

# Comparison of ASPIRE Mechanical Thrombectomy Versus AngioJet Thrombectomy System in a Porcine Iliac Vein Thrombosis Model

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**Background:** Percutaneous mechanical thrombectomy device has become an important therapeutic armamentarium in the management of venous thromboembolism. In this study, we compare the efficacy and safety profile of the AngioJet thrombectomy device and ASPIRE thrombectomy system in a porcine venous thrombosis model.

**Methods:** Twelve adult pigs underwent bilateral iliac venous thrombosis created by using a stent graft thrombosis model and subsequently underwent either AngioJet ( $n = 6$ ) or ASPIRE mechanical thrombectomy ( $n = 6$ ) 1 week later. Intravascular ultrasound (IVUS) was used to assess thrombectomy efficacy, and computed tomography was used to evaluate pulmonary embolism (PE). Hemolytic effect was measured by plasma-free hemoglobin (PfHgb). Iliac vein thrombogenicity was evaluated with radiolabeled platelet and fibrin deposition. Veins were harvested and evaluated with light microscopy and scanning electron microscopy (SEM).

**Results:** Similar thrombectomy efficacy by IVUS evaluation was noted in both groups. Significant greater PE and hemolysis were identified in the AngioJet group compared to the ASPIRE group. The AngioJet group had greater reduction in WBC and platelet compared to the ASPIRE group. No difference was found in thrombogenicity, light microscopic evaluation, or SEM.

**Conclusions:** Both devices had similar thrombectomy efficacy and thrombogenicity response. The ASPIRE catheter incurred less PE and hemolysis compared to the AngioJet device. Vessel wall response by histological analysis and SEM was similar in both groups.

## INTRODUCTION

Deep venous thrombosis (DVT) remains a major health care challenge as it is responsible for more than 60,000 deaths annually in the United States, as a consequence of pulmonary embolism.<sup>1,2</sup> Long-term complications of DVT such as postthrombotic syndrome with venous stasis ulcer can lead to lifelong disability and diminution of quality of life. Various treatment modalities, including systemic anticoagulation, surgical thrombectomy, endovascular thrombectomy, and catheter-directed thrombolytic therapy have been shown to provide a therapeutic role in patients with symptomatic DVT.<sup>3,4</sup> Recent advances in minimally invasive endovascular therapy have broadened the therapeutic

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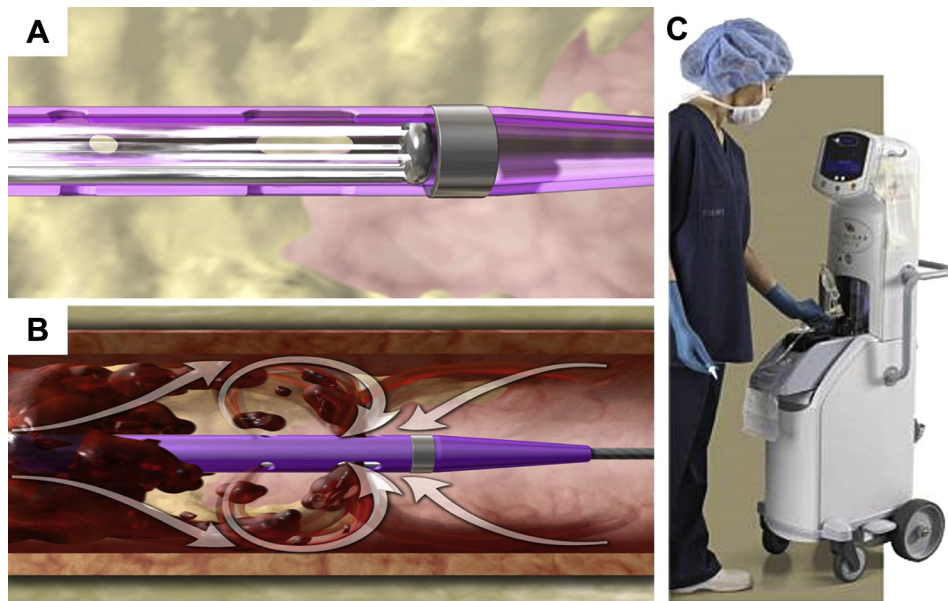
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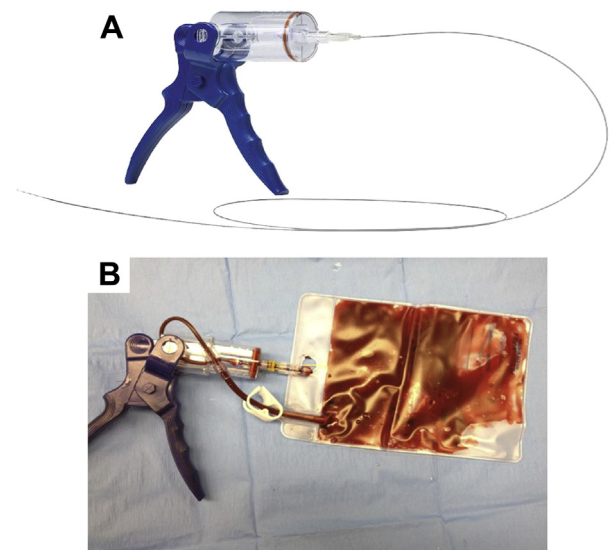


