Original Paper

Comparison of Subacute Vascular Damage Caused by ADAPT versus Stent Retriever Devices after Thrombectomy in Acute Ischemic Stroke: Histological and Ultrastructural Study in an Animal Model

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Keywords

ADAPT · Arterial wall · Stent retriever · Stroke · Thrombectomy · Vascular wall damage

Abstract

Objectives: To assess the delayed (15 days) histological and ultrastructural changes occurring following endovascular treatment with a direct aspiration first pass technique (ADAPT) or stent retrievers (SRs) and to compare the findings in order to determine which is the least harmful technique and what changes occur. **Materials and Methods:** Damage to the wall of swine extracranial arteries was evaluated after ADAPT with the Penumbra system or thrombectomy with various SRs. The procedures were performed using two pigs as animal models; extracranial cervical arteries were selected based on their diameters in order to reproduce the procedures as in human intracranial arteries, and endovascular thrombectomies were done after the injection of autologous thrombi. Two weeks later, the animals were euthanized, and 60 arterial samples were obtained for analysis by optical and electron microscopy. **Results:** Optical and electron microscopy revealed that both techniques cause, in different way, alterations to the structure of the vessel wall. **Conclusions:** Both techniques caused damage to the vessel wall. The main damages were localized at the level of the tunica media and adventitia, instead of the tunica intima as in the acute phase. Further investigation is required to better understand whether these alterations could have chronic consequences.

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Introduction

Endovascular ischemic stroke procedures have evolved over the years making use of stent retrievers (SRs) (i.e., Solitaire [Medtronic, Irvine, CA, USA] in 2009, Trevo [Stryker, Kalamazoo, MI, USA] in 2010, and Revive [Codman, Raynham, MA, USA] in 2011), until ADAPT (a direct aspiration first pass technique) in 2013, associated initially with use of the Penumbra aspiration system (Penumbra, Alameda, CA, USA) and now with the new large-bore aspiration catheters (ACE68, Penumbra Inc/SOFIA, MicroVention Inc/AXS Catalyst Distal Catheter, Stryker). Several studies demonstrated the notable revascularizing capacity and good clinical outcome of these techniques, and the first results of the use of larger-bore aspiration catheter were published recently [1].

After our first experience [2], the aims of this study were to assess the delayed histological and ultrastructural changes occurring following endovascular treatment with ADAPT or SRs and to compare the findings in order to determine which is the least harmful technique and what changes occur.

Assessment of the evolution of delayed vascular damage was performed in the past using digital subtraction angiography (DSA) or magnetic resonance imaging (MRI) follow-up to evaluate the decrease in arterial diameter at the level at which the thrombectomy had been performed. However, to our knowledge, no study has compared the delayed histopathological and ultrastructural effects induced by SRs and ADAPT. This could be interesting considering that focal endothelial denudation with substantial medial trauma produces marked delayed intimal thickening.

Materials and Methods

All procedures were performed at the Lab Animal Service of the Vall d'Hebron Institut de Recerca, Barcelona, Spain with a monoplane General Electric angiography system, using two pigs as animal models (C01 and C02). Animals remained under general anesthesia during the procedure. Vital parameters such as arterial blood pressure, heart rate, body temperature, electrocardiogram, and carbon dioxide levels were recorded continuously. Blood samples were collected prior to surgery to control blood baseline parameters.

The protocol was principally designed to assess the degree and type of vascular damage and to compare it with our previous study (Table 1) [2]. Recanalization rate, vasospasm, arterial perforation, and distal embolism were also reported (Table 2).

Clot Preparation

Twenty-four hours before the procedures, autologous whole blood samples were collected into standard tubes without sodium citrate solution to prepare the artificial clot: 60 mL were incubated at 4 °C for 24 h. The solid component was separated from the plasma, broken into several pieces, and subsequently stored at 37 °C until the time of the procedure.

