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Vascular injury and occurrence of microthrombi after endovascular therapy for acute ischaemic stroke in a thromboembolic model

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ABSTRACT

Background Endovascular catheters and devices used for thrombectomy in patients who had a stroke can damage the vessel lumen leading to microthrombi. During stroke recanalisation, microthrombi could migrate distally and occlude cerebral microvasculature, potentially limiting the benefit of recanalisation therapy.

Objectives To describe vascular injury occurring after endovascular therapy (EVT), with stent retrievers (SR) and direct aspiration (DA), to open up avenues for further improvement of EVT technique.

Methods SR and DA were performed according to clinical procedures in extracranial vessels in a swine model of thromboembolic arterial occlusion. Treated vessels were collected at 2 hours or 3 days post-EVT to assess respectively acute injury and early healing (remnant vascular injury) as assessed by Evans-Blue (EB) dye exclusion. The presence of microthrombi was quantified using scanning electron microscopy. Markers of coagulation activation were measured periprocedurally in plasma.

Results Both SR and DA induced vascular injury. SR tended to result in larger EB positive areas than DA at 2 hours (99.5 vs 84.5; p=0.072) which reached statistical significance at day 3 (78.6 vs 48.6; p=0.040) post-EVT. Both EVT methods similarly yielded microthrombi in treated areas which were still observed at 3 days post-EVT. In addition, both EVT methods immediately increased systemic plasma levels of complexes of intrinsic-pathway coagulation activation: thrombin, Factor IX and Factor Xa:Antithrombin.

Conclusions In this preclinical thromboembolic model, SR thrombectomy and DA lead to acute vascular injury, yield microthrombi and trigger contact activation of the coagulation system. At 3 days after intervention, healing remains incomplete, showing remnant vascular injury in the treated arteries, especially in SR thrombectomy.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Endovascular therapy is routinely used to achieve recanalisation in patients who had a stroke, but can cause iatrogenic vascular damage during treatment.

WHAT THIS STUDY ADDS

⇒ We have quantified the extent of injury and size and number of microthrombi following artery recanalisation using stent retrievers (SR) and direct aspiration (DA) catheters to remove the occluding clot. Both techniques induced vascular damage, showed numerous adherent microthrombi, and activated coagulation. While SR induced overall a larger extent of injury, DA yielded larger microthrombi that remained present at 3 days following treatment.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Having observed microthrombi and activation of coagulation following treatment, the next steps in research might be to determine whether they occur clinically and whether they impact outcome. Aiming to improve stroke care and using sensitive methods to quantify vascular injury and its sequelae, our study opens up avenues for improvement of catheter and device design. Further refinement of technique and optimisation of devices might target reduced microthrombi formation and attenuation of coagulation activation.

INTRODUCTION

Endovascular therapy (EVT) is a very effective technique to achieve recanalisation in patients suffering from acute ischaemic stroke (AIS) with proximal intracranial large vessel occlusion. In the USA, EVT is used in approximately 30% of patients who had an AIS with large-vessel or medium-vessel occlusions, and it is estimated to increase to up to 50% in the coming years.[1] Some complications of EVT, such as symptomatic intracranial haemorrhage, vasospasm and distal embolisation of (macroscopic) clots,[2 3] are well recognised as clinical entities. However, experimental data shows that EVT also induces vascular injury

Table 1 EVT technical characteristics, complications and recanalisation

	Stent retriever (n=16)	Direct aspiration (n=14)	P value
Treated artery (n (%))			
SCA	10 (63)	8 (57)	0.76
LA	6 (37)	6 (43)	
Artery diameter (mm)			
SCA	2.8 (2.0–3.4)	2.6 (2.0–3.0)	0.51
LA	2.3 (1.9–3.6)	2.0 (1.8–2.8)	0.32
Attempts (n (%))			
One attempt	4 (25)	4 (29)	0.82
Two attempts	11 (69)	7 (50)	0.29
Three attempts	1 (6)	3 (21)	0.22
Complications (n (%))			
Spasm	6 (38)	3 (21)	0.33
Dissection	2 (13)	1 (7)	0.62
Perforation	0 (0)	1 (7)	1
Recanalisation (n (%))			
Recanalisation>50%	13 (81)	10 (71)	0.52

Differences between stent retriever and direct aspiration for categorical variables (treated arteries, attempts, complications and recanalisation) were studied by χ^2. Differences between the diameter of SCA and LA between the two groups were studied by Mann-Whitney U.
EVT, endovascular therapy; LA, lingual artery; SCA, superficial cervical artery.

on a microscopic level in clinically 'normal' vessels.[4–6] While this type of injury might be difficult to identify in the clinical setting, it does not mean that it is not of relevance, particularly when considering the microvascular reperfusion.

