Lack of thrombus organization in nonshrinking aneurysms years after endovascular abdominal aortic aneurysm repair

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Objective: **During endovascular abdominal aortic aneurysm repair (EVAR), blood is trapped in the aneurysm sac at the moment the endograft is deployed. It is generally assumed that this blood will coagulate and evolve into an organized thrombus. It is unknown whether this process always occurs, what its time span is, and how it influences aneurysm shrinkage. With magnetic resonance imaging (MRI), quantitative analysis of the aneurysm sac is possible in terms of endoleak volume as well as unorganized thrombus volume and organized thrombus volume. We investigated the presence of unorganized thrombus in nonshrinking aneurysms years after EVAR.**

Methods: **Fourteen patients with a nonshrinking aneurysm without endoleak on computed tomography/computed tomography angiography underwent MRI with a blood pool agent (gadofosveset trisodium). Precontrast T1-, precontrast T2-, and postcontrast T1-weighted images (3 and 30 minutes after injection) were acquired and evaluated for the presence of endoleak. The aneurysm sac was segmented into endoleak, unorganized thrombus, and organized thrombus by interactively thresholding the differently weighted images. The classification was visualized in real-time as a color overlay on the MR images. The volumes of endoleak, unorganized thrombus, and organized thrombus were calculated.**

Results: **Median time after EVAR was 2 years (range, 1-8.2 years). The average aneurysm sac volume of the patients was 167 ± 107 mL (mean ± standard deviation). Nine patients had an endoleak on the postcontrast T1-w images 30 minutes after injection. On average, the aneurysm sac contained 78 ± 61 mL unorganized thrombus, which corresponded to 51 ± 21 volume-percentage, irrespective of the presence of an endoleak on the blood pool agent enhanced MRI images (independent *t*-test, $P = .8$).**

Conclusions: **In our study group, half of the nonshrinking aneurysm sac contents consisted of unorganized thrombus years after EVAR. (J Vasc Surg 2012;56:938-42.)**

The aneurysm size of patients after endovascular abdominal aortic aneurysm repair (EVAR) is closely monitored. Aneurysm shrinkage as well as the lack of aneurysm growth usually carries a good prognosis. In case of a growing aneurysm, rupture risk is increased. Many growing aneurysms are due to an endoleak. However, some aneurysms exhibit aneurysm growth without evidence of endoleak on computed tomography angiography (CTA) and delayed CT.[1-3] This phenomenon has been termed endotension. Different etiologies for endotension have been proposed, such as slow flow endoleak below the detection threshold of CTA, intermittent (eg, position-dependent) endoleak, or stent graft porosity.[4] Magnetic resonance imaging (MRI) is more sensitive for endoleak than CT.[5-10] Slow flow endoleaks and graft porosity can be diagnosed with MRI after injection of a blood pool contrast agent.[11-14] Images with blood pool enhancement can then be acquired as long as 60 minutes after injection.[15]

Prior to EVAR, there is a large interpatient variation in the presence of thrombus in the aneurysm and its degree of organization.[16] During endograft deployment, a certain amount of blood is trapped between the intra-aneurysmal thrombus and the endograft. It is generally assumed that this blood will coagulate and evolve into an organized thrombus. The time span in which this occurs as well as its influence on aneurysm shrinkage is unknown. The evolution of aneurysm sac contents is not monitored in the current, mostly CTA-based follow-up. In contrast, with MRI, visualization of thrombus organization is possible; unorganized thrombus has a high signal intensity on T2-weighted imaging, while thrombus organization leads to a decrease in signal intensity.[17] The changing appearance of the intra-aneurysmal thrombus in time has been described by Engellau et al.[18]

Recently, a new method for aneurysm sac monitoring with MRI has been described, which combines both the capabilities of MRI in terms of quantifying unorganized thrombus and in terms of endoleak imaging.[19] We used this

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method to investigate the presence of unorganized thrombus in nonshrinking aneurysms years after EVAR.