**Fig. 1.** (A) The AngioJet system emits high-velocity saline jets that are directed backward from the tip of the device to outflow channels in a coaxial fashion. (B) This generates a vacuum force, which draws the thrombus

into the catheter achieving the rheolytic thrombectomy effect. (C) The thrombectomy device requires a console unit which generates pressurized saline to the thrombectomy catheter tip.

armamentarium of percutaneous thrombectomy devices, as many clinical studies have reported the clinical efficacy of numerous percutaneous thrombectomy devices in the management of DVT.<sup>4,5</sup> Although these devices are effective in removing intravascular thrombus, complications associated with these devices, including vessel injury, hemolysis, endothelial denudation, and late intimal hyperplasia have been described.<sup>4–6</sup>

The AngioJet rheolytic thrombectomy system (Boston Scientific, Marlborough, MA; Fig. 1) was introduced in 1996 and has become a widely utilized thrombectomy device in the management of peripheral arterial or venous thromboembolism. This mechanical thrombectomy catheter utilizes a complex mixture of rapid fluid streaming and hydrodynamic forces to fracture thrombus, allowing extraction at the catheter tip using negative pressure based on the so called Bernoulli principle. The clinical efficacy of this device in DVT management has been proven in many large clinical studies.<sup>3,7–9</sup> Our laboratories have previously reported the physiological response and endothelial vasoreactivity of the AngioJet system in various in vivo investigations.<sup>10–13</sup> A percutaneous thrombectomy device, the ASPIRE MAX Mechanical Thrombectomy System (Control Medical, Park City, UT; Fig. 2) was recently approved for thrombus removal, which utilizes a similar rheolytic



**Fig. 2.** (A) The ASPIRE thrombectomy system consists of a hand-held aspirator, which is attached to an aspiration catheter for thrombus removal. The thrombectomy force is generated by the hand-held aspiration apparatus. (B) The ASPIRE Aspirator is connected to a fluid drainage bag to store aspirated fluid containing thrombus.

thrombectomy principle. This is a novel hand-held device incorporating a syringe apparatus, which provides a manually controlled aspiration force to remove intraluminal thrombus. Although early

clinical reports showed therapeutic efficacy of this device, little is known regarding the physiological response to this device. The purpose of our study was to compare the efficacy and safety of the ASPIRE and AngioJet mechanical thrombectomy systems in a porcine iliac DVT model.

