter-captured thrombus in each group, which did not limit blood flow and were completely removed through aspiration thrombectomy. Furthermore, angiography performed 28 days postthrombectomy on 3 cases (6 iliac veins) in each group confirmed patent iliac veins with no rethrombosis (Fig. 4). Throughout the procedure, all the animals remained stable and free from complications.

Laboratory measurements, including prothrombin time (PT), fibrinogen (FIB), partial pressure of oxygen (PO2), partial pressure of carbon dioxide (PCO2), haemoglobin (Hb), and creatinine (CRE), were performed. Considering the small sample size, the changes in data (postthrombectomy minus baseline levels) were not compared between the two groups. Instead, within each group, post-thrombectomy data were compared with the baseline data. No significant differences were found in either the Zylox or AcoStream groups ($P > 0.05$) (Table 2).

In both groups, the iliac veins, pulmonary arteries, and major organs were dissected without any pulmonary embolism, iliac vein perforation, or haematoma. Pathological examinations of the iliac veins revealed similar degrees of inflammation, vessel injury, endothelialization, fibrosis, and intimal thickening in 0 day (Fig. 5A–D) and 28 days (Fig. 5E–H) postoperation in both groups. However, both devices were found to cause some degree of venous wall damage, triggering an inflammatory response. Notably, at 28 days postthrombectomy, both the fibrotic score of the vessel wall (1.29 ± 0.61 vs. 0.96 ± 0.61) and the intimal thickening score (0.92 ± 0.76 vs. 0.79 ± 0.64) were significantly elevated and were completely normal on Day 0 after thrombectomy (Table 3). This finding indicates that both devices may lead to delayed damage to the venous wall.

4. Discussion

This study describes a modified swine model of iliac vein thrombosis using a proximal–distal balloon occlusion technique combined with autologous venous thrombus injection and thrombin injection methods. To our knowledge, this model has not been previously described. The protocol was successfully reproduced in 12 animals (24 iliac veins), with 6 animals followed for up to 28 days without any complications. Moreover, this study explored the effectiveness and safety of a newly developed thrombectomy system (Zylox) using this animal model, with the Acostream thrombectomy system serving as the control group. The results showed complete thrombus removal in both groups. Although the Zylox group did not demonstrate superior thrombus removal capability, it resulted in significantly better outcomes in terms of blood loss.

With the evolution of thrombus removal devices [4], there is a growing need for ideal animal models to provide adequate vehicles for the evaluation of new devices. Various methods for creating swine DVT models have been reported, including two-balloon occlusion with or without thrombin injection [19,23], the placement of foreign material (stents, coils, and IVC filters) [18,24,25], and open surgery ligation/suture [26]. However, current models have issues such as technical complexity, instability in model establishment, and time consumption. In this study, a modified swine model of iliac vein thrombosis was established using a "sandwich" method involving proximal–distal balloon occlusion combined with autologous venous thrombus and thrombin injections. This method achieved a 100 % technical success rate. The mean thrombus lengths for the two groups in the present study were 98.42 ± 17.56 mm and 84.12 ± 13.30 mm, greater than the 2.98 ± 0.16 cm^3 reported in other studies [24]. Thrombus-induced luminal occlusion was quantified using a venography-based four-segment scale. The median scores for the two groups were 10 (8–12) and 10.5

Table 2
Comparison of pre- and post-operative laboratory measurements in Zylox group and AcoStream group, respectively.

	Pre-thrombectomy	Post-thrombectomy	P value
PT (n = 12)			
Zylox	15.40 ± 2.14	17.35 ± 4.22	0.22
AcoStream	15.62 ± 1.51	18.08 ± 1.96	0.10
FIB (n = 12)			
Zylox	1.11 ± 0.11	0.85 ± 0.24	0.094
AcoStream	1.00 ± 0.16	0.91 ± 0.16	0.36
PO2 (n = 12)			
Zylox	250 (211–645)	240.5 (178–534)	0.35
AcoStream	241.67 ± 64.80	226.17 ± 26.12	0.57
PCO2 (n = 12)			
Zylox	76.83 ± 25.98	66.92 ± 21.11	0.17
AcoStream	54.4 (35.4–79.8)	48.7 (44.1–77.1)	0.75
Hb (n = 6)			
Zylox	118.67 ± 8.50	111.00 ± 10.44	0.11
AcoStream	102.33 ± 7.02	94.67 ± 17.95	0.38
CRE (n = 6)			
Zylox	150.00 ± 24.27	152.33 ± 27.54	0.89
AcoStream	166.67 ± 33.98	179.67 ± 6.43	0.54

