Ann Vasc Dis Vol. 17, No. 4; 2024; pp 389–395
Online October 23, 2024
doi: 10.3400/avd.oa.24-00044

Original Article

Feasibility and Clinical Outcomes of Vasa Vasorum Embolization for Atypical Type 2 or Type 5 Endoleaks after Endovascular Aneurysm Repair

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Objectives: The purpose of this study is to evaluate the feasibility and clinical outcomes of vasa vasorum embolization for preventing continuous aneurysmal expansion after endovascular aneurysm repair (EVAR).
Methods: We retrospectively reviewed the medical records of patients who underwent vasa vasorum embolization between August 2018 and May 2022. Vasa vasorum embolization was attempted in cases of continuous aneurysmal expansion after EVAR, where the vasa vasorum was identified through catheter angiography. The vasa vasorum was accessed and embolized with a microcatheter. The outcomes of vasa vasorum embolization were evaluated based on technical success, defined as the successful completion of the embolization procedure, and clinical success, defined as the prevention of continuous aneurysmal expansion after the embolization.
Results: Seven cases of endoleak with developed vasa vasorum were confirmed by catheter angiography. The mean age was 83.7 years, and the mean aneurysmal diameter was 60.6 mm. Technical success was achieved in 6 cases, while clinical success was not achieved in any of the cases. The mean observation period was 16.5 months, and the mean increase in aneurysmal diameter was 9.7 mm.
Conclusions: Although the vasa vasorum embolization is a technically feasible procedure, it is not effective in preventing continuous aneurysmal expansion.

Keywords: vasa vasorum, embolization, EVAR, endovascular

Introduction

Endovascular aneurysm repair (EVAR) is a widely accepted treatment option for managing abdominal aortic aneurysm (AAA) alongside traditional open surgical repair. Although EVAR is considered beneficial for its minimally invasive nature, its long-term result is less favorable due to the continuous aneurysmal expansion associated with endoleaks.[1)]

Type 2 endoleak (T2EL) can be subdivided into conventional T2EL and atypical T2EL, based on the appearance of contrast enhancement area within the aneurysmal thrombus on contrast-enhanced computed tomography (CECT).[2)] Conventional T2EL is marked by a clearly demarcated contrast enhancement area within the aneurysmal thrombus with a connection to inflow arteries. By contrast, atypical T2EL is characterized by the heterogeneous contrast enhancement within the aneurysmal thrombus without a clear connection to inflow arteries. Type 5 endoleak (T5EL), characterized by continuous aneurysmal expansion without a detectable leak in the aneurysmal thrombus on imaging, has been under discussion regarding its pathophysiological mechanism. One potential mechanism of T5EL includes blood inflow into the aneurysmal thrombus, which is difficult to detect by current imaging technologies.[3)]

Vasa vasorum is a tiny network-like blood vessel around the vascular wall, responsible for supplying blood to nourish the vascular wall. The development of the vasa vasorum after EVAR has recently been highlighted, and the past case series have demonstrated a direct relationship

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Received: April 25, 2024; Accepted: September 29, 2024
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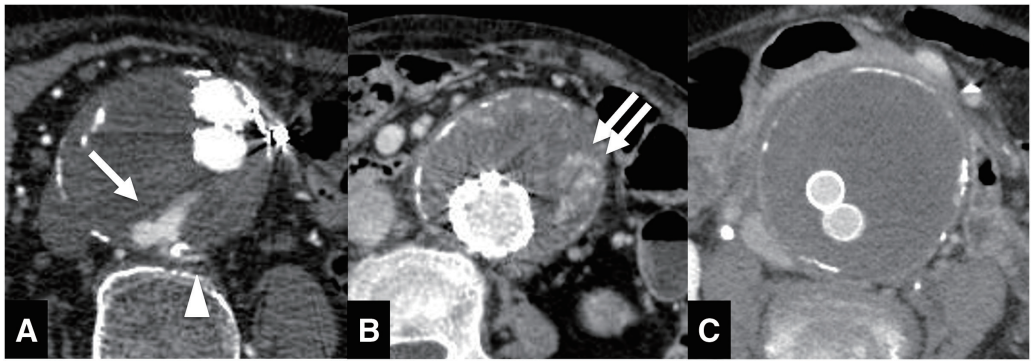