In this sense, among other potential consequences of EVT, the local formation of microthrombi[7] and the activation of the coagulation system triggered by endothelial injury are of special interest. Microthrombi formed in the EVT-treated lumen could occlude microvessels in case of distal embolisation, hindering the complete reperfusion of the affected vascular tree. Moreover, the activation of coagulation can have (clotting) consequences beyond the area of vascular damage and further contribute to poststroke thromboinflammation. The occurrence and magnitude of these phenomena after clot retrieval with currently used EVT tools is not known yet. Stent retriever (SR) and direct aspiration (DA) thrombectomy are both widely used as a means of mechanical recanalisation and have similar clinical profiles in terms of success and acute safety. Nonetheless, any clinical technique is, of course, amenable to improvement. To support further development, more quantitative information at a micro level is needed to gain a more comprehensive understanding of the vascular damage and healing response. Swine are the gold standard for testing safety and efficacy of arterial interventions. We therefore used a swine model of arterial thromboembolic occlusion and EVT to study endothelial injury and repair, microthrombi formation and coagulation activation as induced by standard clinical techniques and devices. Our study aims to open up avenues for further improvement of EVT technique, as well as catheter and device design.

MATERIALS AND METHODS

Experiments were performed in specific pathogen-free female farm-bred swine (n=11, 7 days acclimatised, Yorkshire-Landrace, 46–60 kg). The study was approved by the animal ethics committee of the Erasmus MC University Medical Center, complied with the 'Guide for the care and use of laboratory animals',[8] and is reported according to the ARRIVE (Animals in Research: Reporting In Vivo Experiments) guidelines.[9]

Experimental design

To test whether EVT by SR induced more vascular injury than DA, 42 extracranial arteries were randomly assigned to thrombus embolisation and EVT (SR or DA) or control (no thrombus, no intervention). Treatment allocation was by predetermined randomised blocks for both vessel and treatment, with 2 hours or 3 days follow-up (www.randomizer.org). Procedures were performed in left and right superficial cervical (SCA) and lingual arteries (LA) to mimic M1 or M2 segments of human middle cerebral arteries, easily accessible for post-sacrifice harvesting.

The primary outcome, extent of injury, was determined using Evans-Blue (EB) dye-exclusion tests. Sample size was calculated using previously published data[10] allowing detection of 15±10% differences (mean±SD, 80% power) in EB area. Secondary outcomes of the study were quantification of presence and size of luminally adherent microthrombi, descriptive assessment of vascular damage, temporal dynamics of coagulation activation and procedural and angiographic parameters.

Swine model of arterial thromboembolism and EVT

Autologous aged blood clots were created 24–48 hours before EVT (online supplemental methods). On the day of intervention, animals were sedated and mechanically ventilated. A 9 French sheath was percutaneously placed and used for continuous invasive blood pressure registration, arterial blood sampling and access for introduction of catheters. Animals were monitored by means of EKG, pulse oximetry and invasive blood pressure.

To create arterial thromboembolic occlusions, a balloon guide was advanced proximally to the targeted arteries. After baseline angiography, the autologous thrombus was injected into the artery. The location of the occluding thrombus was then confirmed by angiography. EVT, either SR or DA, was performed 2 hours after injection of thrombi according to clinical routine methodology. In short, for SR, the balloon guide was placed just distal to the origin of the occluded artery. A microcatheter was advanced past the thrombus using a guidewire. The SR was deployed, left in place for 5 min and then retracted under flow reversal. For DA, a sheath was positioned at the origin of the occluded artery, a reperfusion catheter