Data are presented as mean ± standard deviation for normally distributed data or median (range) for non-normally distributed data. $P < 0.05$ was considered statistically significant.
PT = prothrombin time; FIB = fibrinogen; PO2 = partial pressure of oxygen (PO2); PCO2 = partial pressure of carbon dioxide, Hb = hemoglobin, CRE = creatinine.

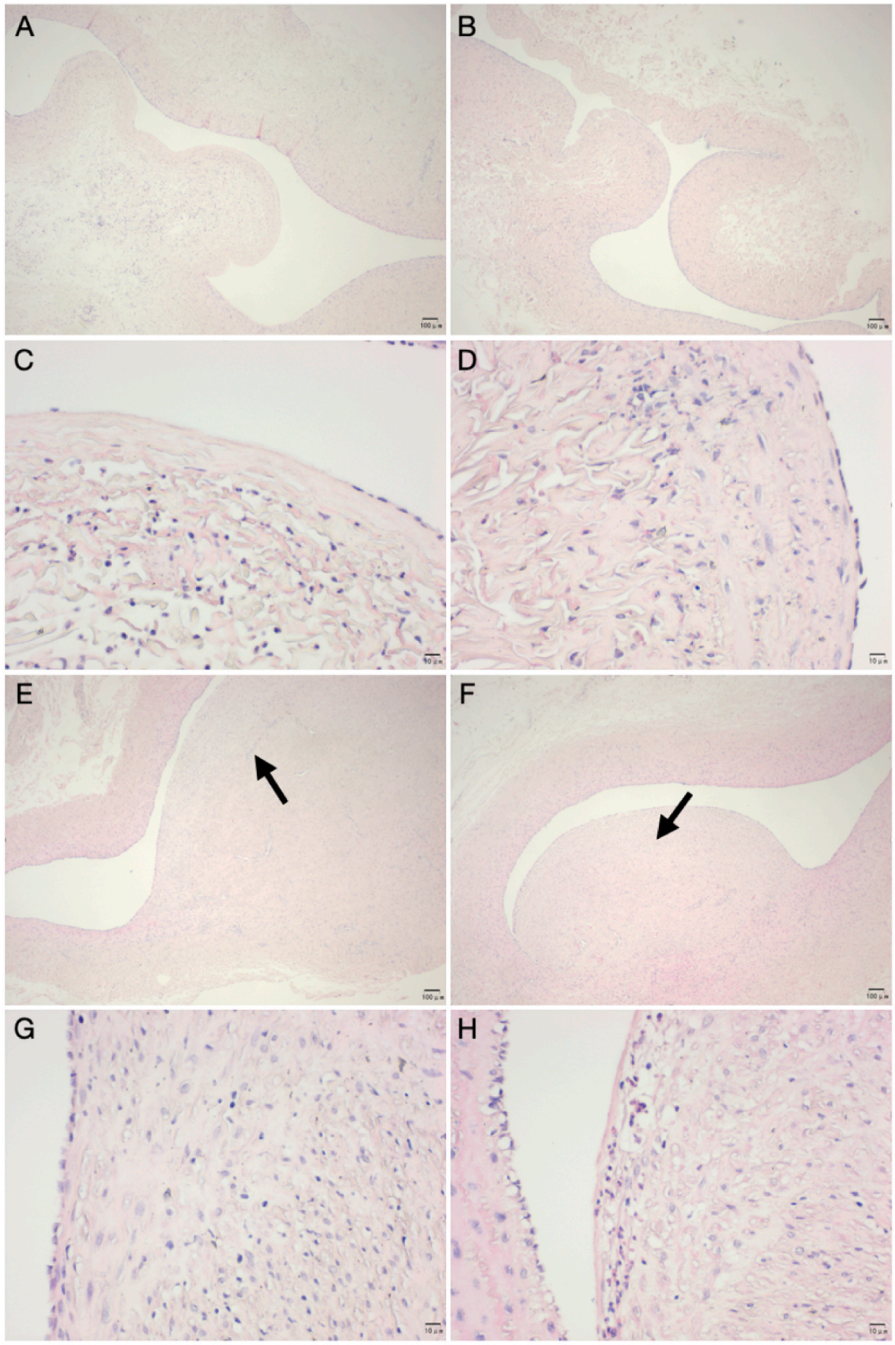

Fig. 5. H&E stain of iliac vein section at 0 day and 28 days postoperation. H&E (4 × and 40 × magnifications) of a subject from the Zylox group (A, C) and a subject from Acostream group (B, D) at 0 day postoperation show significant infiltration of inflammatory cell. H&E staining (4 × and 40 × magnifications) of iliac vein sections from the Zylox group (E, G) and the Acostream group (F, H) at 28 day post-operation highlight areas of intimal thickening, indicated by the arrows. H&E, haematoxylin and eosin.

(9–12), respectively. Indeed, these scores are satisfactorily high, indicating robust and consistent thrombus formation. Overall, the model used in this study involves only simple endovascular procedures and achieves stable thrombus formation. Therefore, it may serve as a replicable animal model and can be widely applied in endovascular device testing.

An important advantage of PCDT is its ability to combine mechanical disruption of the thrombus with direct infusion of a lytic agent. Thrombolytic therapy may support fragmentation, as the thrombus surface area is increased by mechanical treatment [27,28]. However, the lytic agent may not adequately disperse within the thrombus if the catheter is positioned eccentrically within the lumen.

Table 3
Histological assessments at days 0 and 28.

		Day 0			Day 28		
		Zylox (n = 20)[a]	AcoStream (n = 24)	P value	Zylox (n = 24)	AcoStream (n = 24)	P value
Histological assessment	Inflammation (0–4)	2.10 ± 0.54	1.71 ± 0.54	0.063	1.08 ± 0.57	0.92 ± 0.40	0.32
	Vessel injury (0–4)	0.40 ± 0.58	0.92 ± 0.86	0.057	0.96 ± 0.73	0.63 ± 0.70	0.089
	Endothelialization (0–4)	0.95 ± 0.97	0.92 ± 0.64	0.779	0.04 ± 0.20	0.00 ± 0.00	0.32
	Fibrosis (0–4)	0.00 ± 0.00	0.00 ± 0.00	1.00	1.29 ± 0.61	0.96 ± 0.61	0.087
	Intimal Thickening (0–4)	0.00 ± 0.00	0.00 ± 0.00	1.00	0.92 ± 0.76	0.79 ± 0.64	0.65

