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ORIGINAL ARTICLE

Intra-aneurysmal air after flow diversion treatment in intracranial aneurysms: incidence, characteristics and clinical significance

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Abstract

Objective To describe the rate and characteristics of air bubble retention (ABR) within cerebral aneurysms treated by flow diversion.

Methods Procedural flat detector CT (FDCT) studies were scrutinized for the presence of air bubbles (density < − 200 HU) in patients treated by flow diversion. Patients with intrasaccular treatment or previous clipping were excluded. Clinical outcomes, procedural angiograms, aneurysm characteristics and imaging features of air within the aneurysm were evaluated.

Results Bubbles were noted in 17.1% of 105 aneurysms in 85 FDCTs. Aneurysms with ABR were significantly larger (mean diameter: 18.9 versus 7.5 mm, $P < 0.0001$). There was a trend for the use of multiple devices during the treatment of these aneurysms (72.2% vs 49.4%, $P = 0.071$). All of the bubbles were located rostrally in the aneurysm sac and were smaller than 6 mm (mean diameter: 2.1 ± 1.3 mm). None of the patients had post-procedural neurological deterioration. The air had spontaneously disappeared on follow-up CT images (available in 12 patients) obtained at a mean follow-up duration of 48 h.

Conclusions ABR is not infrequent in cerebral flow diversion procedures. It is a clinically silent and self-limited technical complication. We propose air entrapment or filtration through the flow diverter as causative factors.

Keywords Air embolism · Aneurysm · Flow diversion · Endovascular · Flat detector computed tomography

Introduction

Flow diversion, an effective treatment option for cerebral aneurysms is associated with some peculiar adverse events, such as perforator infarction, distal intraparenchymal hemorrhage, fish-mouthing, and delayed aneurysm rupture [1–5]. We describe a previously unreported adverse event involving flow diversion: intra-aneurysmal air retention. Cerebral air embolism is a well-known complication of various endovascular procedures and is most commonly seen after cerebral angiography [6]. It is generally asymptomatic, but rarely can lead to devastating neurologic consequences. There are few in vitro studies about air bubble formation during coil detachment [7] but no data exist about intra-aneurysmal air bubble retention (ABR) after cerebral aneurysm embolization. We evaluated the incidence, imaging features and clinical outcomes of this phenomenon.

Materials and methods

This retrospective study was approved by the Ethics Committee of our institution and conducted in accordance with the Helsinki Declaration. Patients with cerebral aneurysms treated by flow diversion (flow diverter or overlapping braided stents) at a single institution between September 2015 and May 2018 were retrospectively evaluated. Patients were excluded if an intrasaccular treatment was performed before or during the same session. Among the remaining patients, those with post-procedural flat detector CT (FDCT) images with or without intra-arterial contrast administration were identified.

We routinely obtain thin slice (0.1 mm slice thickness) FDCT images with or without intra-arterial diluted contrast infusion, after flow diversion. However, in some

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cases, only selected volume rendered technique (VRT) images or maximum intensity projection (MIP) images were deposited in our PACS. We included the patients only if all of the 0.1 mm thick sections of the post-procedural FDCT studies were available for review. FDCT studies were excluded if images were degraded by surgical or endovascular materials. Patients were not excluded if they had more than one device (> 1 flow diverter or conjoined use of a flow diverter and a stent or overlapping braided intracranial stents) in place.

All aneurysm treatment procedures were performed by a single operator under general anesthesia using biplane flat panel digital subtraction angiography (DSA) machines (Artis zee biplane; Siemens). During all interventional procedures a meticulous technique was followed; guiding catheters and sheaths were connected to high-pressure (300 mmHg) saline bags, syringes were filled from an open basin set and laid on the angiographic tray for several minutes and any visible air was expelled before injection. The following FDCT data acquisition parameters were used: rotation: 20 s, angular range: 200°, increment: 0.4°/image; 1240 × 960 pixels and 496 projections. In those cases, with intra-arterial contrast administration, 33–44 mL of 10% non-ionic contrast agent (Iohexol; Omnipaque 350) was injected with a power injector at a flow rate of 1.5–2 mL/s intra-arterially through the distal access catheter. FDCT data were transferred to a dedicated workstation (Leonardo DynaCT, Inspace 3D software, Siemens Medical Solutions).