Fig. 1 CT images of different types of endoleaks. (**A**) Conventional type 2 endoleak: Early phase CECT reveals well-demarcated contrast enhancement within the aneurysmal thrombus (arrow), along with a clear connection to inflow and outflow arteries (arrowhead). (**B**) Atypical type 2 endoleak: delayed phase CECT shows heterogeneous contrast enhancement within the aneurysmal thrombus (double-arrow). (**C**) Type 5 endoleak: CECT displays no detectable contrast enhancement within the aneurysmal thrombus despite continuous expansion of the aneurysm after EVAR. CECT: contrast-enhanced computed tomography; EVAR: endovascular aneurysm repair

between the developed vasa vasorum and atypical T2EL through angiography achieved by catheterization of these vessels.[2)]

We hypothesized that blood flow into the aneurysmal thrombus from the developed vasa vasorum may be the primary cause of continuous aneurysmal expansion after EVAR in cases of atypical T2EL and even T5EL. If this hypothesis is correct, blocking blood flow through the vasa vasorum could effectively prevent continuous aneurysmal expansion after EVAR in such cases. This study aims to evaluate the feasibility and clinical outcomes of the vasa vasorum embolization in cases of atypical T2EL and T5EL.

Materials and Methods

This study was a retrospective, single-center study that reviewed the medical records of patients who underwent attempts at the vasa vasorum embolization between August 2018 and May 2022. The vasa vasorum embolization was indicated in cases of atypical T2EL and T5EL with continuous aneurysmal expansion after EVAR, where the developed vasa vasorum was identified through catheter angiography. This study was approved by the Institutional Review Board of Saitama Medical University International Medical Center (Approval number: 2023-054).

Definition of atypical T2EL and T5EL

All endoleaks after EVAR were checked by CECT images in both early and delayed phases. Conventional T2EL was defined as well-demarcated contrast enhancement within the aneurysmal thrombus in early phase CECT, along with a clear connection to the major branches of the abdominal aorta, such as the lumbar and inferior mesenteric arteries (IMAs; **Fig. 1A**). Atypical T2EL was defined as heterogeneous enhancement within the aneurysmal thrombus in delayed phase CECT without clear connection to the major branches in abdominal aorta (**Fig. 1B**). T5EL was defined as the absence of detectable contrast enhancement within the aneurysmal thrombus despite continuous expansion of the aneurysm after EVAR (**Fig. 1C**).

Angiography and embolization procedure

Sheaths and catheters were inserted into the common femoral artery. Initially, an aortogram was obtained by contrast injection through the pig-tail catheter positioned at the level of the proximal edge of the main body of the stent graft. Subsequently, the major branches of the abdominal aorta were accessed by the microcatheters to search the developed vasa vasorum around the AAA.

If the developed vasa vasorum was found by the angiography, the microcatheter was advanced into the vasa vasorum for embolization. The embolization was achieved by coiling or glue injection (**Fig. 2**). Glue was prepared by mixing N-butyl cyanoacrylate and ethiodized oil (Lipiodol; Guerbet Japan, Tokyo, Japan).

Evaluation items

Technical success was assessed based on the procedural success or failure of inserting the microcatheter into the developed vasa vasorum and its subsequent embolization. The successful embolization was defined as the disappearance of the vasa vasorum on the angiogram following the embolization. Clinical success was assessed based on the change in aneurysmal diameter during the follow-up period after the embolization. The aneurysmal diameter measurements were obtained using non-contrast CT or CECT images.