## MATERIALS AND METHODS

### Animal Model and Interventions

Twelve adult domestic swine each weighing 65–75 kg were used in all experiments. The native-vessel domestic swine model was chosen because animal weight, blood volume, and vessel diameters are comparable to that in adult humans. All animal procedures and care were performed in accordance with the Guide for the Care and Use of Laboratory Animals, Eighth Edition (Institute of Laboratory Animal Resources, National Research Council, Washington; National Academy Press; 2011). Institutional Animal Care and Use Committee approval was obtained for this study. Animals were given intravenous thiopental sodium (10 mg/kg). Endotracheal intubation was performed, and anesthesia was maintained with 1% isoflurane. Under sterile conditions, bilateral groin cutdowns were performed to expose the superficial femoral veins, followed by the placement of a 14F introducer sheath (Terumo Medical, Phoenix, AZ). Bilateral DVT was created using an endovascular model previously described in our laboratory.<sup>10–12,14</sup> Briefly, a self-expanding nitinol stent graft (Symphony Stent, Boston Scientific Vascular, Natick, MA) that incorporated an intra-stent stenosis was deployed in the bilateral common iliac veins. The intra-stent stenosis was created by a tapered PTFE graft (WL Gore, Flagstaff, AZ), which caused flow stasis with a resultant DVT. A venogram was performed which documented the presence of DVT in the bilateral iliac veins. The introducer sheaths were next removed, and the venotomy was closed with a 6–0 polypropylene suture followed by a layered groin wound closure. The animals were allowed to be extubated and recovered following the stent-graft deployment. All animals underwent a bilateral stent-graft placement to induce iliac DVT. After 2 weeks of DVT, these animals were divided into 2 groups, which were treated with either AngioJet thrombectomy (AngioJet group,  $n = 6$ ) or ASPIRE thrombectomy system (ASPIRE group,  $n = 6$ ).

### AngioJet Thrombectomy

The rheolytic thrombectomy using the AngioJet system was performed using techniques, which we had

previously described.<sup>11</sup> Briefly, 7F introducer sheaths (Terumo) were placed in bilateral femoral veins, which was followed by the placement of a 0.035" Bentson guidewire (Terumo) through the femoral introducer sheath to cannulate the stent-graft device in the iliac vein under fluoroscopic guidance (OEC 9900 Neurovascular System, GE Medical, Milwaukee, WI). An AngioJet Xpedior Rheolytic Thrombectomy catheter (Boston Scientific) was inserted over the guidewire. Mechanical thrombectomy was performed by advancing the catheter across the iliac vein thrombotic segment at a rate of 1 mm/sec. Catheter passage across the thrombotic segment was performed 4 times per minute with a total device activation time of 30 min. Following the thrombectomy intervention, balloon angioplasty using a 12 mm × 4 cm balloon (Boston Scientific) was performed to dilate the tapered stent graft which eliminated the intra-stent stenosis and restore the venous flow. Iliac venous patency was assessed with venogram and intravascular ultrasound (IVUS).

### ASPIRE Thrombectomy

Animals in the ASPIRE group were treated with the ASPIRE aspiration thrombectomy system. Briefly, 7F introducer sheaths (Terumo) were placed in bilateral femoral veins, which was followed by the placement of a 0.035" Bentson guidewire (Terumo) through the femoral introducer sheath to cannulate the stent-graft device in the iliac vein under fluoroscopic guidance (OEC 9900 Neurovascular System). An ASPIRE Aspiration Mechanical Thrombectomy device (Control Medical) was inserted over the guidewire. Mechanical thrombectomy was performed by advancing the aspiration catheter across the iliac vein thrombotic segment at a rate of 1 mm/sec. A hand-held aspirator device was activated to generate the aspiration force for mechanical thrombectomy. Catheter passage across the thrombotic segment was performed 4 times per minute with a total device activation time of 30 min. Following the mechanical aspiration thrombectomy, balloon angioplasty using a 12 mm × 4 cm balloon (Boston Scientific) was performed to dilate the tapered stent graft, which eliminated the intra-stent stenosis and restore the venous flow. Iliac venous patency was assessed with IVSU and contrast venogram.

### Computed Tomography

To evaluate the risk of procedural-related pulmonary embolism, computed tomography (CT) scan was performed following thrombectomy procedure.