METHODS

Patients. Data from an institutional review board-approved study into the use of a blood pool contrast agent for the detection of slow flow endoleak were reviewed for this study.[11,12] Written informed consent was obtained from all participants. Fourteen patients with a nonshrinking aneurysm without endoleak on CT/CTA more than 1 year after EVAR with an MR-compatible endoprosthesis underwent MRI with intravenous administration of a blood pool contrast agent (gadofosveset trisodium, Vasovist; Bayer Healthcare, Berlin, Germany). The MRI examinations were conducted on a clinical 1.5-T MR scanner (Achieva; Philips Healthcare, Best, The Netherlands).

MRI acquisition. Transverse precontrast T1-weighted spin echo (repetition time [TR] 580 ms; echo time [TE] 14 ms; acquisition time 5.27 minutes), precontrast T2-weighted turbo spin echo (TR 6130 ms; TE 100 ms; echo train length 17; acquisition time 4.30 minutes), and postcontrast T1-weighted spin echo (as precontrast) acquisitions were acquired both 3 minutes (early postcontrast) and 30 minutes after injection (late postcontrast) with 3-mm slice thickness, no slice gap, 60 slices, field of view of 270 × 385 mm^2, a 179 × 256 acquisition matrix, voxel size 1.5 × 1.5 mm, covering the entire aortic aneurysm. A regional saturation slab was placed on the ventral abdominal wall to prevent ghosting artifacts from breathing. Phase-encoded arrhythmia rejection (PEAR; Philips Healthcare) was used to further minimize breathing artifacts.

Image analysis. Aneurysm volumes and the volumes of the intra-aneurysmal thrombus were measured with OsiriX (open source software, version 3.8.1, www.osirix-viewer.com) on the CTA data, which were acquired before EVAR. To correct for patient motion between the MRI sequences, all images were rigidly registered to the early postcontrast T1-w images using the Elastix software.[20] As a first step in the quantification of aneurysm sac contents, the aneurysmal thrombus was manually segmented from the level of the proximal attachment of the endograft to the native aortic bifurcation; iliac aneurysms were not included. A few voxels in the direct vicinity of the stent graft suffered from signal loss due to susceptibility artifacts.[21] These voxels were not included in the segmentation of the aneurysm sac. Then, the aneurysm sac voxels were classified based on the precontrast T1- and T2-weighted and late postcontrast T1-weighted images in the categories endoleak, unorganized thrombus volume, or organized thrombus volume. This was done interactively by thresholding the multispectral images relative to the signal intensity of fat according to the scheme shown in Table I. This method and its interobserver agreement were described earlier.[19] To eliminate interobserver variability, two observers classified the aneurysm sac voxels in consensus in this study. The volumes of all voxels in each category were calculated and expressed in milliliters.

Table I. Combination of signal intensities for the different categories used for voxel classification

	T1-weighted	*T2-weighted*	*T1-weighted postcontrast*
Endoleak	Low	Mostly high	High
Unorganized thrombus	Low/high	High	Same as precontrast
Organized thrombus	Low	Low	Low

The postcontrast images acquired 3 and 30 minutes after contrast injection were evaluated for the presence of endoleak by two experienced observers. In case of discrepant ratings, a third observer decided whether endoleak was present.[12]

The amount of unorganized thrombus in patients with and without evidence of endoleak on postcontrast T1-w images was compared with the independent *t*-test after normality was assessed with the Kolmogorov-Smirnov test. A P value $<.05$ was considered significant. Statistical analysis was performed using SPSS 16.0 (SPSS, Chicago, Ill).

RESULTS

The results of the individual patients are given in Table II. Example images are shown in Figs 1-3. The presence of unorganized thrombus was confirmed in patient 10, who had a large growing aneurysm containing a large volume of unorganized thrombus (Fig 1). In this patient, a CT-guided thrombin injection was performed, which was preceded by aspiration of aneurysm sac contents. Approximately 300 mL of blood was aspirated from the aneurysm sac, confirming the presence of unorganized thrombus.[22] In two patients, more than 70% of the aneurysm sac consisted of unorganized thrombus. The average aneurysm sac volume of all patients was 167 ± 107 mL. The average unorganized thrombus volume was 78 ± 61 mL, which corresponded to 51% ± 21% of aneurysm sac volume (Table III). In two patients, the aneurysm sac already had high signal intensity on the T1-weighted images before contrast injection (Fig 3). In nine patients, endoleak was visualized on the postcontrast images 30 minutes after injection.[11,12] In patients with endoleak, the mean unorganized thrombus volume was 71 ± 44 mL (52% ± 19% of aneurysm sac volume), which was not significantly different from 91 ± 89 mL (49% ± 26% of aneurysm sac volume) in patients without endoleak. The three growing aneurysms were larger than the stable aneurysms (303 ± 110 mL compared with 130 ± 72 mL; $P = .007$, independent *t*-test). Mean unorganized thrombus volume in patients with a growing aneurysm was 137 ± 112 mL (42% ± 29% of aneurysm sac volume) compared with 62 ± 32 mL (53% ± 19% of aneurysm sac volume) in patients with a stable aneurysm ($P = .4$, independent *t*-test).