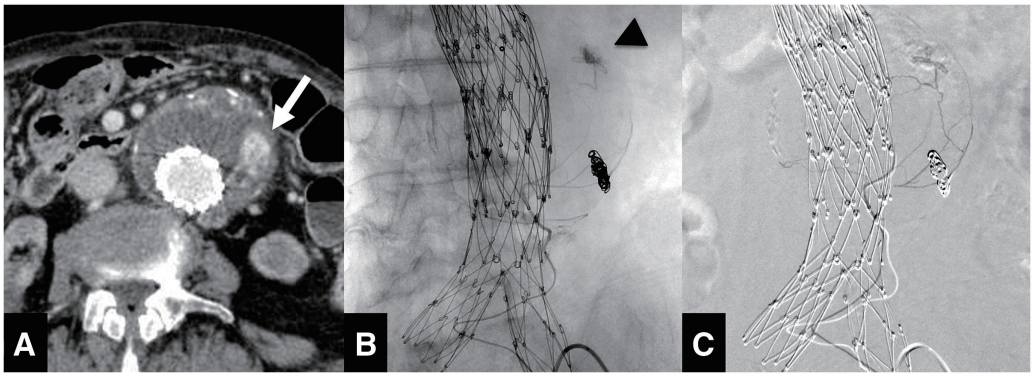

Fig. 2 Vasa vasorum embolization for atypical T2EL. (**A**) Delayed phase CECT showed atypical T2EL characterized by heterogenous enhancement in the aneurysmal thrombus (arrow). (**B**) Catheter angiography displayed a network-like structure of the vasa vasorum, originating from the left common iliac artery and encircling the aneurysmal wall. The enhanced area on the angiography (arrowhead) corresponded to the enhanced area observed on CECT. (**C**) The vasa vasorum was successfully embolized with glue injected through the microcatheter. T2EL: type 2 endoleak; CECT: contrast-enhanced computed tomography

Table 1 Patients' characteristics

Case number	Age/sex	Aneurysm diameter before EVAR (mm)	Endograft type	Antithrombic therapy
1	79, male	54	Zenith	Edoxaban
2	89, male	41	Zenith	No
3	75, male	54	Endurant	No
4	86, female	50	Endurant	No
5	91, female	46	Aorfix	No
6	80, male	43	AFX	No
7	86, male	41	AFX	No

EVAR: endovascular aneurysm repair

Table 2 The result of the vasa vasorum embolization

Case number	Types of endoleak	Origin of vasa vasorum	Technical success in embolization	Embolization material	Aneurysm diameter (mm)		Observation period (month)	New type endoleak after embolization	Additional treatment after embolization
					Before embolization	After embolization			
1	aT2EL	IMA	Success	Glue	63	81 (rupture)	8	1a + 1b	LOC
2	aT2EL	IMA	Success	Glue	61	67	18	No	Follow-up
3	T5EL	IMA	Success	Glue	59	67	15	No	LOC
4	aT2EL	IMA	Success	Coils	56	63	19	1b + 3b	EVAR
5	T5EL	IMA	Failure	–	76	–	–	–	–
6	T5EL	LA	Success	Glue	52	68	31	No	LOC
7	aT2EL	CIA	Success	Glue	57	60	8	3b	EVAR

aT2EL: atypical T2EL; T5EL: type 5 endoleak; IMA: inferior mesenteric artery; LA: lumbar artery; CIA: common iliac artery; LOC: late open conversion; EVAR: endovascular aneurysm repair

Results

Seven cases of attempts at the vasa vasorum embolization were enrolled in this study, and patient characteristics are presented in **Table 1**. The mean age was 83.7 years, and the aneurysmal mean diameter before EVAR was 47.0 mm. One patient was treated with an anticoagulant agent, while the other patients had no history of antiplatelet and anticoagulation therapy. The implanted stent-graft for EVAR included Zenith (Cook Medical, Bloomington, IN, USA) in 2 cases, Endurant (Medtronic, Minneapolis, MN, USA) in 2 cases, Aorfix (Lombard Medical, Oxfordshire, UK) in 1 case, and AFX (Endologix, Irvine, CA, USA) in 2 cases. The IMA was embolized with coils during the initial EVAR operation in 2 cases. The lumbar artery (LA) was neither catheterized nor embolized with coils during the initial EVAR in any case.