Postoperative Monitoring

After surgery, animal recovery from anesthesia was constantly monitored. Animals were monitored daily throughout the study period. This control included appearance and body condition, behavior and habits, food and water intake, clinical monitoring, and any abnormality or incident. Animal monitoring was done by caretakers, technicians, veterinarians, and animal welfare advisers. Twenty-four-hour remote surveillance by webcam and recording system allowed study of the animal's behavior. Twelve days after the endovascular procedure, C02 was found dead due to a deep subcutaneous hematoma from the left inguinal area to the mid abdomen, caused by a broken pseudoaneurysm. C01 was euthanized on day 14.

Endovascular Procedure

In both pigs, an 8-Fr guiding catheter (Neuron MAX.88; Penumbra) was used, continuously flushed with physiological saline in the right femoral artery, and a 5-Fr femoral sheath in the left femoral artery was used

Table 1. Arterial wall damages reported in optic and electron microscopy

Sample	Endothelial damage	Damage to the internal elastic lamina	Damage to the tunica media/adventitia	Electron microscopy
C01				
<i>R</i>				
ICA _{SO}	no	++ (focally fragmented)	+++ (thin, wavy, and scattered EMs and EEL)	++ (irregular endothelial surface, superficial scars, some platelets at the surface)
M1 _{SO}	+++ (endothelial layer absent, thickened subendothelial space)	+++ (exposed and focally fragmented)	+++ (thickened EMs, thickened and discontinuous EEL)	+++ (almost totally denuded endothelial surface)
<i>L</i>				
ICA _{TR}	+ (thickened endothelial layer)	++ (focally fragmented)	+++ (thin, wavy, and scattered EMs, discontinued EEL)	++ (irregular endothelial surface, superficial scars, some platelets at the surface)
M1 _{TR}	++ (thickened subendothelial space)	+++ (thickened with multiple foci of fragmentation)	+++ (thickened EMs, thickened and discontinuous EEL)	+ (regular thickened endothelial surface)
C02				
<i>R</i>				
ICA _{ADAPT}	+ (flat endothelial layer)	+ (thin and focally fragmented)	+ (thickened EMs)	+ (regular endothelial surface, superficial scars, some filamentous material at the surface)
M1 _{ADAPT}	++ (extremely flat endothelial layer, lax subendothelial layer)	+ (flat)	+ (thickened EMs)	+++ (almost totally denuded endothelial surface, platelets at the surface)
ICA _C	+ (flat endothelial layer)	+ (discontinuous)	no (thickened EMs)	+ (regular endothelial surface, superficial scars, some filamentous material at the surface)
M1 _C	+ (flat endothelial layer)	+ (thin and focally discontinuous)	no (thickened EMs)	regular endothelial surface
<i>L</i>				
ICA _{ET}	+++ (thickened endothelial layer, thickened subendothelial space)	+++ (wavy, focally, and slightly discontinuous)	+++ (little evident, scattered, and thin, thin and discontinuous EEL)	++ (irregular endothelial surface, superficial scars, some platelets at the surface)
M1 _{ET}	+++ (flat endothelial layer, thickened subendothelial space)	++ (focally fragmented)	+++ (thickened EMs, discontinuous EEL)	++ (irregular endothelial surface, superficial scars, some platelets at the surface)

Red: the structure was severely damaged; yellow: the structure was moderately damaged; green: the structure was slightly damaged. EEL, external elastic lamina; EMs, elastic membranes; ICA_{ADAPT}, ICA segment in which ADAPT was performed; ICA_C, ICA control; ICA_{ET}, ICA segment in which EmboTrap was used; ICA_{SO}, ICA segment in which Solitaire was used; ICA_{TR}, ICA segment in which Trevo was used; M1_{ADAPT}, M1 segment in which ADAPT was performed; M1_C, M1 control; M1_{ET}, M1 segment in which EmboTrap was used; M1_{SO}, M1 segment in which Solitaire was used; M1_{TR}, M1 segment in which Trevo was used.