All CT examinations were performed using a 16-slice scanner (CT660, GE Healthcare, Cleveland, OH) using the following acquisition parameters: 120 kV, 200 mAs, pitch = 1.063, rotation speed = 0.5 rounds/sec, and 1-mm slice thickness. Contrast medium injection (Imeron 400) was performed using a mechanical double-head injector (Medrad Mark V ProVis Injector, Bayer, Leverkusen, Germany) with a flow rate of 3.5 mL/sec through the sheaths in the femoral vein in all cases. The examination was triggered for the arterial phase with the region of interest in the pulmonary artery, a threshold of 180 Hounsfield units, and an automatic minimal delay calculated by the scanner. The venous phase was acquired 110 sec after the arterial phase was started to visualize the veins.

### Intravascular Ultrasound

A 3.5F 20-MHz IVUS catheter was inserted over the guidewire for IVUS assessment (iLab System, Boston Scientific). Before the thrombectomy procedure, IVUS was used to assess the iliac venous thrombus. The IVUS examination was performed by an individual who was blinded to the respective treatment groups of the animals. The IVUS catheter was first inserted in the proximal iliac vein just below the stent graft, and 5 different images were obtained in the proximal 2 cm of each iliac vein for thrombus measurement. After thrombectomy intervention, the IVUS catheter was again positioned within the proximal 2 cm of the iliac vein to obtain 5 different images for residual thrombus measurement. Spot fluoroscopic image was used to confirm the location of the IVUS transducer within the proximal iliac vein. The luminal dimensions before and after thrombectomy interventions were traced on the IVUS image using a tracking device, which allowed calculation of a cross-sectional area:

$$\begin{aligned} \text{Efficacy of thrombectomy therapy (\%)} \\ = 1 - (\text{Area}_{\text{After}} / \text{Area}_{\text{Before}}) \times 100 \end{aligned}$$

### Thrombogenicity

Sample of blood from each animal was obtained and placed in anticoagulant citrate dextrose solution (ACD solution Modified; Squibb Diagnostics, New Brunswick, NJ) for centrifuge to acquire platelet pellet. The platelet sample was resuspended with ACD solution followed by indium (In) 111 oxyquinoline (Amersham Corporation, Arlington Heights, IL) to create radiolabeled platelets. Freeze-dried human fibrinogen labeled with radioactive iodine

(<sup>125</sup>I; Amersham Corporation) was reconstituted in 1.1 mL ACD solution and 1.9 μCi/kg. Following the harvesting of one ileofemoral vein for organ chamber analysis, the radiolabeled platelet and fibrinogen were injected into the animal and allowed to circulate for 3 hr prior to harvesting of the contralateral iliofemoral vein. The vein segment was cut into 3 sections with documented surface areas. Depositions of <sup>111</sup>In-platelets and <sup>125</sup>I-fibrinogen were analyzed in each iliac vein segment in accordance with the surface area with a gamma counter (Packard Instruments, Downers Grove, IL). Hemocytometer was used to determine the platelet concentration. The formulas used to calculate platelet and fibrin deposition were chosen from reports that were published earlier.<sup>15,16</sup>

### Blood Sampling for Hemolytic Effect

Plasma-free hemoglobin (PfHgb) was measured to determine the effect of hemolysis, a phenomenon known to occur with the AngioJet mechanical thrombectomy device.<sup>17,18</sup> PfHgb levels were measured immediately before thrombectomy treatment, every 5 min during treatment, and after thrombectomy treatment. Pretreatment samples for determination of the hematocrit level, white blood cell (WBC) count, platelet count, and creatinine levels were drawn after placement of the femoral sheaths and before thrombectomy treatment. Posttreatment samples were obtained after conclusion of the final angiogram and IVUS analysis. Samples were analyzed by a commercial laboratory (AniLytics, Gaithersburg, MD).

### Histologic and Immunohistochemical Analysis

Segments of the iliac vein were fixed in 10% buffered formalin overnight and then transferred to 70% alcohol. The specimens were dehydrated using sequentially increasing concentrations of ethanol followed by xylene and embedded in paraffin. Five-micrometer cross sections were cut and prepared as previously described.<sup>19,20</sup> Histological staining with hematoxylin and eosin, methylene blue, and Verhoeff-Masson stain were performed. Immunohistochemical analysis was performed using the avidin-biotin complex immunoperoxidase procedure (LSAB Kit, Dako Co, Carpinteria, CA) as previously described.<sup>19,20</sup> Immunostaining for α-actin and factor VIII-related antigen was performed to identify smooth muscle cells and endothelial cells, respectively.