Table 2 presents the data before and after vasa vasorum embolization. The aneurysmal mean diameter before

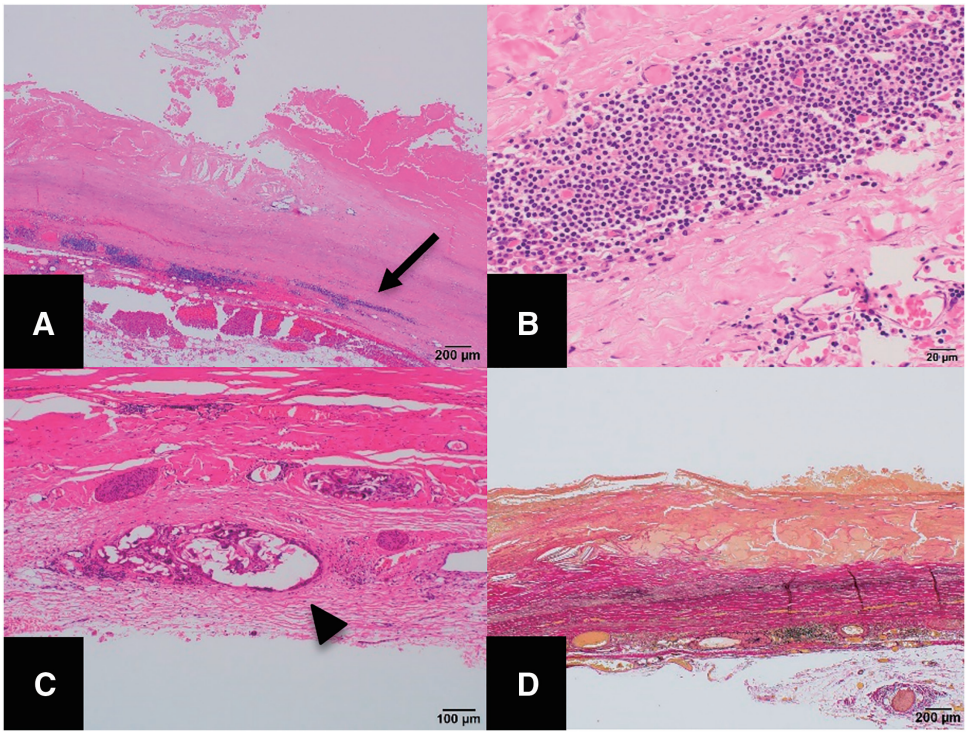

Fig. 3 Microscopic examination of the aneurysmal wall after the vasa vasorum embolization and late open conversion with HE staining and GVH staining. (**A** and **B**) Lymphocyte infiltration (arrow) is observed in the tunica media and adventitia of the aneurysmal wall. (**C**) Reactive granulation tissue (arrowhead), likely induced by the injection of the glue, is found within the lumen of the developed vasa vasorum. (**D**) A remarkable thinning of the tunica media in the aneurysmal wall is noted, along with a significant loss of elastin fibers and smooth muscle cells. HE: hematoxylin and eosin; GVH: Gomori's Van Gieson

embolization was 60.6 mm. Four cases were categorized as atypical T2EL, while 3 cases were T5EL. The vasa vasorum originated from the IMA in 5 cases, the LA in 1 case, and the common iliac artery in 1 case. The vasa vasorum from the IMA was connected to the distal segment of the IMA in 3 cases, and to the transitional segment between the IMA and the left colic artery in 2 cases. In the case involving the vasa vasorum from the LA, it was connected to the proximal segment of the LA near the aortic aneurysm.

Technical success was achieved in 6 out of 7 cases. In 1 case, the embolization procedure failed despite the successful visualization of the developed vasa vasorum, due to minor vascular dissection when navigating the microcatheter. The embolization was achieved by glue injection in 5 cases and coiling in 1 case. A double coaxial microcatheter system was used in 5 cases, while a single microcatheter system was in 2 cases. The mean time between the initial insertion of the sheath into the femoral artery and the first recognition of the vasa vasorum supplying the aneurysmal wall was 118.9 minutes (range: 14–277 minutes). The time from the first recognition of the vasa vasorum to its catheterization averaged 26.2 minutes (range: 3–98 minutes). The total procedure time was 185.2 minutes (range: 67–343 minutes).