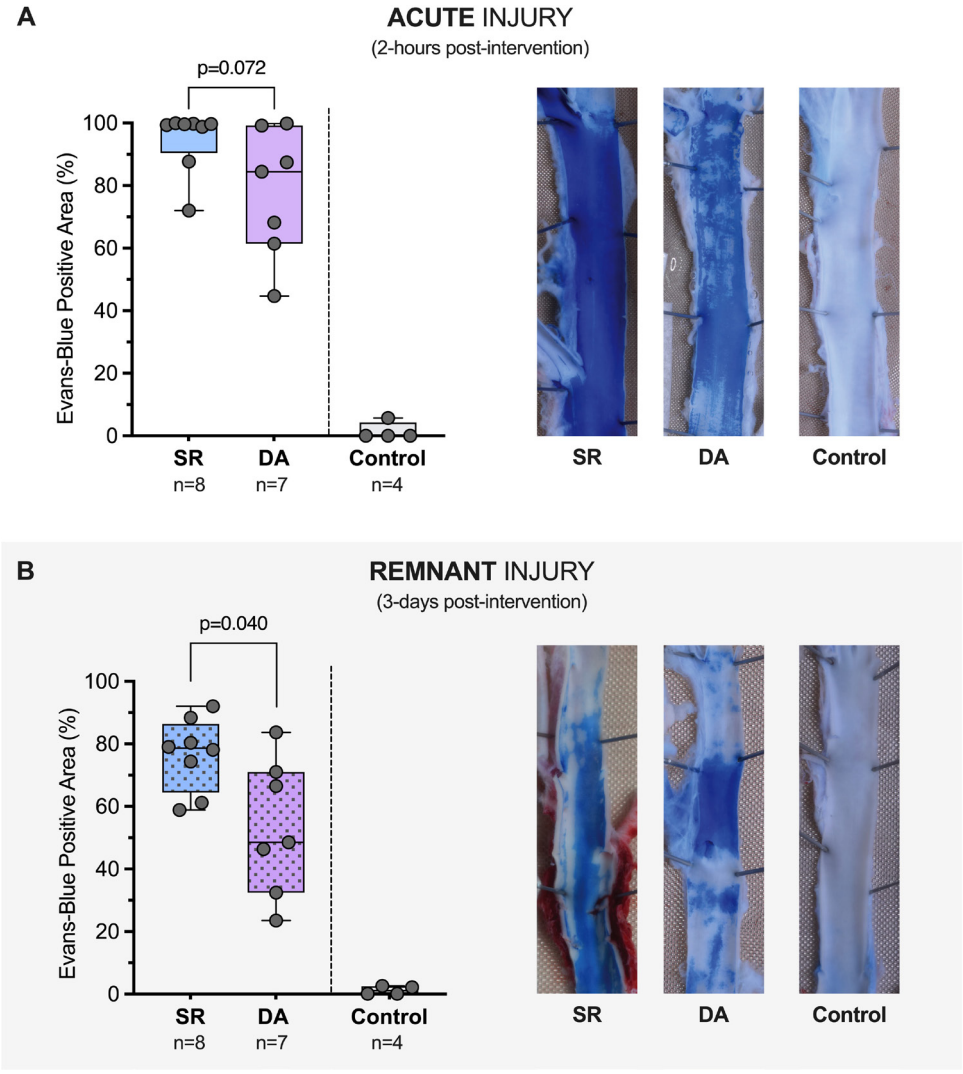

Figure 1 Vascular injury induced by EVT. Both SR and DA induced significant vascular injury as visualised by Evans-Blue. At 2 hours after EVT, vascular injury tended to be lower for DA as compared with SR (Panel A). Differences between treatments were more pronounced and statistically significant at 3 days after EVT (Panel B). Representative images of treated and non-treated vessels (Control) are shown in Panel A and B. Box plots represent Evans-Blue positive areas as median (box, 25th–75th percentiles; whiskers, 5th–95th percentiles). Differences between groups at each time point were studied by Mann-Whitney U. DA, direct aspiration; EVT, endovascular therapy; SR, stent retrievers.

was advanced against the thrombus and connected to the pump. After 2 min of suction, the catheter was pulled back while manually applying suction on the sheath for flow reversal. Control vessels were left untouched. For both SR and DA, a maximum of three recanalisation attempts were performed. Second and third attempts were only performed in case of incomplete recanalisation (<50%) of the main branch. For details, see online supplemental methods.

Endothelial permeability: EB dye exclusion test

The EB dye only penetrates permeable or damaged endothelium, staining the artery blue. To prevent post-mortem clotting, unfractionated heparin (10 000 IU, intravenous bolus) was administered. Following euthanasia (pentobarbital, 100 mg/kg, intravenous bolus), the dye-exclusion test was performed as described before.[7] Target arteries were harvested, longitudinally dissected and photographed. For details, see online supplemental methods.

The extent of vascular permeability was defined as the percentage of EB-positive luminal surface within the distal 4 cm of the treated area. If it was impossible to collect sufficient tissue, arteries were excluded from analysis. The damaged area was determined by semiautomated colour threshold analysis (ImageJ) and expressed as a percentage.

Quantification of microthrombi and assessment of microinjury

Scanning (SEM) and transmission (TEM) electron microscopy were used to study microthrombi and vascular injury respectively, see online supplemental methods. The central part (≈5 cm) of the treated area was processed for SEM and studied as described before.[10] Microthrombi were counted using SEM and ImageJ. SEM samples were

Table 2 Scanning electron microscopy outcomes

	Acute injury (2 hours post-EVT)			Remnant injury (3 days post-EVT)		
	SR (n=8)	DA (n=7)	P value	SR (n=8)	DA (n=7)	P value
Presence of microthrombi (n (%))	8 (100)	7 (100)	1.00	3 (37.5)	6 (85.7)	0.057
Microthrombi (n/cm²)	4.1 (0.6–11.8)	4.6 (1.6–13.9)	0.53	0.0 (0.0–1.3)	0.6 (0.0–4.8)	0.12
Microthrombus-covered surface (μm²/cm²)	1.7×10^5 (5.5×10^3–7.6×10^5)	2.6×10^5 (4.7×10^3–5.8×10^6)	0.53	0.0 (0.0–2.3×10^3)	1.2×10^3 (0.0–2.6×10^5)	0.021
Leucocyte adhesion (n (%))	7 (87.5)	7 (100)	1.00	5 (62.5)	7 (100)	0.20
Platelet adhesion (n (%))	8 (100)	7 (100)	1.00	6 (75)	5 (71.4)	1.00

Differences between SR and DA for categorical variables (presence of microthrombi, leukocytes, platelet adhesion) were studied by χ^2. Differences between the number of microthrombi and microthrombus-covered surface between groups were studied with Mann-Whitney U.
DA, direct aspiration; EVT, endovascular therapy; SR, stent retriever.

then processed for TEM to study luminal integrity, endothelial morphology, leucocytes and platelets.

Histology

The proximal and distal 5 mm segments of the treated areas were fixed in buffered 4% paraformaldehyde, dehydrated in graded ethanol series and cleared by xylene prior to paraffin embedding. Sections were stained using H&E as an overview stain and Resorcin-Fuchsin as an elastin stain.