Table 2. Additional information

	ICA _{SO}	M1 _{SO}	ICA _{TR}	M1 _{TR}	ICA _{ADAPT}	M1 _{ADAPT}	ICA _{ET}	M1 _{ET}
Vasospasm	–	–	–	mild	–	–	–	–
Distal embolism	–	–	–	–	–	+	–	–
Arterial perforation	–	–	–	–	–	–	–	–
Recanalization rate	TICI 3	TICI 3	TICI 3	TICI 3	TICI 3	TICI 2A	TICI 3	TICI 3

ICA_{ADAPT}, ICA segment in which ADAPT was performed; ICA_{ET}, ICA segment in which EmboTrap was used; ICA_{SO}, ICA segment in which Solitaire was used; ICA_{TR}, ICA segment in which Trevo was used; M1_{ADAPT}, M1 segment in which ADAPT was performed; M1_{ET}, M1 segment in which EmboTrap was used; M1_{SO}, M1 segment in which Solitaire was used; M1_{TR}, M1 segment in which Trevo was used.

for monitoring. A diagnostic angiogram was performed to select, on the basis of their diameter, common carotid arteries as models of the internal carotid artery (ICA) and the middle segment of the superficial cervical arteries for the middle cerebral artery (M1) model.

Mechanical thrombectomy was carried out by two experienced neurointerventionists with both ADAPT and SRs in these arteries (Fig. 1d). After each passage, cutaneous color marks and surgical metal staples were used as landmarks for arterial samples (Fig. 1a).

For selective thromboembolization, the preformed clot was injected directly into the vessel through the 8-Fr guiding catheter immediately before the thrombectomy; a subsequent DSA control was done to confirm the arterial occlusion and the localization of the clot. The ADAPT technique was performed in the arterial models ICA_{ADAPT} and M1_{ADAPT} (Fig. 1b) with the Neuron MAX delivery catheter, an ACE68 aspiration catheter, and the Penumbra aspiration pump. Mechanical thrombectomy was performed in the arterial models ICA_{SO}, ICA_{TR}, ICA_{ET}, M1_{SO}, M1_{TR}, and M1_{ET} with the Neuron MAX delivery catheter, a PXSlim microcatheter (Penumbra), a Syncro 2 microguide (Stryker), and different SRs: Solitaire revascularization device (SO) (Medtronic) 6 × 20 mm for ICA_{SO} and 4 × 20 mm for M1_{SO}, Trevo ProVue Retrieval System (TR) (Stryker Neurovascular) 6 × 25 mm for ICA_{TR} and 4 × 20 mm for M1_{TR}, and EmboTrap (ET) (Neuravi, Ireland) 5 × 21 mm for both ICA_{ET} and M1_{ET}. A single attempt was made for each of the procedures and was conducted according to the manufacturers' instructions and clinical practice. In the majority of the cases a TICI 3 score were obtained (Table 2).

Histological Analysis

After euthanasia, arterial segments were sectioned for the purpose of analysis by optical and electron microscopy, according to the criteria reported in Figure 2: ICA_{ADAPT}, the tract of the right ICA between the distal tip of the aspiration catheter (which was in contact with the clot) and the delivery catheter, in C02; M1_{ADAPT}, the main branch of the right thyrocervical trunk, between the distal tip of the aspiration catheter and the origin of the vessel, in C02; ICA_C, the tract of the right ICA distal to the clot, in C02; M1_C, the main branch of the right thyrocervical trunk, distal to the clot, in C02; ICA_{SO} and M1_{SO}, respectively, the right ICA and the main branch of the right thyrocervical trunk, from the point at which the stent was released to the distal tip of the delivery catheter, in C01; ICA_{TR} and M1_{TR}, respectively, the left ICA and the main branch of the left thyrocervical trunk, from the point at which the stent was released to the distal tip of the delivery catheter, in C01; ICA_{ET} and M1_{ET}, respectively, the left ICA and the main branch of the left thyrocervical trunk, from the point at which the stent was released to the distal tip of the delivery catheter, in C02. Five tissue samples were taken from each artery; the distal and the proximal portion of each sample were embedded in paraffin 4% and sent to optic microscopy study, and the central portion was embedded in paraffin 1% and sent to electron microscopy study (Fig. 1b). Both the histological analysis and the scanning electron microscopy were performed and reviewed by independent pathologists.

Results

Optical and electron microscopy of the tissue samples revealed changes to the arterial walls (Table 1).