For scanning electron microscopy (SEM), the iliac vein segment was incised to allow en face

imaging. This tissue specimen was placed in 2% glutaraldehyde and fixed overnight. The specimens were rinsed in phosphate-buffered saline 3 times and then dehydrated in a graded series of ethanol (30–100%). The tissue samples were placed with a graded series of hexamethyldisilazane, air dried, and gold sputter coated before imaging (SEM microscope; Cambridge 360). Endothelial loss based on SEM image was scanned and evaluated by a blind observer using an SEM image software (Bioview Image, Atlanta, GA).

### Statistical Analysis

Values are expressed as mean  $\pm$  standard error of the mean. Differences in vessel relaxation and contraction in organ chamber study was determined by 1-way analysis of variance or Student's *t*-test where appropriate. Unless otherwise stated, *n* refers to the number of vessels. As a normal distribution cannot be assumed for both morphologic parameters and percent changes in thrombectomy efficacy, the Kruskal-Wallis, and Friedman or Wilcoxon signed rank-sum tests were used to compare mean group values. Significant differences are presented in terms of mean and 95% confidence intervals. The independent variable, maximal Pfhgb was analyzed with analysis of variance by using the same independent variables as previously mentioned. All tests were 2-sided, and results were considered statistically significant at the 0.05 level. An SAS statistical package was used for analysis (version 5.0, Abacus Concepts, Berkeley, CA). Significance was considered when the *P* value was less than 0.05.

## RESULTS

### Radiological Evaluation

Successful iliac vein occlusion was demonstrated in all animals by venography and IVUS following the implantation of the iliac stent graft for DVT induction. Iliac veins from 2 groups remained patent based on both angiographic and IVUS assessment following thrombectomy treatment. IVUS evaluation revealed a wide disparity of residual iliac venous thrombosis following interventions among various groups. No difference was found in the thrombectomy efficacy based on IVUS assessment between the AngioJet and ASPIRE group, which was 58.3%, and 53.7% (*P* > 0.05), respectively. Thrombus areas in prethrombectomy and post-thrombectomy IVUS assessment between the 2 groups were summarized in [Table I](#).

### Computed Tomography

Pulmonary embolism was detected in 4 animals (66.7%) in the AngioJet group, in contrast to 1 animal in the ASPIRE group (16.7%, *P* = 0.03) based on CT scan of the chest. Among the 4 animals in the AngioJet group, bilateral pulmonary emboli was present in 3 animals, whereas unilateral or segmental pulmonary embolism was identified in 1 animal. In contrast, the only animal who developed PE in the ASPIRE group had unilateral embolism in the right inferior segment of the pulmonary vein. No animal exhibited hemodynamic derangement attributable to pulmonary embolism during the course of the thrombectomy procedure or perioperative period.