Soluble markers of coagulation activation following EVT

Soluble markers of coagulation activation were studied for the first treated artery per animal. For details, see online supplemental methods. Samples for Thrombin:Antithrombin (TAT), Factor Xa (FXa):AT, Factor IXa (FIXa):AT, Factor XIa (FXIa):AT and Factor VIIa (FVIIa):AT complexes were taken directly prior to the first recanalisation attempt and after each attempt.

Radiological and procedural outcomes

Angiography was performed at baseline, directly post-occlusion, pretreatment (after 2 hours occlusion) and after each attempt (max three attempts). The following radiological outcome measures were independently scored by two experienced neurointerventional radiologists blinded for treatment group: baseline diameter at occlusion site, recanalisation of main branch after final attempt (<50% or >50%), spasms, dissections and perforations. In case of disagreement, a third blinded experienced neurointerventional radiologist was consulted.

Patient and public involvement

There was no 'Patient and public involvement'.

Statistical analysis

Data were analysed using SPSS (V.28.0.1.0) and GraphPad Prism (V.9.5.1). Differences between SR and DA regarding %EB and microthrombi were assessed by Mann-Whitney U. Acute and remnant injury data were analysed separately. Linear regression analysis was performed for predictors of EB percentage, including all treated arteries (independent variables: treatment, follow-up duration and attempts; dependent variable: EB percentage). Plasma levels of coagulation activation complexes were compared between time points (baseline, first, second attempt) using Kruskal-Wallis and pairwise comparisons with Bonferroni correction (excluding a single artery that required a third EVT attempt). Mann-Whitney U was used to study differences between SR and DA in coagulation activation by comparing the fold change increase ((First Attempt − Baseline)/Baseline) of each complex following a first recanalisation attempt between both treatments. For comparison of categorical data (eg, presence/absence of leucocytes), a χ^2 test was used.

Continuous data are given as 'median [95%CI]'. Categorical data are given as 'n (%)'. A p value of≤0.050 was considered statistically significant.

RESULTS

All 11 animals (42 arteries) completed the study. After excluding 4 vessels, see online supplemental results, 38 arteries were included for analysis: 19 at 2 hours and 19 at 3 days postintervention. EVT outcome is summarised in table 1.

In terms of efficacy, both EVT treatments were associated with similar rates of success, with more than 50% recanalisation (ie, thrombolysis in cerebral infarction (TICI) score of 2b or higher) achieved in 81% of SR and 71% of DA (p=0.52). Successful recanalisation was commonly achieved after a second attempt for both techniques (SR vs DA; 69% vs 50%; p=0.29). No differences were observed between the two EVT techniques regarding