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Fig. 1. **a** Superficial markers of arterial samples. **b** The ADAPT technique in swine model C02; arterial segment in red. The portion between the white lines was sent to electron microscopy analysis. **c** Retroperitoneal hematoma in swine model C02. **d** Initial study protocol. ICA_{ADAPT}, ICA segment in which ADAPT was performed; ICA_C, ICA control; ICA_{ET}, ICA segment in which EmboTrap was used; ICA_{SO}, ICA segment in which Solitaire was used; ICA_{TR}, ICA segment in which Trevo was used; M1_{ADAPT}, M1 segment in which ADAPT was performed; M1_C, M1 control; M1_{ET}, M1 segment in which EmboTrap was used; M1_{SO}, M1 segment in which Solitaire was used; M1_{TR}, M1 segment in which Trevo was used.

Optical Microscopy

ICA_C. Focal endothelial denudation with attached erythrocytes and focally exposed internal elastic lamina (IEL); the endothelium was extremely flat; the IEL was wavy, fragmented, and seemed to overlap in points with the more superficial elastic membrane (EM) of the tunica media. In the tunica media, the smooth muscle cells (SMCs) appeared disrupted, with increased cytoplasmic eosinophilia and nuclear condensation, the EM little evident throughout the section of the wall, and the external elastic lamina (EEL) seemed discontinuous probably due to postoperative handling.

M1_C. The endothelium appeared flat, the IEL wavy, focally fragmented, with few represented EM, the SMCs disrupted, with increased cytoplasmic eosinophilia and nuclear condensation, and the EEL discontinuous.

Fig. 2. Vascular wall composition in humans: intracranial versus extracranial vessels. EEL, external elastic lamina; IEL, internal elastic lamina.

Fig. 3. **a** ICA_C sample. **b** M1_{S0} with absent endothelial layer, thickened subendothelial space, exposed IEL (red arrow), and thickened EEL (white arrow). **c** ICA_{ET} with thickened endothelial layer and subendothelial space (ellipse). **d** M1_{ET} with degenerated and thickened EM. **e** M1_{TR} with fragmented IEL (arrow), thickened EM, and fragmented EEL (ellipse). **f** M1_{ET} with mononuclear infiltrates into the endothelial layer (arrows). EEL, external elastic lamina; EM, elastic membrane; ICA_C, ICA control; ICA_{ET}, ICA segment in which EmboTrap was used; IEL, internal elastic lamina; M1_{ET}, M1 segment in which EmboTrap was used; M1_{S0}, M1 segment in which Solitaire was used; M1_{TR}, M1 segment in which Trevo was used.

ICA_{ADAPT}. In all samples the endothelium appeared extremely flat, the IEL had lost its wavy appearance, was thin and fragmented (Fig. 3). The EM was thick and very evident; in the medium tunica there was a lax and basophilic matrix with thick nonundulating EM and the SMCs not very evident. The EEL appeared discontinuous, and intersects with the EM in the deep edge of the tunica media and an adventitial perivascular mononuclear inflammatory infiltrate were evident.

M1_{ADAPT}. Endothelium appeared extremely thin, focally discontinuous, and the subendothelial space had a lax appearance. The IEL was confused with the more superficial EM. In the tunica media, the luminal part was basophilic lax material in the stroma, and SMCs had lost cytoplasmic eosinophilia and characteristic packing; the EM appeared thick, while the EEL was focally discontinuous.

ICA_{SO}. The endothelial layer appeared normal, while the IEL was wavy and focally fragmented. In the tunica media, the EM was displayed thin, wavy, and scattered. The EEL appeared thin, wavy, and interrupted in some points.

M1_{SO}. Focal invagination of the endothelial layer, with white blood cells and foreign material adhering, that appeared partially denudated (Fig. 3a); the IEL was exposed; the tunica media had a thick EM and at the edge crisscrossed with the adventitia. The EEL was clearly similar to the EM.

ICA_{TR}. Focal thickening of the inner lamina was observed. The IEL was wavy but focally fragmented. In the tunica media, the EM was very thin, wavy, and scattered; the EEL appeared discontinued.