Clinical success was not achieved in any of the cases despite the successful embolization of the developed vasa vasorum. The mean observational period and increase in aneurysmal diameter after the embolization were 16.5 months and 9.7 mm. In 1 case, an aneurysm ruptured 8 months after the embolization. Additional treatment for continuous aneurysmal expansion, including either further EVAR or late open conversion, was performed in 5 cases after the embolization. The indication of additional EVAR in 2 cases was the emergence of new type endoleaks, besides existing atypical T2EL. The late open conversion was performed for 2 cases of T5EL with continuous aneurysmal expansion. Additionally, the ruptured case, which encountered a newly arisen type 1 endoleak, was also treated with emergent open surgery.

Pathological specimens of the aneurysmal wall after the vasa vasorum embolization were acquired in cases where the late open conversion was performed afterward (**Fig. 3**). These specimens revealed a significant increase in both the number and size of the vasa vasorum within the aneurysmal wall. Additionally, reactive granulation tissues were noted in some of these vasa vasorum, whereas others remained intact without any observational change. The aneurysmal wall exhibited a remarkable decrease in

the thickness of the tunica media with a significant loss of elastin fibers and smooth muscle cells. Furthermore, lymphocyte infiltration was observed within tunica media and adventitia of the aneurysmal wall.

Discussion

This study demonstrates that selective catheterization and embolization of the developed vasa vasorum with a microcatheter is a feasible procedure. However, it also indicates that the vasa vasorum embolization is not effective in preventing continuous aneurysmal expansion after EVAR.

The vasa vasorum is typically invisible under normal conditions because it is a remarkably tiny vascular network around the vessel wall. There have been very few case reports where the vasa vasorum was visualized by the catheter angiography.[4,5] However, in our study, the vasa vasorum around the aneurysmal wall was clearly visualized by catheter angiography because the diameter of the vasa vasorum was sufficiently enlarged to be detected by the angiography. The development of the vasa vasorum after stent-graft placement has been reported in both experimental and clinical settings, confirmed by microscopic observation on aortic walls.[6,7] The exact mechanism of its development remains unknown, but the hypoxic condition in the aortic wall after the stent-graft placement might be closely associated with the development of the vasa vasorum.[6] There are 2 pathways for oxygen transport to the aortic wall: the inner layers receive oxygen through direct diffusion from the luminal blood flow, while the outer layers are perfused with blood via the adventitial vasa vasorum.[8] Stent-graft placement and subsequent formation of aneurysmal thrombus possibly reduce the oxygen diffusion from the luminal blood flow, resulting in the compensatory development of the vasa vasorum due to the hypoxic condition in the aneurysmal wall.

The development of the vasa vasorum contributes not only to its visualization by catheter angiography but also to its catheterization and subsequential embolization by microcatheters. Technological and technical advancements in microcatheters, such as the double coaxial microcatheter system, have enabled the catheterization of small vessels by navigating tortuous arterial routes during the embolization procedure for endoleaks.[9] Although there have been only a few case reports demonstrating the successful catheterization of the vasa vasorum,[2] our research serves as additional evidence for the feasibility of its catheterization.

Contrary to our hypothesis, the blockade of the blood flow from the vasa vasorum into the aneurysmal thrombus, achieved by the embolization procedure via the microcatheter, did not effectively prevent continuous aneurysmal expansion. A past case report, where the vasa vasorum embolization was performed as the treatment for the continuous expansion of AAA after EVAR, also indicated ineffective clinical outcomes.[10] The precise reason for this ineffectiveness remains unclear, but several potential mechanisms could be considered to explain this result.