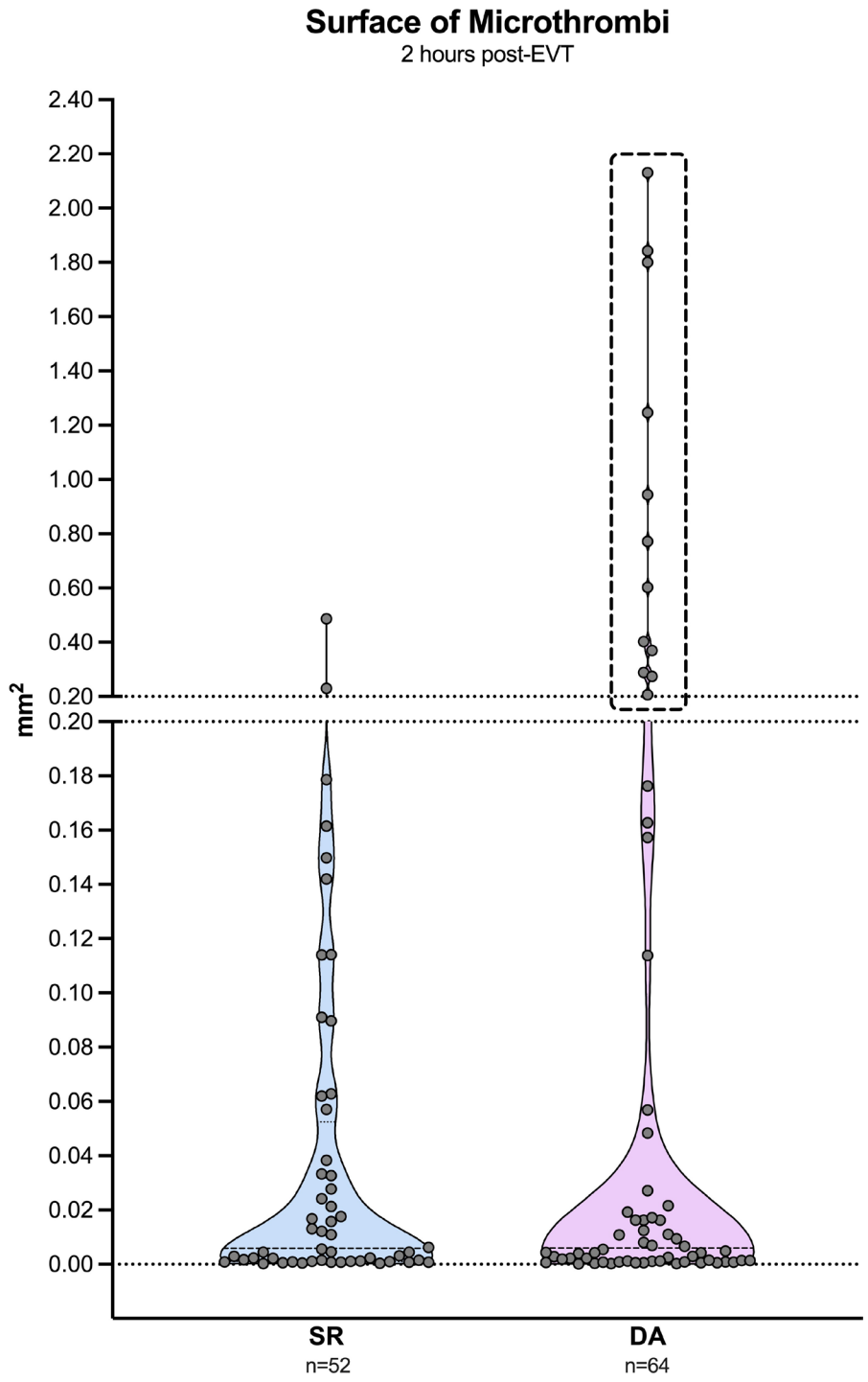

Figure 2 Size distribution of microthrombi observed at 2 hours post-EVT. Rectangle with dashed lines highlights microthrombi with large surface in DA group. Note the difference in scale of the two segments of the Y axis. DA, direct aspiration; EVT, endovascular therapy; SR, stent retrievers.

complications such as vessel spasms (p=0.33), dissections (p=0.62) or perforations (p=1.00).

SR induces a larger area of vascular injury than DA

The EB dye-exclusion test revealed that both SR and DA altered endothelial permeability of the treatment area. When assessed acutely (primary outcome), the luminal area with increased permeability covered almost the complete treatment segment when using SR to perform EVT (99.5% (72.1–99.9%) EB-positive area). In comparison to SR, treatment with DA resulted in 84.5% (44.7–99.8%) of the treated area stained with EB. This difference did not reach statistical significance when assessed at 2 hours (p=0.072). However, at 3 days, differences between SR and DA were larger and statistically significant (78.6% (58.8–92.1%) for SR and 48.6% (23.5–83.7%) for DA; p=0.040). Results are summarised

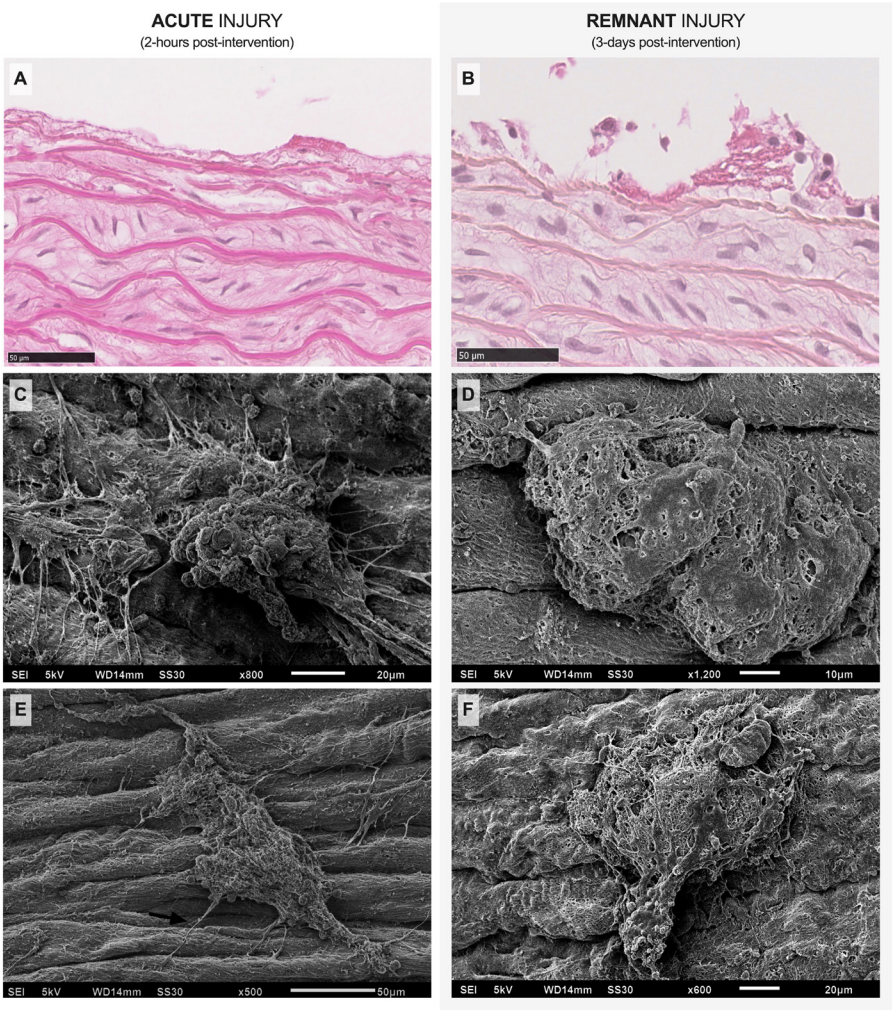

Figure 3 Presence of microthrombi on the luminal surface after endovascular therapy. Histology (A,B) and scanning electron microscopy (C,F) of adherent microthrombi acutely (A,C,E) and at 3 days (B,D,F) following endovascular treatment. Microthrombi contain fibrin, leukocytes and platelets. Scanning electron microscopy shows that microthrombi are tethered to the arterial wall by fibrin strands.