DISCUSSION

Aneurysm sac contents after EVAR naturally change in time. Blood is trapped in the aneurysm sac during the

Table II. Individual patient results

Patient	*Gender*	*Age (years)*	*Preop AAA vol (mL)*	*Preop thrombus vol (mL)*	*Time after EVAR (years)*	*Endoprosthesis*	*Endoleak volume (mL)*	*Unorganized thrombus (%)*	*Size change*
1	M	82	151	19	1.9	OGE	16	74	Stable
2	M	73	177	80	1.3	Talent	≤1	51	Stable
3	F	70	NA	NA	8.0	EVT/Ancure	4	62	Stable
4	M	81	NA	NA	2.9	OGE	≤1	63	Stable
5	M	82	206	17	2.0	Talent	≤1	8	Growth
6	F	82	125	25	1.0	LPGE	0	79	Stable
7	M	71	289	199	1.9	Talent	11	44	Stable
8	M	58	313	211	2.9	OGE	23	44	Stable
9	M	76	NA	NA	8.2	Guidant AUI	6	61	Stable
10	M	90	413	207	1.0	Talent	0	56	Growth
11	M	76	152	66	1.0	Talent	0	39	Stable
12	M	81	175	48	3.1	Talent	0	9	Stable
13	M	62	197	0	2.0	Talent	27	62	Growth
14	M	79	180	103	0.9	Talent	0	61	Stable

EVT/Ancure (Guidant, Menlo Park, Calif); *Guidant AUI*, aorto-uniiliac Guidant (Guidant); *OGE*, Original Excluder (W. L. Gore, Flagstaff, Ariz); *Talent*, Talent endoprosthesis (Medtronic Vascular, Minneapolis, Minn).
Preop AAA vol represents the total aneurysm volume (including the lumen) before EVAR. Preop thrombus volume represents the thrombus volume measured on the preoperative CTA examination. In three patients, no digital preoperative CTA scan was available. The column endoleak volume represents endoleak volume measured on blood pool agent enhanced MRI images 30 minutes after injection. Unorganized thrombus is given as volume percentage of nonluminal aneurysm sac volume.