Data are presented as mean ± standard deviation.
$P < 0.05$ was considered statistically significant.
[a] Since the iliac vein on one side of a subject in the Zylox group was not subjected to device testing, a total of five iliac veins were utilized. Four sections were taken from each vein for H&E staining, resulting in a total of 20 sections used for evaluation.

Additionally, the lytic agent may not be retained sufficiently if the proximal vessel is not completely obstructed by the thrombus. These factors collectively can reduce the efficacy of PCDT. The Zylox device addresses these limitations by enabling thrombus fragmentation while simultaneously occluding the vessel lumen, thus enhancing lytic retention and effectiveness. The overall results of this study were satisfactory, with a high thrombus removal rate and no complications. Significant thrombus fragmentation and thrombolysis were observed in many subjects after the occlusion-thrombolysis-fragmentation process. Given these outcomes, the Zylox device presents a promising solution in the design of thrombus removal devices.

Blood loss is an unavoidable issue in current thrombus removal treatments and is caused mainly by the aspiration thrombectomy procedure. At the heart of this issue is the mechanism of action in aspiration thrombectomy, which has the potential to suction and remove large volumes of blood quickly. Some studies have reported that using the Indigo aspiration system results in blood loss exceeding 400 ml in 26.9 % of patients [15]. In the present study, half the amount of blood loss in the Zylox group was observed compared with that in the control group. This reduction is attributed to two main factors: first, the effective debulking of large thrombi through a combined fragmentation and thrombolysis procedure minimizes the number of aspiration procedures needed; second, the fragmentation procedure physically breaks down the structure of the thrombus, which reduces the challenge of manual aspiration thrombectomy. These factors result in decreased blood loss during the aspiration thrombectomy procedure. Unfortunately, in this study the number and duration of aspiration were not calculated or compared between the two groups because of concerns about accuracy.