in figure 1. Linear regression analysis using treatment, follow-up duration and number of attempts as independent variables (analysis of variance (ANOVA) p=<0.001; Adj. R^2 0.49) showed that SR induced more injury than DA (p<0.001); damage decreased over time (p<0.001); and showed a strong trend for more damage with increasing number of attempts (p=0.055). SR induced near complete denudation on the first attempt. Regression analysis for DA alone, using follow-up duration and number of attempts as independent variables (ANOVA p=0.007; Adj. R^2 0.52) indicated that damage indeed increased with the number of attempts (p=0.011) and decreased in time (p=0.016). Vessel location (SCA vs LA) did not affect outcome (online supplemental results).

SR and DA result in luminal microthrombi at the treatment area

SEM revealed microthrombi in all treated areas collected at 2 hours after EVT. However, no differences were observed between the two treatment modalities: neither in the total number of lumen-adhered microthrombi nor in the luminal surface that they covered. Three days after intervention, microthrombi were still adherent but now in 37.5% of SR-treated arteries versus 85.7% for DA (p=0.057), with a larger surface of the treated area covered by microthrombus following (p=0.021). Quantitative data are summarised in table 2 and illustrated in figure 2. No microthrombi were detected in any of the control arteries.

Besides quantitative analysis of microthrombi, SEM analysis and histology also provided insights into ultrastructural microthrombus characteristics (figure 3). Overall, microthrombi were composed of a mix of fibrin, platelets, leucocytes and red blood cells. However, some also presented unidentified (biological) structures, compatible with clumps/aggregates of endothelial cells (online supplemental figure 1). The microthrombi present in the arteries collected 2 hours after EVT showed complex geometries and elongated shapes, with sharp angles and protuberant structures like fibrin strands tethering them to the lumen

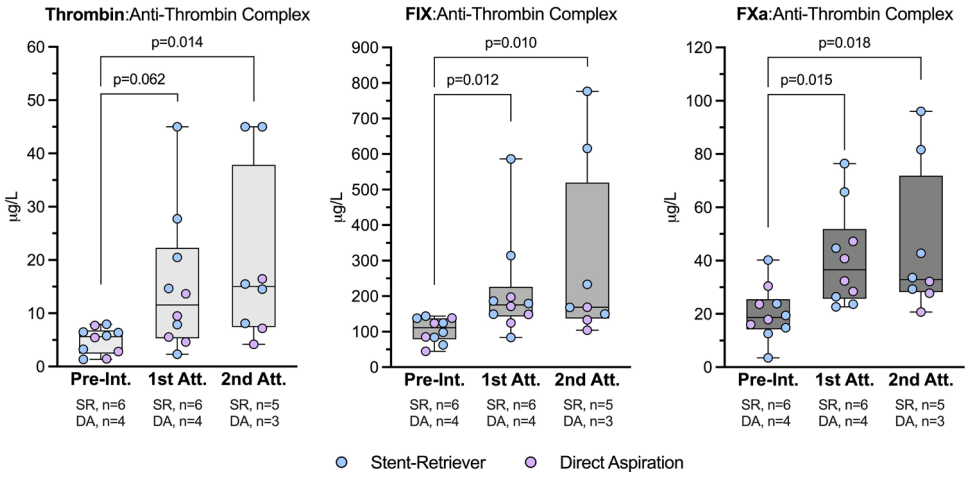

Figure 4 Effect of EVT on contact activation of coagulation. Box-whisker plots represent median concentration (box, 25th–75th percentile; whiskers, 5th–95th percentile) of plasma markers of contact activation, TAT, FIX:AT and FXa:AT, which significantly increased already after the first pass of EVT. Light blue dots represent the animals where SR was performed and light purple dots animals that received DA. No differences were observed between the two treatments regarding the increase in these plasma markers of contact activation of coagulation. Differences between the concentration of each complex among the time points were studied with Kruskal-Wallis, followed by pairwise comparisons with Bonferroni correction. AT, Antithrombin; DA, direct aspiration; EVT, endovascular therapy; FIX, Factor IX; FXa, Factor Xa; SR, stent retriever; TAT, Thrombin:Antithrombin.

(figure 3C,E). Conversely, microthrombi observed at 3 days postintervention were characterised by a more flattened geometry, smooth surfaces and fewer fibrin strands (figure 3D,F).