### Thrombogenicity and Hemolytic Effect

The preoperative hematocrit or platelet counts were similar between the 2 groups. The platelet counts in the AngioJet and ASPIRE group were  $268,000 \pm 79,200/\mu\text{L}$  and  $283,500 \pm 89,400/\mu\text{L}$ , respectively ([Table II](#)). The hematocrit counts in the AngioJet and ASPIRE group were  $36.8 \pm 7.4\%$  and  $42.5 \pm 8.9\%$ , respectively ([Table II](#)). Pfhgb values increased with thrombectomy time in both groups and reached peaked values immediately following cessation of the thrombectomy procedure ([Fig. 3](#)). The AngioJet group generated greater Pfhgb than the ASPIRE cohorts (average maximum value,  $1,254 \pm 375$  vs.  $268 \pm 75$  mg/dL; *P* < 0.001; [Table II](#)). Compared with the AngioJet treatment group, ASPIRE device was associated with significant less changes from prethrombectomy to post-thrombectomy values in WBC count (*P* = 0.002) and platelet count (*P* = 0.004). With the ASPIRE thrombectomy device, there was no significant difference between prethrombectomy and postthrombectomy values for hematocrit count (*P* = 0.422), WBC count (*P* = 0.436), platelet count (*P* = 0.457), and creatinine level (*P* = 0.317; [Table III](#)). In contrast, AngioJet device was associated with a significant postprocedural decrease in WBC count (mean,  $-5,800/\mu\text{L}$ ; *P* = 0.02) and platelet count (mean,  $-65,200$ ; *P* = 0.01). There was no change in the creatinine level before and after the thrombectomy in both groups. With regard to the posttreatment hematocrit level, there was no significant difference between the 2 groups (*P* > 0.5). The difference between pretreatment and posttreatment hematocrit levels was not significantly different for both devices (*P* > 0.5). Radiolabeled platelet deposition did not differ between the AngioJet and ASPIRE group following thrombectomy interventions, which was  $8,258 \pm 3,525$  and  $9,862 \pm 5,852$ ,

**Table I.** Comparison of thrombectomy efficacy based on IVUS evaluation following AngioJet and ASPIRE thrombectomy treatment

Analyzed IVUS variable	AngioJet	ASPIRE
Prethrombectomy thrombus area (mm <sup>2</sup> )	78.2 ± 19.5	83.5 ± 23.7
Postthrombectomy thrombus area (mm <sup>2</sup> )	32.6 ± 16.8	38.6 ± 19.3
Thrombectomy efficacy (%)	58.30%	53.70%

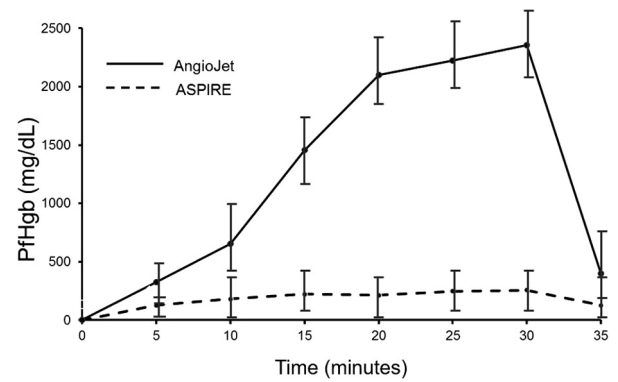
**Table II.** Comparison of Pfhg, hematocrit, WBC, platelet, and creatine levels following AngioJet and ASPIRE thrombectomy treatment

Analyzed IVUS variable	AngioJet	ASPIRE
Animal weight (kg)	68.3 ± 7.9	64.5 ± 6.2
PfHgb (maximum value, mg/dL)	1,254 ± 375	268 ± 75
Hematocrit (%)		
Before thrombectomy	36.8 ± 7.4	42.5 ± 8.9
After thrombectomy	33.6 ± 4.8	38.4 ± 6.3
WBC count (WBC/μL)		
Before thrombectomy	17,400 ± 5,200	2,600 ± 7,100
After thrombectomy	11,600 ± 4,700	24,200 ± 6,400
Platelet count (platelet/μL)		
Before thrombectomy	268,500 ± 79,200	283,500 ± 89,400
After thrombectomy	203,300 ± 36,400	273,600 ± 45,000
Creatinine level (mg/dL)		
Before thrombectomy	1.4 ± 0.3	1.3 ± 0.5
After thrombectomy	1.6 ± 0.4	1.2 ± 0.4

respectively (Table III). Radiolabeled fibrin deposition did not differ between the AngioJet and ASPIRE group following thrombectomy interventions, which were  $9.6 \pm 5.8$  and  $5.3 \pm 3.4$ , respectively (Table III).