Distal embolization is a prevalent issue with current mechanical thrombectomy devices [29], highlighting the need for next-generation technology to minimize this risk. Although some devices have been developed to reduce the occurrence of distal embolization, their intricate structure and the requirement for jugular vein access present challenges for clinical application [29,30]. While the Zylox device can prevent distal embolization during thrombus fragmentation, it requires the occlusive balloon to be deflated before aspiration, which still carries a risk of distal embolization. In our study, a nonflow-limiting filter-captured thrombus was discovered in 3 subjects in both the Zylox group and the AcoStream group. Fortunately, the filter-captured thrombus was effortlessly cleared in all the animals, avoiding the need for a detailed histologic analysis at the end of the study. Currently, the placement of a retrievable filter may be an important method to prevent distal embolism in PMT patients. Even if a filter-captured thrombus occurs, many methods can be used to handle it [31,32]. In the future, reducing the risk of distal embolization is an important challenge in the design of thrombectomy devices.

Vein wall damage caused by rotational devices is a critical variable when considering procedural safety and outcomes [29]. In this study, histopathological evaluations were conducted, revealing elevated levels of inflammation, vessel injury, and endothelialization in the vessel walls of both groups immediately after the operation. It remains challenging to determine whether these changes were directly caused by the devices since thrombus formation inherently involves the infiltration of inflammatory cells [24]. The longer a DVT is in contact with the vein wall the greater the degree of damage [33,34]. Additionally, similar fibrosis and intimal thickening, which were not present on the day of the operation, were observed in both groups at 28 days postoperation. These changes are highly likely influenced by the device because the thrombus has already been completely removed after thrombectomy. However, angiographic observations at 28 days did not reveal any new thrombus formation or iliac vein stenosis. Certainly, whether this venous wall damage will increase long-term risks requires further study.

The limitations of the study should also be mentioned. 1. The small sample size limits the broad applicability of the conclusions. Preclinical studies with larger samples and more extensive data are needed to further substantiate the advantages of the device. 2. Owing to the nature of preclinical animal studies, the effects of thrombus removal and the laboratory and pathological results of these two devices may not be applicable to clinical practice. Future clinical trials are needed to validate the safety and efficacy of the Zylox device. 3. Differing device principles lead to unavoidable differences in experimental procedures, such as differences in thrombolytic duration and aspiration catheter size. Consequently, the results cannot accurately reflect the differences in thrombus removal efficiency between the two devices. Therefore, more diverse control group designs such as the AngioJet system, are needed to further determine the clinical value of the device.

5. Conclusion

In conclusion, the newly developed Zylox device enables thrombolysis and thrombus fragmentation under balloon occlusion, introducing a novel pharmacomechanical thrombectomy method for DVT treatment. In a modified swine model, the Zylox device was demonstrated to be effective and safe for thrombus removal, with a notable advantage in controlling blood loss compared with the control device. However, to fully validate these findings, future expanded preclinical studies and randomized controlled trials in human subjects are essential. Overall, the Zylox thrombectomy system shows great potential as a safer and more effective option for the clinical treatment of acute DVT in the future.

Ethics statement

The animal care and experimental procedures in this study were approved by the Institutional Animal Care and Use Committee (IACUC) of Gateway Medical Innovation Center (Shanghai, China) (approval number: SH2023-07003). The study adhered strictly to the U.K. Animals (Scientific Procedures) Act, 1986 and associated guidelines, the National Institutes of Health-Office of Laboratory Animal Welfare policies and laws, and the ARRIVE guidelines.

Data availability

Data associated with the study has not been deposited into a publicly available repository. Data are available from the corresponding author on reasonable request.

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CRediT authorship contribution statement

Qiu Zeng: Writing – review & editing, Writing – original draft, Visualization, Resources, Methodology, Investigation, Formal analysis, Data curation. **Zheng Chen:** Resources, Methodology, Investigation, Formal analysis, Data curation. **Biyun Teng:** Software, Resources, Formal analysis, Data curation. **Fenghe Li:** Writing – review & editing, Supervision, Formal analysis. **Yu Zhao:** Writing – review & editing, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e38692.

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