Aneurysm characteristics, imaging features of air within the aneurysm and clinical outcomes were evaluated. Aneurysms less than 10 mm in diameter were considered small, those between 10 and 25 mm in largest dimension were noted as large and any aneurysm larger than 25 mm was considered as giant. Intra-aneurysmal air was defined as voxels with absorption values of < − 200 HU inside the aneurysm sac. In patients with a documented ABR, DSA images were evaluated retrospectively in an effort to explore the mechanism of air entrapment into the aneurysm.

For statistical evaluation, all measurements were presented as the mean ± standard deviation for parametric variables. Chi-square analysis was used to test associations between categorical variables. Univariate and multivariate logistic regression analyses were used to identify risk factors of air bubble retention. *P* values less than 0.05 were considered significant.

Results

A total of 85 FDCT studies in 85 patients with 105 aneurysms were identified and investigated for the presence of air in the aneurysm. 32 of these aneurysms were large or giant and 19 were fusiform/dissecting.

Intra-aneurysmal air bubble retention was noted in 18 out of a total of 105 aneurysms treated during 85 procedures (17.1%). Table 1 shows the characteristics of patients

Table 1 Characteristics of the patients with air bubble retention

Patient	Aneurysm morphology	Devices used (including flow diverters, stents)	Aneurysm location (anterior vs posterior circulation)	Flow diverter	Aneurysm size	Air bubble size (mm) /number
1	Saccular	Single	Anterior	DV	Large	1.5/1
2	Fusiform	Multiple	Posterior	SP	Large	1.5–3/3
3	Saccular	Multiple	Anterior	DV	Large	1.5–2/2
4	Fusiform	Multiple	Posterior	SP	Large	4–4.5/2
5	Saccular	Multiple	Anterior	SP	Large	1/1
6	Saccular	Multiple	Anterior	DV	Large	1.5–2.7/2
7	Saccular	Multiple	Anterior	SP	Giant	5/1
8	Fusiform	Single	Posterior	Silk	Small	1/1
9	Fusiform	Multiple	Anterior	SP	Giant	4/1
10	Saccular	Multiple	Anterior	SP	Large	4/1
11	Fusiform	Multiple	Posterior	SP	Large	2/1
12	Fusiform	Multiple	Anterior	OBS	Giant	1–3/m
13	Fusiform	Multiple	Anterior	SP	Giant	s-6/m
14	Saccular	Single	Anterior	DV	Large	2.4/1
15	Saccular	Single	Anterior	DV	Small	2.8/1
16	Saccular	Single	Anterior	DV	Large	1–2/2
17	Saccular	Multiple	Anterior	SP	Large	1.5/1
18	Saccular	Multiple	Anterior	SP	Large	1.4/1

DV derive device, *SP* surpass device, *Silk* silk plus device, *OBS* overlapping braided stents, *s* submillimeter, *m* multiple

with air bubble retention. Eleven of these aneurysms were saccular and the remaining seven were fusiform/dissecting. Fourteen were located in the anterior circulation. All but two of these aneurysms were large or giant and ABR occurred more frequently in large aneurysms versus small aneurysms ($P < 0.0001$). The mean diameter of aneurysms with ABR was 18.9 and that for aneurysms without ABR was 7.5 mm. Although not statistically significant, there was a trend for ABR in aneurysms treated with multiple devices (72.2% vs 49.4%, $P = 0.071$). Even though fusiform aneurysms were associated with air bubble retention on univariate analysis ($P = 0.016$), multivariate analysis showed aneurysm size is the only significant risk factor (Table 2). Air bubbles were associated with all types of flow diverters currently used in our department (Surpass, Stryker Neurovascular; Silk, Balt Extrusion; Derivo, Acandis GmbH).

There was a single air bubble in eleven patients, two bubbles in four patients, three bubbles in one patient and multiple (more than five and mainly submillimeter in size) air bubbles in two patients. All of the bubbles were in the rostral portion of the aneurysm sac and smaller than 6 mm in maximum diameter (mean diameter: 2.1 ± 1.3 mm) (Online resource-figures). None of the patients with intra-aneurysmal air had a post-procedural deterioration in neurological status. The air had spontaneously disappeared on all post-procedure follow-up CT images with 0.6 mm slice thickness (available in 12 patients) at a mean CT follow-up duration of 48 h (range 4–123 h).