### Light Microscopy and SEM

Histological evaluation of the thrombus revealed similar degree of recanalized and organized thrombus in the AngioJet group (58.3%, 7/12 vessel specimens) and ASPIRE group (66.7%, 8/12 vessel

**Fig. 3.** Device-related hemolytic effect is compared between the AngioJet and ASPIRE device based on PfHgb levels versus thrombectomy activation time.

specimens). Immunohistochemical evaluation revealed a similar pattern of factor VIII staining in all groups without obvious evidence of endothelial cell loss. Immunohistochemical staining of  $\alpha$ -actin showed positive staining pattern in the thrombus as well as the media without evidence of intimal proliferation in all groups. SEM evaluation revealed similar patterns of endothelial cell loss among the 2 thrombectomy groups (AngioJet,  $37.4\% \pm 16\%$ ; ASPIRE,  $39.7\% \pm 24\%$ ). With further histological assessment in regard to the inflammatory response, no difference was found with regards to WBC, macrophage, and neutrophil levels between the AngioJet and ASPIRE group.

### DISCUSSION

Since the first reported case of intraluminal thrombus removal was performed successfully in a patient using an inflatable balloon catheter by Dr. Fogarty in 1963,<sup>21</sup> it opened a new era in the management of thromboembolism. Despite the efficacy of this surgical thrombectomy approach, this technique of thrombus removal has been shown to result in denudation injury and endothelial dysfunction with subsequent thrombus recurrence.<sup>22,23</sup> Recent advances in endovascular therapy have created many catheter-based thrombectomy devices in an effort to maximize the efficacy of thrombus removal while reducing procedural-related complications.<sup>24–26</sup> The efficacy of these thrombectomy devices has been evaluated in various animal thrombosis models.<sup>10–12,14</sup> In this report, we compared the device performance, including thrombectomy efficacy, thrombogenicity, hemolysis, and device-associated pulmonary embolism of the AngioJet thrombectomy system and ASPIRE thrombectomy device using a porcine DVT model.

**Table III.** Iliac vein thrombogenicity following AngioJet and ASPIRE thrombectomy treatment

Analyzed IVUS variable	AngioJet group	ASPIRE group
Platelet deposition (platelet/cm <sup>2</sup> )	8,258 ± 3,525	9,862 ± 5,852
Fibrin deposition (ng/cm <sup>2</sup> )	9.6 ± 5.8	5.3 ± 3.4

The AngioJet thrombectomy catheter received the Food and Drug Administration (FDA) approval for thrombectomy application in 1999, and its utility has been widely examined in both clinical literature and animal studies.<sup>7,11,18</sup> This device requires a console unit to generate a high-velocity fluid stream, which is delivered to the catheter to achieve the thrombectomy functionality. In contrast, the ASPIRE thrombectomy system, which received its FDA approval for clinical application in 2014, has not received a significant focus in neither clinical literature nor device-related *in vivo* analysis. The ASPIRE catheter is a stand-alone device system, which generates an aspiration force based on a hand-held syringe apparatus. Although both systems utilize a coaxial aspiration-based thrombectomy principle, we postulate that these thrombectomy systems generate differential hemodynamic force which invariably can affect surrounding physiological and hematological responses. This hypothesis therefore formed the impetus of this *in vivo* investigative analysis to compare their respective device performance.

We found that, although both catheter systems have similar thrombectomy efficacy in this porcine DVT model, the ASPIRE catheter sustained less procedural-related pulmonary embolism compared to the AngioJet system based on CT evaluation. Both catheter systems utilized a coaxial aspiration mechanism for thrombus removal. Although the ASPIRE system's aspiration force is generated by a simple hand-controlled syringe apparatus, the AngioJet catheter uses a complex mixture of rapid fluid streaming and hydrodynamic forces to fracture thrombus, allowing extraction at the catheter tip using negative pressure based on the Bernoulli principle.<sup>27</sup> Numerous studies have validated the treatment efficacy using the AngioJet system in removing thrombus and restoring intraluminal flow, as the jet streams within the AngioJet catheter system can generate an effective pressure of 2,000 psi at a flow velocity of 360 km per hour within the catheter.<sup>28–30</sup> Although these high-velocity jet streams create a low-pressure zone which results in thrombus maceration and aspiration, we have previously