M1_{TR}. Subendothelial focal thickening was observed (Fig. 3d). The IEL was thick, with multiple foci of fragmentation; the EM of the tunica media also appeared thick and at the deep edge mixed with the EEL.

ICA_{ET}. A very flattened endothelium, detached at some points, was observed (Fig. 3b). The subendothelial space was focally thickened. The IEL was wavy and focally discontinuous. The EM of the tunica media appeared scattered and thin; basophilic lax material within the stroma was observed, and SMCs were little packed. The EEL was thin and discontinuous.

M1_{ET}. The endothelium was very flattened, the subendothelial space was focally thickened, and the IEL appeared fragmented, confused with the superficial EM of the tunica media (Fig. 3c). In the tunica media a basophilic matrix was evident within the stroma, the SMCs were focally disorganized, and the EM was thickened. The EEL was thin and discontinuous at various points.

Electron Microscopy (Fig. 4)

ICA_C. The vascular surface maintained the longitudinal direction of the blood vessel, with some spaces between endothelial cells, partially covered by platelets and fibrin filaments (Fig. 4a).

M1_C. The vascular surface appeared regular and maintained the longitudinal direction of the blood vessel.

ICA_{ADAPT}. An endothelial orientation was maintained, but with discontinuities between the cells. This denudation seemed to be partially covered by cell processes and fibrin filaments.

M1_{ADAPT}. Marked disruption of the vascular surface with filamentous or fibrillar appearance; there were no appreciable endothelial cells. Pores and some platelets were evident (Fig. 4b).

ICA_{SO}. The vascular surface maintained the longitudinal direction of the blood vessel, but was irregular, with variable cellular dimensions, focal intercellular spaces exposed, and platelets dispersed.

Fig. 4. **a** ICA_C with regular endothelial surface. **b** M1_{ADAPT} with an irregular endothelial surface superficial pores (thin arrows) and some filamentous material at the surface (thick arrows). **c** M1_{SO} with the vascular surface distorted and irregular and with denudation covered by cellular processes (arrows). **d** ICA_{TR} with irregular endothelial cells with variable dimensions and intercellular spaces, possible tissue desquamation or processing artifacts, and few scattered adhered platelets. The vascular surface maintains the longitudinal direction of the blood vessel but seems distorted, with intercellular spaces (thin arrow), possible scaling of tissue or processing artifacts (thick arrows), and scarce dispersed plaques adhere. ICA_C, ICA control; ICA_{TR}, ICA segment in which Trevo was used; M1_{ADAPT}, M1 segment in which ADAPT was performed; M1_{SO}, M1 segment in which Solitaire was used.

M1_{SO}. The vascular surface appeared distorted and irregular, with focal denudation, covered by cellular processes (Fig. 4c).

ICA_{TR}. The vascular surface maintained the longitudinal direction of the blood vessel, but seemed distorted, with focally exposed intercellular spaces, probably scaling of tissue or processing artifacts, and scarce dispersed adhered plaques (Fig. 4d).

M1_{TR}. The vascular surface maintained the longitudinal direction of the blood vessel and seemed regularly thickened. The endothelium appeared continuous.

ICA_{ET}. The vascular surface maintained the longitudinal direction of the blood vessel, but seemed irregular with some spaces between endothelial cells. Platelets and some erythrocytes on the surface were evident.

M1_{ET}. The vascular surface appeared markedly disorganized, with filamentous or fibrillar aspect, tissue waste, and platelet aggregates.