Activation of the coagulation system is triggered by EVT

EVT induced a significant increase in the complexes TAT, FIXa:AT and FXa:AT, which was observed already following the first attempt and reached levels of statistical significance after the second attempt (figure 4). No statistically significant differences were observed between the two EVT techniques when comparing the fold-change of these complexes. FXIa:AT, FVIIa:AT and FXIIa:AT did not show any modification of their plasma levels following EVT.

EVT-induced vascular injury is characterised by endothelial denudation with platelet and leucocyte adhesion

Microscopic analysis by light microscopy, SEM and TEM (figure 5A–F) showed that EVT resulted in vascular injury with extensive areas of complete endothelial denudation (figure 5A). Moreover, some injured areas presented platelet and leucocyte adhesion (figure 5C,E, online supplemental figure 2), both in vessels obtained at 2 hours and at 3 days follow-up (figure 5C–E). Minimal damage was observed to the internal elastic laminae, but frank medial rupture was not observed. The endothelium had partially regrown at 3 days on top of an eosinophilic layer (figure 5B), showing clear signs of endothelial activation as illustrated by surface folds observed by SEM and TEM (figure 5D,F). There were no significant differences between SR and DA in qualitative assessment of histology and ultrastructure of vascular injury.

DISCUSSION

By means of a swine model of arterial thromboembolic occlusion, we showed that both SR and DA led to vascular injury with extensive areas of increased vascular permeability, particularly in SR. We also demonstrated that both SR and DA yielded a remarkable number of lumen-adherent microthrombi in the treated artery and triggered the activation of the coagulation system. We observed that both injury and the presence of microthrombi were less prominent when assessed 3 days after the intervention, indicating an active healing process of the artery.

EVT-induced vascular injury

Our main aim was to study the incidence of vascular injury induced by EVT. While SR tended to injure the whole treatment area, DA did not (99 vs 84%; p=0.072). The latter was also remarkably higher than another catheter-based technique such as intravascular ultrasound (IVUS) imaging (~35%).[7] While the presence of a thrombus may have influenced the outcome, data from a previous study without thrombus embolisation show a very similar percentage of 85% endothelial damage following permanent stenting.[7] We cannot, however, exclude that coagulation activation may have further impacted endothelial damage. In addition, the relation between dimensions of the device and the vessel could also play a role in the extent of damage. In this study, we used a 7Fr aspiration catheter which results in a higher luminal surface contact area in comparison to IVUS (3.6Fr).[7] The suction forces applied in DA may also have modified vessel geometry, further increasing the surface of contact between inner vessel lining and device. Other factors such as catheter flexibility or the number of passes could also contribute