When we reviewed the DSA images retrospectively, the entrapment of intra-aneurysmal air was evident in three cases. In two of these, the air bubble was noted before placement of the FD and was then trapped by FD. In the other patient, the air bubble appeared to be formed as a result of the coalescence of the air trapped within the flow diverter interstices during device deployment. We refer to air bubble that forms in this way as "air filtration".

Discussion

Cerebral arterial air embolism is associated with various vascular and non-vascular interventional procedures [8–10] and most commonly with during catheter flushing, wire manipulation and contrast medium injections during cerebral angiography [11]. Although this is asymptomatic in most affected patients, it may result in symptoms, ranging from headache to death, in those with diabetes mellitus, and atherosclerosis [6, 12, 13]. Even large air gradually dissolves in the arterial system as long as it is smaller than the caliber of the arterial lumen [14]. The only intra-aneurysmal air reported to date, was found on CT inside a large aneurysm immediately after diagnostic angiography and the patient was asymptomatic [15]. We were unable to find a report in the literature describing the phenomenon of air embolism with flow diversion.

Flow diverters cause the gradual occlusion of the aneurysm by altering the pattern and velocity of blood flow [16]. Complications of flow diverters include thromboembolic events, parenchymal hemorrhage, in-stent stenosis and delayed rupture [1–3]. The temporary air bubble retention inside the aneurysm, as we report in this study, is a new adverse event related to flow diversion. Its incidence was 17.1% in our cohort. Some aneurysms had more than one bubble, all of the air bubbles were in the rostral part of the aneurysm and all were smaller than 6 mm. We showed that the entrapped air dissolves fast. All of the air bubbles had dissolved in the patients who underwent early follow-up imaging and none of the patients had air embolism-related symptoms.

We demonstrated that at least two mechanisms lead to ABR. Firstly, the microemboli, generated during endovascular device manipulation as reported by Bendzus et al, get into the aneurysm and are then entrapped within the stagnated aneurysm by the high-mesh flow diverter (Fig. 1 and Online resource video 1). The second mechanism is that the tiny air bubbles that occur after flow diverter placement are "filtered" through the flow diverter and move to the least-dependent portion of the aneurysm, then they coalesce to form larger bubbles. This hypothesis would also explain the higher rate of air entrapment observed in larger and fusiform aneurysms, which have a larger "filtration" surface, and those in which we used multiple devices, such as a second flow diverter or a stent placed for apposition the flow diverter (resulting in more angiographic runs, catheter removals, etc., and therefore recruiting more air bubbles to

Table 2 Predictors of air bubble retention according to univariate and multivariate regression analyses

	Univariate logical regression analysis			Multivariate logical regression analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Aneurysm morphology (fusiform)	3.977	1.289–12.271	**0.016**	–	–	–
Stent number	2.786	0.915–8.485	0.071	–	–	–
Aneurysm location (posterior)	2.200	0.604–8.007	0.232	–	–	–
Aneurysm size	47.439	6.844–328.830	**< 0.001**	32.941	6.904–157.167	**< 0.001**