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Table 3. Comparison between acute and delayed damages of the arterial vascular wall

Arterial model	Endothelial damage		Damage to the internal elastic lamina		Damage to the tunica media/adventitia	
	acute	delayed	acute	delayed	acute	delayed
ICA _C	no	+ (flat endothelial layer)	no	+ (discontinuous)	no (thickened EMs)	no (thickened EMs)
M1 _C	no	+ (flat endothelial layer)	no	+ (thin and focally discontinuous)	no (thickened EMs)	no (thickened EMs)
ICA _{S0}	+++ (endothelial layer absent)	no	+++ (thickened)	++ (focally fragmented)	+++ (altered elastic fibers)	+++ (thin, wavy, and scattered EMs and EEL)
M1 _{S0}	+++ (endothelial layer absent)	+++ (endothelial layer absent, thickened subendothelial space)	+++ (thickened)	+++ (exposed and focally fragmented)	+++ (degenerated elastic fibers)	+++ (thickened EMs, thickened and discontinuous EEL)
ICA _{ADAPT}	no	+ (flat endothelial layer)	no	+ (thin and focally fragmented)	+ (focal elastic fiber alterations)	+ (thickened EMs)
M1 _{ADAPT}	+ (focal denudation)	++ (extremely flat endothelial layer, lax subendothelial layer)	no	+ (flat)	++ (some elastic fiber alterations)	+ (thickened EMs)

Red: the structure was severely damaged; yellow: the structure was moderately damaged; green: the structure was slightly damaged. EEL, external elastic lamina; EMs, elastic membranes; ICA_{ADAPT}, ICA segment in which ADAPT was performed; ICA_C, ICA control; ICA_{S0}, ICA segment in which Solitaire was used; M1_{ADAPT}, M1 segment in which ADAPT was performed; M1_C, M1 control; M1_{S0}, M1 segment in which Solitaire was used.

Discussion

The publication of recent trials about the positive results of mechanical thrombectomy in terms of recanalization rate and outcome [3, 4], represented a starting point for the introduction of a variety of devices available for neurointerventionists to perform this type of treatment. At the same time, there were the enrichment of the well-demonstrated SR technique with new SRs and the evolution of a new technique (ADAPT), based on the use of large-bore catheters to suck blood clots [1, 5]. Both methods have been shown to be effective with regards to revascularization and improving the patients' clinical outcomes [1], but little is known about the exact mechanism of arterial injury caused by these procedures. Assessment of the delayed evolution of vascular damage was performed by Kurre et al. [6], using DSA follow-up to evaluate the decrease in arterial diameter at the level at which the thrombectomy was performed, and by Power et al. [7] who, using MRI, observed arterial wall thickening in the treated part of the vessel. However, to our knowledge no study has compared the delayed histopathological and ultrastructural effects induced by SRs and ADAPT.

Yuki et al. [8] first described the normal histological characteristics of porcine extracranial arteries, offering the possibility of evaluating pathological lesions. Recently, based on initial studies about this topic [9], we published a paper about the acute vascular wall damage caused by the ADAPT technique versus the SR technique, demonstrating that although both techniques cause various vascular injuries, SRs produce much more aggressive damage to the endothelium and tunica media in the acute phase [2].

On this background, we designed an animal model to assess the delayed vascular wall alterations after mechanical thrombectomy treatment, comparing the ADAPT technique with Penumbra catheters (Penumbra) and the SR technique with three devices: Solitaire (Medtronic), Trevo (Stryker, The Netherlands), and EmboTrap (Neuravi). It was shown that both techniques, in different way, cause alterations to the structure of the vessel wall (Table 1); in detail, it was observed that the main damages were localized at the level of the tunica media and adventitia, instead of the tunica intima as reported in the acute phase (Table 3).

There was severe damage to the tunica intima with almost complete denudation of the endothelium together with thickening of the subendothelial space in the vessels treated with the Solitaire and EmboTrap devices ($M1_{SO}$, ICA_{ET} , $M1_{ET}$); strangely, this severe damage shown in the $M1_{SO}$ model was not confirmed in the ICA_{SO} model, in which no damage was found (Table 1). Maybe it happened because Solitaire 4×20 mm, which was used in an M1 model, has a greater radial force density than Solitaire 6×20 mm, which was used in an ICA model (0.00448 vs. 0.00351 N/mm). ICA_{TR} and $M1_{TR}$ showed similar results. In ET models, there was thickening of the subendothelial space, but only in ICA_{ET} and $M1_{ET}$ there was involvement of the endothelial layer, with altered shape of endothelial cells; this could just be related to biological interindividual differences. In no ADAPT sample hypertrophy of the subendothelial space was found (Table 1).