First, the strength and integrity of the aneurysmal wall might be impaired by ischemic conditions caused by blocking blood flow from the vasa vasorum. The combination of stent-graft placement and the vasa vasorum embolization could potentially lead to severe hypoxia in the aneurysmal wall due to the loss of oxygen supply from both luminal blood flow and the vasa vasorum. Several studies have indicated that a hypoxic environment in the arterial wall is significantly responsible for the generation and progression of AAAs, primarily due to the loss of smooth muscle cells and elastin fibers within the tunica media.[11] Recent molecular biological studies have also demonstrated the increased production of hypoxia-inducible factor 1-alpha (HIF-1α), which is closely related to the hypoxic condition, and matrix metalloproteinases, which break down extracellular matrix components.[12] Thus, the vasa vasorum embolization after stent-graft placement may exacerbate hypoxic conditions in the aneurysmal wall, potentially promoting the mechanism of aneurysmal expansion.[13]

Second, the embolization procedure might not achieve a sufficient blockade of blood flow from the vasa vasorum. The vasa vasorum in the abdominal aorta originates from the mesenteric artery and LA, forming a complex network-like distribution around the aortic wall.[14] Given the intricate network of the vasa vasorum, it may be difficult to achieve a complete blockade of blood flow through coiling and glue injection. Indeed, histological investigation of the aneurysmal wall after the embolization in our study revealed a mixture of 2 types of the vasa vasorum: 1 type which was embolized and filled with reactive granulation tissues, and the other type maintaining luminal patency. If it is true that the blood flow from the vasa vasorum into the aneurysmal thrombus is responsible for the continuous aneurysmal expansion, then remaining blood flow in the vasa vasorum after the embolization would hinder its prevention. Embolizing the vasa vasorum from either the IMA or the LA may be insufficient to cease blood flow in the vasa vasorum on the aneurysmal wall because the remaining vessel could still supply blood to it, and vice versa.

Third, there might be no direct relationship between the continuous aneurysmal expansion and blood flow in the developed vasa vasorum. In our study, continuous aneurysmal expansion had already been observed before the vasa vasorum embolization, and this trend was sustained even after the embolization. Moreover, 3 out of 4 atypical

T2EL cases encountered newly emerged endoleaks, such as type 1 and 3, after the embolization. Given these outcomes, it seems rational to assume that these newly emerged endoleaks were the primary cause of continuous aneurysm expansion, rather than the blood inflow from the vasa vasorum. The concept of an occult endoleak, which includes delayed type 1 and 3 endoleaks not initially identified but discovered later, has sparked intense discussion due to its challenging diagnosis.[15] Early detection of the occult endoleak is difficult because they do not show clearly on current imaging technology. If the continuous aneurysmal expansion is caused by invisible blood inflow like occult endoleaks, rather than from the vasa vasorum, the aneurysm expansion would be continued regardless of the vasa vasorum embolization. Additionally, if this presumption is correct, the management of atypical T2EL should focus more on early and accurate detection of currently invisible blood inflow into the aneurysm.

Given the ineffective outcome of the vasa vasorum embolization, alternative treatment strategies should be explored for cases of atypical T2EL and T5EL. Surgical late open conversion is certainly 1 option for managing endoleaks with continuous aneurysmal expansion after EVAR, but high perioperative mortality was also reported in the previous studies.[16] The potential of pharmacotherapy for AAA, such as HIF-1α inhibitor and anti-inflammatory drugs, is currently being investigated, with the expectation of suppressing the pathogenetic process of aneurysmal formation.[17,18] The discovery in our study regarding the technical feasibility of catheterizing the developed vasa vasorum may lead to possible future treatment advancements by enabling direct drug delivery to the aneurysmal wall through the vasa vasorum.

Conclusion

Although vasa vasorum embolization is a technically feasible procedure, it is not effective in preventing continuous aneurysmal expansion.

Declarations

Acknowledgments

None.

Disclosure statement

The authors declare no conflicts of interest associated with this manuscript.

Author contributions

Study conception: MT, KN, YU
Data collection: MT
Analysis: MT, KN, YU, TS, NS
Research: MT, KN, YU
Manuscript preparation: MT
Critical review and revision: all authors
Final approval of the article: all authors
Accountability for all aspects of the work: all authors.

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