Statistically significant results are shown as bold

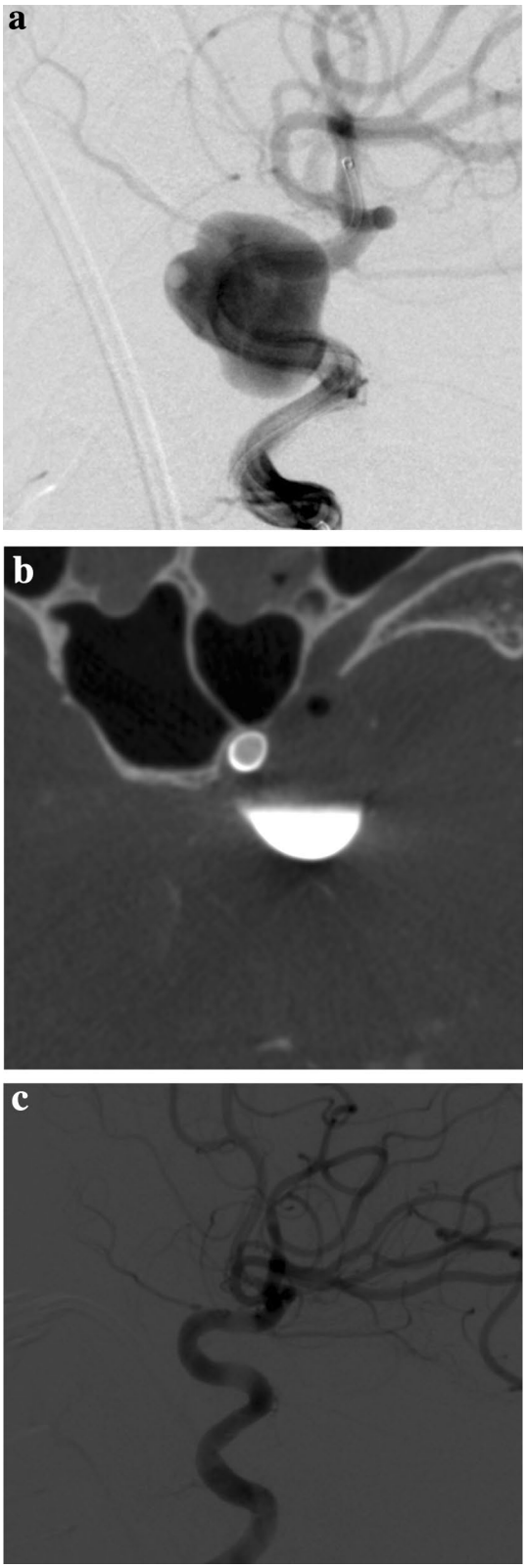

Fig. 1 **a** An air bubble is noted in the rostral portion of the aneurysm on left ICA arteriogram (in working projection). **b** FDCT with administration of intra-arterial contrast approximately 30 min after deployment of the flow diverter shows that air bubble is entrapped by the flow diverter within what appears to be a newly developed thrombus in the aneurysm. **c** Post-procedural arteriogram demonstrates only minimum opacification of the aneurysm (please see same patient as in Online resource video 1)

be filtered). The source of filtered air may be the tiny bubbles that are injected into the arterial system after the FD is deployed. Yet we believe that a more frequent source of air is the tiny bubble (or bubbles) that remains entrapped within the tight interstices of the undeployed FD during its transfer from the delivery sheath into the microcatheter and gets released and filtered as the device is being deployed (Fig. 2 and Online resource video 2). Alternatively, filtered air can potentially arrive from the proximal circulation via the afferent artery as well. We tried to simulate this condition in vitro (Online resource Fig. 2 and video 4). It is possible that the air bubble in this case may have been trapped between the saline and the contrast medium secondary to contamination between the syringe and connector, there also remains a possibility that it was trapped and transferred together with the device within the delivery catheter. Rigorous flushing of the FD outside the body before insertion into the guiding catheter does not guarantee the disposal of such air (Online resource video 2). A final possibility is that when a FD is already deployed at a site of arterial junction such as the vertebrobasilar junction or anterior communicating artery complex, contrast injection via the jailed arterial branch (e.g., contralateral vertebral artery or A1 segment of anterior cerebral artery on the contralateral side) may result in air entry into the aneurysm which has stagnated flow due to the FD that is already placed through the unjailed branch. This may have potentially resulted in the entrapment of a bubble in the patient with giant vertebrobasilar junction aneurysm in our cohort.

Since flow diverters do not cause any significant CT artifacts [17], IIA is easily visualized on an FDCT obtained immediately after flow diverter placement. These tiny air emboli can occur during other forms of endovascular cerebral aneurysm treatment as well, but it may not be possible to visualize them on cross-sectional imaging because they are either immediately washed out or cannot be detected due to the artifacts caused by coils. As an intraprocedural cross-sectional imaging tool yielding volume-rendered images within the angiography suite during endovascular procedures [18, 19], FDCT allows excellent visualization of intra-aneurysmal air. We obtain FDCT images at the end of the procedure to check the apposition of the flow diverter, aneurysm neck coverage and the status of side branches. Streak artifacts secondary to endovascular or surgical materials, such as coils or metallic clips, can cause image-quality