The IEL resulted seriously damaged in three SRs samples, as reported in the acute phase [2]: it was exposed and focally fragmented in $M1_{SO}$, thickened and fragmented in $M1_{TR}$, and wavy and fragmented in ICA_{ET} (Table 1). Lesions at this level are very important for intracranial arteries, because as reported by Ritz et al. [10], they are muscular-type arteries that generally exhibit a thicker and denser IEL and do not have an EEL. The EEL is still present in the petrous portion of the ICA, but disappears within the cavernous portion, which forms a hotspot of stenosis.

As stated above, the tunica media and the adventitia were the major layers affected, resulting seriously damaged in almost all samples: only $M1_{ADAPT}$ showed slight damages with

a thickened and discontinuous EEL. The EM resulted altered in all samples in which SRs were used: thickened in all M1 samples and thin, wavy, and scattered in all ICA samples.

Evaluation of the vascular wall surface with electron microscopy did not show significant differences between the ADAPT and SR techniques in the delayed phase; complete endothelial denudation at 15 days was reported only in M1₅₀. This study confirms that different early damages have different evolutions: the extent and depth of a vascular lesion may be contributing factors in promoting early atherosclerotic and accelerated hyperplastic intimal and medial changes [6]; indeed, large areas of endothelial denudation without substantial medial trauma caused only mild intimal thickening, whereas focal endothelial denudation with substantial medial trauma produced marked delayed intimal thickening [11]. As reported by Power et al. [7], the pattern of concentric arterial wall thickening and enhancement of the vascular wall observed at MRI in patients treated with mechanical thrombectomy is similar to the MRI appearance of inflammatory conditions such as primary central nervous system vasculitis, due to endothelial denudation with inflammation of the tunica media, as seen in optic microscopy of some arterial samples.

Given these results, in the delayed phase both techniques seem to be traumatic to the vascular wall, with different damages to all three layers. Interestingly, it is clear that damages observed in the endothelial layer recover faster, considering that in almost all samples the endothelial surface was evident. It is known that within the first 24 h following denudation the replication cycle starts, from the leading edge of the denuded area and from the ostia of collateral arteries, to restore endothelial continuity, ceasing 3–6 weeks later, depending on the entity of vascular damage. The mechanisms leading to neointimal hyperplasia are not known, but it was observed that deep injury to the media with limited endothelial cell loss and re-endothelialization within a few days may also induce intimal thickening mechanisms [12].

Limitations

This study's main limitations consist in the small size of the sample, but the aim of this study was just a preliminary experience; it was not possible to obtain a sufficiently large number of samples to be able to perform a statistical analysis. The anatomical limitations of this study are the ultrastructural composition of the swine model vascular wall [8]. The arteries of the human intracranial circulation have a much thinner adventitia and do not have an elastic lamina between this and the muscle layer [13]. Additionally, human intracranial arteries are known to have thinner vessel walls and a lower wall:lumen ratio than the small arteries in other parts of the human body [8, 13]. Like in the previous study, we analyzed the delayed damage to the vessel wall after a single attempt at clot removal, and probably there is a correlation between the number of passages and vascular wall damage.

Conclusions

In this animal model, we found that both ADAPT and SR devices, in different ways, caused damage to the vascular wall, particularly at the level of the tunica media and adventitia. The involvement of the tunica media associated to focal endothelial denudation causes marked delayed intimal thickening whose chronic effects need to be studied. Further investigation with eventually concomitant MRI study are required to better understand the cause and effect relationship between thrombectomy maneuvers and tissue reaction/damage observed in treated arteries.

Statement of Ethics

All procedures were conducted in accordance with international guidelines as well as the ARRIVE guidelines and were approved by the responsible local authorities.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

S. Peschillo: conception and design, data analysis, data interpretation; S. Peschillo, F. Diana: data acquisition, drafting of the manuscript; F. Diana: literature review; M. Rosal-Fontana, M. Esteves Coelho: animal lab support; A. Tomasello, D. Hernandez: manuscript oversight. All authors critically reviewed the manuscript and approved its final submission.

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