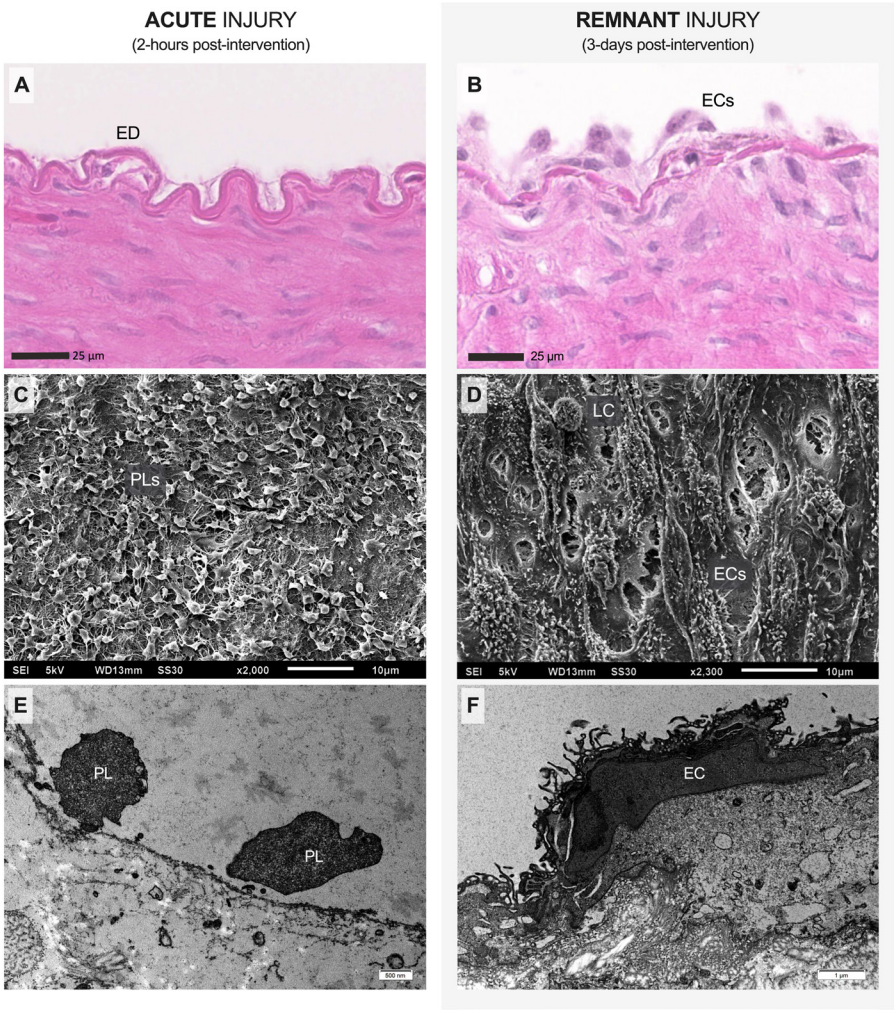

Figure 5 Endothelial denudation with platelet and leucocyte adhesion. Histological assessment of the treated arteries was performed using light microscopy (A,B), scanning electron microscopy (C,D) and transmission electron microscopy (E,F) acutely (A,C,E) and 3 days (B,D,F) following endovascular treatment. Microscopy illustrates endothelial denudation and regrowth (A,B), platelet adhesion (C,E), leukocyte adhesion (D) and endothelial activation (D,F) characterised by surface folds. EC(s) indicates endothelial cell(s); LC, leukocyte; and PL, platelet. ED, endothelial denudation.

to differences observed between the two catheter procedures. SR data is more difficult to compare to other techniques involving stents as the procedures significantly differ. However, the introduction of a stent in an artery is invariably associated with a large extent of endovascular damage.

Injury associated with SR and DA was decreased at 3 days post-EVT, with DA now showing significantly less injury than SR. However, both techniques still show a significant area of vascular permeability. How long it will take for the injury to be completely healed still needs to be determined, but a forward projection indicates that this may take between 12 and 21 days for SR and between 6 and 15 days for DA.[11] It is unclear what the consequences of this relatively long period will be. Our data also indicate that more attempts could increase the injured surface, which is in line with another study that demonstrated increased damage with multiple attempts for SR, using different techniques.[6] This additional damage can be taken into account when considering another attempt, although we realise the possible benefits of an extra attempt generally outweigh this additional focal damage.

Effects of EVT on (micro)thrombosis

As secondary outcomes, we studied the potential effects of EVT on the number and extent of microthrombi and activation of coagulation. At 2 hours following EVT, we detected microthrombi in all treated arteries, in similar amounts for both SR and DA. Our study does not distinguish between locally formed microthrombi and residual thrombus material (ie, of the original occluding clot) and we can only speculate on their origin. However, other studies[5 7] confirm the presence of microthrombi after performing SR, DA and other interventions in non-occluded arteries, suggesting that newly formed microthrombi are a major contributor. It remains uncertain if we would consider we are dealing with de novo thrombus formation, which mechanisms might drive the de novo formation of microthrombi. The clear increase in FIXa:AT, FXa:AT and TAT complexes may have been

the result of contact activation, for example, related to neutrophil and platelet activation,[12] but other activators of the coagulation system cannot be ruled out. Regardless of the origin of the microthrombi, embolisation to the distal microcirculation could pose a threat and increase IMR, although we did not directly measure this. In addition, increased systemic coagulation activity could lead to de novo formation of microthrombi in the distal microvasculature, which is already compromised by ischaemia-reperfusion injury. The neurocognitive and behavioural deficits resulting from ischaemic lesions in the microvasculature might be subtle and difficult to quantify by clinical outcome scales. Nonetheless, a recent study aimed to target this incomplete microvascular reperfusion by means of intra-arterial recombinant tissue plasminogen activator[10] after EVT and showed improved functional outcome, even in the case of complete angiographic revascularisation. The results of the present study also indicate that the potential threat of microthrombus embolisation, whether remnant or de novo, remains active for at least 3 days post-EVT. While the number of microthrombi decreased in both treatment groups, the thrombus load was significantly higher in DA than SR at 3 days. This could be explained by a higher number of larger microthrombi in DA-treated arteries initially. Hypothetically, it takes longer for larger microthrombi to lyse. To our knowledge, this is the first study to thoroughly quantify microthrombi on the luminal surface, which provides opportunities to study embolisation patterns, healing and treatment effects.

Translational outlook

The impact of our observations on stroke outcome in terms of small infarctions and effects on cognition remains to be determined, but can be considered hypothesis-generating for human studies. The next steps should focus on confirming the occurrence of these preclinical observations in the clinical setting. Then, our outcome measures can be used to further optimise EVT technique and device development. By designing more vessel-friendly endovascular devices or specific (pharmaco) therapeutic strategies to mitigate endothelial injury and microthrombus formation, for instance, targeting the decrease of large microthrombi following DA.

Limitations

In our study, sheaths were flushed using heparinised saline, which could lead to an underestimation of the amount and size of newly formed microthrombi. However, heparin use is not uncommon in daily practice of EVT in AIS.[13] During interventions, no recombinant tissue plasminogen activator or platelet aggregation inhibitors were administered, so findings can only be extrapolated to patients under the same circumstances. We cannot exclude that systemic coagulation activation may have been triggered by the embolised clots as we did not include a control sample without thrombectomy. Finally, we only included female animals, which does not represent the human stroke population.

CONCLUSIONS

In this swine model of arterial thromboembolic occlusion, EVT by SR and DA led to vascular injury and activation of the coagulation system. Both treatments yielded luminal microthrombi. After 3 days, there is less vascular injury and less microthrombi with either treatment, but vascular healing is still incomplete. Further refinement of EVT technique and optimisation of devices might target these unwanted sequelae.

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