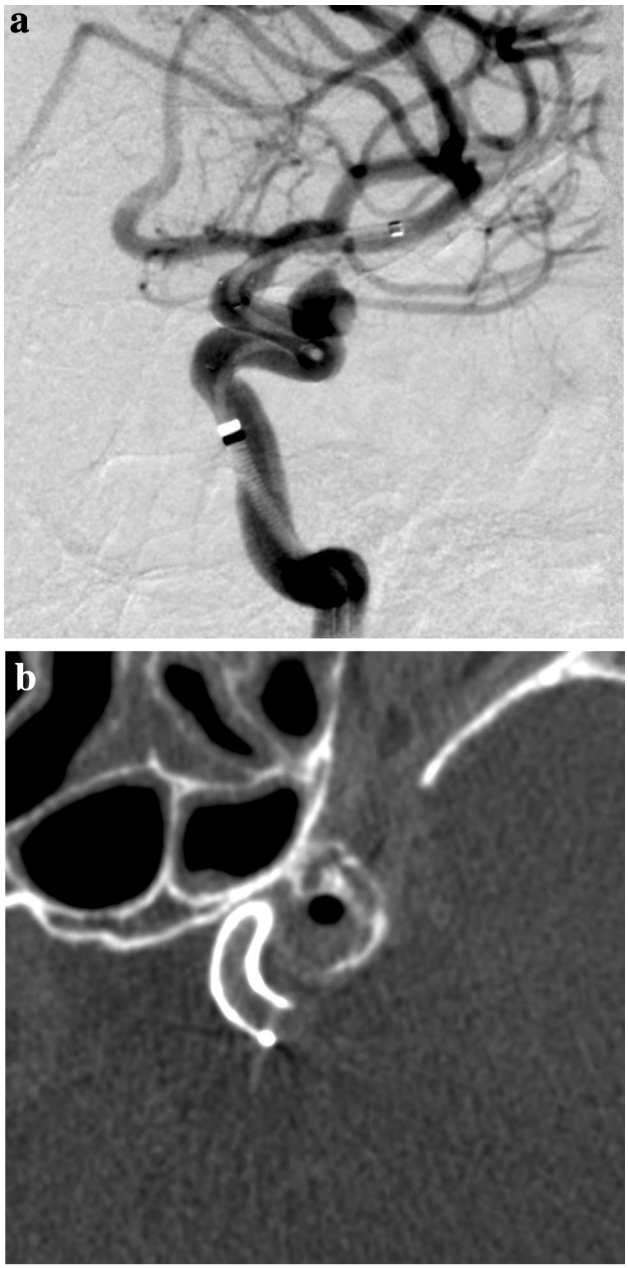

Fig. 2 **a** Left internal carotid artery (ICA) arteriogram in oblique projection shows the intra-aneurysmal air bubble (arrow) in the rostral portion of the aneurysm after the placement of the flow diverter. **b** FDCT without intra-arterial contrast administration of the head reveals entrapment of the air bubble by the flow diverter (please see the same patient in Online resource video 2)

degradation and mimic air within an aneurysm. Thus, we excluded patients who were previously treated with clipping or coiling if they interfered with image interpretation.

It is important to minimize air embolism during endovascular cerebral procedures. In addition to paying careful attention to technique, the systemic administration of heparin or use of an air filter are measures that can reduce, as much as possible, the incidence of air embolism [11]. In symptomatic cases, hyperbaric oxygen treatment, induced hypertension, and anticonvulsants may be utilized [6]. None of the cases with air retention inside the aneurysm after flow diversion needed any treatment in our series.

There are some limitations to our study. This is a single-center retrospective study in which we included a relatively small number of patients with air retention. We were not able to evaluate all FDCT studies in patients treated with flow diversion because in some patients only selected images were sent to PACS after the procedure, especially if the FDCT study was unremarkable. This probably resulted in an overestimation of the rate of intra-aneurysmal air. Moreover, the proportion of large and giant aneurysms observed in our series was higher than the prevalence of these aneurysms observed in the general population because such aneurysms are currently specifically treated by flow diversion. The incidence of intra-aneurysmal air after endovascular treatment is probably lower.

Intra-aneurysmal air bubble retention is a previously unreported complication of flow diversion. Microscopic air embolization is frequent in patients who undergo endovascular treatments. ABR may be caused by the filtration and/or entrapment of these microemboli. The post-procedure FDCT allows clear visualization of ABR after flow diversion. In this study, this finding was common, incidental, self-limited and without clinical consequences.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This retrospective study was approved by the ethics committee of our university hospital.

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