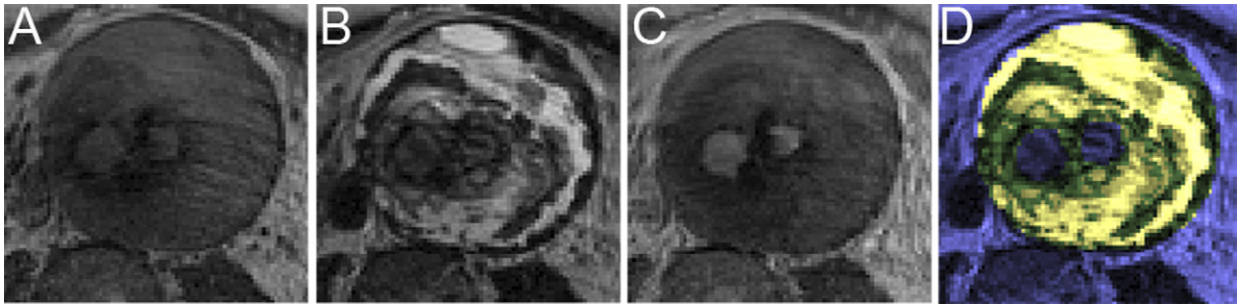

Fig 1. Transverse precontrast T1-w **(A)**, T2-w **(B)**, and T1-w 30 minutes **(C)** after injection of gadofosveset trisodium in patient with Talent endoprosthesis 1 year after endovascular abdominal aortic aneurysm repair (EVAR) (patient 10; Table II). The aneurysm of this 90-year-old patient increased 23 mm in diameter during 1 year without detectable endoleak. Voxel classification overlays are shown in **(D)**; *yellow* represents unorganized thrombus, *green* represents organized thrombus, and *blue* voxels are voxels outside the aneurysm sac. A large unorganized thrombus volume is visible in **(B),** which is *yellow* in **(D)**. Unorganized thrombus volume was 244 mL/56%; organized thrombus volume was 195 mL/44%; the volume of the aneurysm sac was 439 mL. The presence of unorganized thrombus was confirmed by aspiration of approximately 300 mL of blood from the aneurysm sac.

deployment of the endograft, which is assumed to coagulate and to evolve into an organized thrombus.

An improved understanding of the evolution of aneurysm sac contents may increase our insight in aneurysm size changes and endotension. A few studies have demonstrated the capabilities of MRI for assessment of aneurysm sac contents. Recently, a method for quantification of aneurysm sac contents with MRI has been developed. Based on the signal intensity on T1- and T2-weighted images and postcontrast T1-weighted images, the volumes of unorganized thrombus, organized thrombus, and endoleak in the aneurysm sac can be determined.[19]

We used this method in patients with nonshrinking aneurysms without evidence of endoleak on CTA. To reach the highest possible sensitivity for endoleak, we used a blood pool contrast agent and acquired postcontrast images after a long delay of 30 minutes. We found no significant relation between nonorganization of thrombus and endoleak; however, this could represent a type II error, due to a small number of patients.

Our results demonstrate that we do not yet fully understand the evolution of aneurysm sac contents in time. A far lower amount of unorganized thrombus would be expected after several years if the aneurysm sac merely represented an organizing thrombus. Perhaps these areas with high signal intensity on T2-weighted images represent a part of the aneurysm sac that will remain fluid and may never lead to thrombus. The use of anticoagulant medication could play a role. All our patients used acetyl salicylic acid (100 mg per day). Two patients used acenocoumarol.

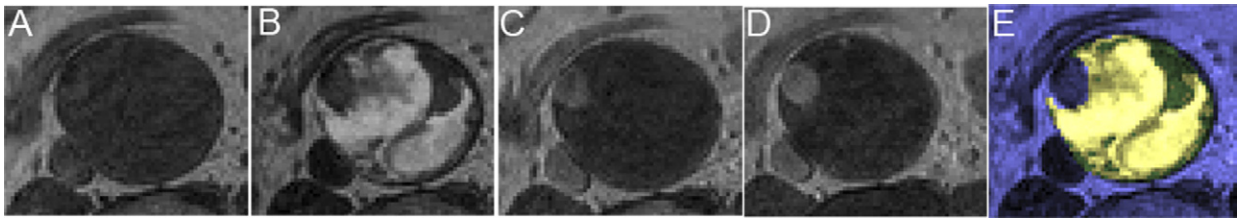

Fig 2. Transverse **(A)** precontrast T1-w, **(B)** T2-w, **(C)** T1-w 3 minutes, and **(D)** 30 minutes after injection of contrast agent in patient 8 years after implantation of a Guidant aorto-uni-iliac device with a stable aneurysm diameter (patient 9; Table II). Voxel classification overlays are shown in **(E)**, *yellow* represents unorganized thrombus, *green* represents organized thrombus, and *blue* voxels are voxels outside the aneurysm sac. This patient had a subtle endoleak peripheral in the aneurysm sac more caudally. The aneurysm sac volume was 130 mL, of which 61% had the aspect of unorganized thrombus.