reported that this hemodynamic system can result in vessel wall injury with subsequent decreased vaso-reactivity and reduced endothelial function.<sup>11</sup> The ASPIRE catheter, while utilizes the similar coaxial aspiration force for thrombus removal based on the Bernoulli effect, generates far less aspiration force due in part to its hand-held syringe apparatus. This consequently accounts for less turbulent disruption of the thrombus and decreased pulmonary embolism compared to the AngioJet group. The risk of procedural-related thromboembolism with subsequent pulmonary embolism in mechanical thrombectomy devices, particularly the AngioJet system, has been reported previously.<sup>26,31</sup> Although our findings of increased incidence of pulmonary embolism in the AngioJet system compared to the ASPIRE system based on this animal model may not be applicable for clinical extrapolation, it is noteworthy that our DVT model was intended to create fresh thrombus, which may result in greater susceptibility for thromboembolism under mechanical thrombectomy and catheter manipulation.

We assessed the PfHgb production to determine the device-related hemolytic effect and found that the ASPIRE device produced approximately one-sixth of the hemolytic effect in contrast to the AngioJet system. Hemolysis is a known procedural-related complication in percutaneous thrombectomy technology.<sup>13,17,32</sup> This is due to structural deformation of the red blood cell membrane caused by the shear stress from turbulent flow through viscous and inertial fluid dynamic forces, as brought on by the aspiration mechanism of thrombectomy devices.<sup>13,17,18,32</sup> The *in vivo* environment performed in our study under free-flow conditions exacerbates the likelihood of hemolysis due to maximal blood-device interface. In a complete occlusive thrombosis model, the risk of hemolysis is low due to little or no blood flow. In a partial flow model due to restoration of blood circulation, the overall effect of hemolysis is affected by various factors, including total run time, device generated shear stress, and ultimate distribution volume of PfHgb produced. We have previously described the biological effect of hemolysis of the AngioJet system.<sup>11,13</sup> In our iliofemoral venous circulation, the ASPIRE device produced PfHgb at an average rate of 35 mg/dL per minute, and the AngioJet produced PfHgb at an average rate of 245 mg/dL per minute. Lang et al. similarly reported that the AngioJet system produced 6 times greater hemolytic effect compared to the OmniWave thrombectomy device, who noted the PfHgb produced by these 2 systems were 23 mg/dL and 140 mg/dL per minute, respectively.<sup>18</sup>

There was no different reduction in hematocrit level in our study, which has been reported in a canine model following AngioJet thrombectomy intervention.<sup>33</sup> Our finding was consistent with our previous reports as well as those by Lang et al., who described that the hematocrit level remained unchanged despite a significantly elevated Pfhgb level following AngioJet thrombectomy.<sup>18</sup> This may be explained by the contractile splenic function in pigs, which can sequester 20–25% of the red blood cell mass under resting conditions, and these erythrocytes can be released rapidly in the circulation when needed.<sup>34</sup>

As with any animal thrombosis model, there are undoubtedly several weaknesses associated with our study. First, due to the species-related phylogenetic differences, results of the hemolytic effect and physiological response between these 2 thrombectomy systems may not be applicable to clinical practice. Second, the severity of histological and hemolytic effect is influenced by many variables including the duration of catheter activation, extent of thrombus burden, and device size relative to vessel caliber. These variables are difficult to replicate uniformly in any experimental investigation. In addition, the thrombectomy activation time in our study was set for 30 min in an effort to establish a uniform parameter for device comparison. In contrast to clinical application, this prolonged activation time can possibly result in an overwhelming physiological and hematological response in this animal model. Despite these limitations, the significance of pulmonary embolism as well as hemolytic profile in our study underscores the biological responses between the AngioJet and ASPIRE system in this porcine DVT model.

In conclusion, our study showed that mechanical thrombectomy can be achieved with similar efficacy between the AngioJet and ASPIRE systems. Although both devices had similar performance with regard to histological response and thrombectomy efficacy, the ASPIRE catheter resulted in less pulmonary embolism and less hemolytic effect compared to the AngioJet device. Further in vivo investigations and clinical comparisons are warranted to further elucidate the ideal thrombectomy system, which can effectively remove intraluminal thrombus while achieving an optimal safety profile.

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