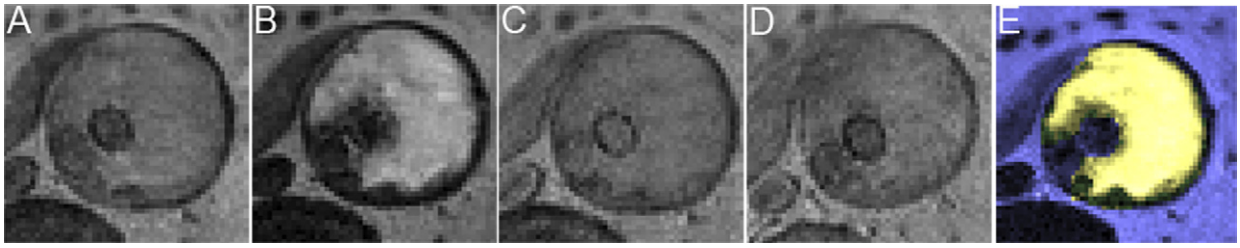

Fig 3. Transverse **(A)** precontrast T1-w, **(B)** T2-w, **(C)** T1-w 3 minutes, and **(D)** 30 minutes after injection of contrast agent in patient 1 year after implantation of an Excluder Low Permeability device (patient 6; Table II). Voxel classification overlays are shown in **(E)**, *yellow* represents unorganized thrombus, *green* represents organized thrombus, and *blue* voxels are voxels outside the aneurysm sac. There was no evidence of endoleak. The aneurysm sac had a high signal intensity before injection of contrast agent. The aneurysm sac volume was 86 mL, of which 79% had a high signal intensity on the T2-weighted images representing unorganized thrombus.

Table III. Summary statistics of endoleak volume, unorganized thrombus volume, organized thrombus volume, and aneurysm sac volume of our patient group

	Endoleak volume	*Unorganized thrombus volume*	*Organized thrombus volume*	*Aneurysm sac volume*
Milliliters (mean ± SD)	6 ± 9 mL	78 ± 61 mL	83 ± 71 mL	167 ± 107 mL
Volume percentage (mean ± SD)	4% ± 6%	51% ± 21%	45% ± 24%	

The unorganized thrombus volume in these two patients was not different from the other patients.

Probably, multiple processes take place simultaneously with buildup and break down of thrombus, leading to an equilibrium situation of organized thrombus and unorganized thrombus volume. To gain more insight in the evolution of the aneurysm sac, we are currently conducting a longitudinal study to investigate early postoperative changes in the thrombus mass with MRI. We think the possibility of endoleak is still not completely excluded in the five patients in whom no endoleak was visualized. Possibly, these patients suffer from endoleaks with different hemodynamics, which cannot be demonstrated even with blood pool agent enhanced MRI (eg, intermittent or position-dependent endoleak). The possibility of occult endoleak is supported by the observation of high signal intensity in the aneurysm sac on T1-weighted images before contrast injection of almost the entire aneurysm sac in two patients. This suggests the presence of methemoglobin in the aneurysm sac, which is a breakdown product of hemoglobin present in recently thrombosed material. Alternatively, other still unknown mechanisms leading to an increase in unorganized thrombus may be present (eg, inflammatory reactions, exudation of fluid through graft fabric, or thrombus fibrinolysis). These differences in composition of the aneurysm sac remain occult on CT because of insufficient contrast resolution.

A limitation of our study is that we did not include patients with shrinking aneurysms. To determine the clinical significance of our findings, future studies in patients with shrinking aneurysms are advocated.

In summary, our data show that the amount of unorganized thrombus in the aneurysm sac several years after EVAR is higher than expected. Thus, the aneurysm sac

does not merely represent an organizing thrombus. More knowledge on the evolution of aneurysm sac contents potentially increases the insight in aneurysm size changes. Therefore, MRI data from larger patient numbers are needed as well as longitudinal data on changing aneurysm sac contents in time. These data can then serve as reference data for patients with complicated sac behavior such as aneurysm growth with or without detectable endoleak.

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AUTHOR CONTRIBUTIONS

Conception and design: SC, HV, FM, LB
Analysis and interpretation: SC, HV, JH, EV, FM, LB
Data collection: SC, HV, JH
Writing the article: SC
Critical revision of the article: HV, JH, EV, LB, FM
Final approval of the article: SC, HV, JH, EV, FM, LB
Statistical analysis: SC
Obtained funding: FM
Overall responsibility: SC

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