ORIGINAL ARTICLE

Diagnostic imaging in patients after endovascular aortic aneurysm repair with special focus on ultrasound contrast agents

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KEY WORDS

abdominal aortic aneurysm, contrast agents, Doppler duplex ultrasonography, multidetector computed tomography, stent graft

ABSTRACT

INTRODUCTION Endovascular treatment of abdominal aortic aneurysms (AAAs) constitutes an alternative to the classic surgical approach. The procedure may be associated with specific complications, including persistent flow within the aneurysm sac, otherwise known as endoleak.

OBJECTIVES The aim of the study was to assess the utility of ultrasound contrast agents in the diagnosis of endoleaks after endovascular AAA repair.

PATIENTS AND METHODS A total of 198 patients with AAA underwent endovascular treatment. Follow-up examinations were performed at 6 and 12 months after the procedure, including pre- and postcontrast ultrasound, followed by computed tomography angiography (CTA) as a reference. Each ultrasound examination consisted of B-flow, color, and power Doppler evaluation before and after contrast injection, supplemented by a contrast-enhanced ultrasound (CEUS) scan.

RESULTS At 6 months, endoleaks were diagnosed in 16 and 22 patients during pre- and postcontrast ultrasound, respectively. CEUS confirmed the presence of 22 previously diagnosed and 4 new (type II) endoleaks. At 12 months, endoleaks were detected in 7 and 13 patients by means of pre- and postcontrast ultrasound, respectively. CEUS confirmed the presence of endoleaks in 17 patients. None of the endoleaks diagnosed solely with CEUS at 6 and 12 months were detected by CTA.

CONCLUSIONS Contrast agents substantially increase the sensitivity of ultrasound in the diagnosis of endoleaks, particularly type II. CEUS proved to have the highest sensitivity for the diagnosis of endoleaks by revealing pathologies undetected by other modalities, including CTA. CEUS may substitute CTA in surveillance of patients after stent graft deployment.

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INTRODUCTION In recent years, the increasing prevalence of abdominal aortic aneurysms (AAAs) has become a challenge for health care providers in rapidly developing countries. The rationale behind this phenomenon is a prolonged life expectancy and a widespread use of ultrasound, which is considered the fundamental diagnostic method for such evaluations. AAA affects 1.9% to 8.6% of the population above the age of 45 years, and is associated with tobacco smoking, hypertension, elevated low-density lipoprotein cholesterol and total cholesterol levels, cardiovascular comorbidities, senility, severe chronic obstructive pulmonary disease, and familial tendency.[1,2] A recent study has indicated that aortic dilation may be also attributed to immunosuppressive treatment (mammalian target of rapamycin inhibitors) in renal graft recipients.[3]

AAAs can be treated either conservatively or surgically. Pharmacological blood pressure control remains the main focus of conservative treatment, while the surgical approach encompasses

both the classic open procedure and endovascular aortic repair (EVAR). The latter consists in aneurysm exclusion from circulation by implanting an endovascular prosthesis (stent graft) into an enlarged aortic lumen.

Current stent grafts include either mass-produced or custom-made technically advanced designs that secure blood flow through the iliac arteries. The modular and telescopically-engageable constructions are found in the majority of devices. Particular models differ by the materials used, strut and mesh design, stent configuration, and fixation techniques.[4,5]

In recent years, endovascular treatment in patients with AAAs has become an established alternative to classic surgery, although it is not free of complications.

Minor adverse events of EVAR include the postimplantation syndrome, which develops in less than 50% of patients. It presents with elevated body temperature, leukocytosis, and elevated heart rate (>90 bpm).[6,7] Endograft infection is a very rare incident, and, according to the literature, it can be directly attributed to failure to maintain sterile conditions within the operating room. Detection of air surrounding the stent graft on computed tomography angiography (CTA) is pathognomonic for an infected prosthesis.[8]

Other serious complications of endograft implantation, even if the procedure was fully successful, include stent graft fracture or tear, migration, kinking, endoleak, endotension, as well as main body and iliac limb thrombosis.[8,9] Stent graft rupture is one of the most severe complications of EVAR.[10] The predisposing factors include type I and type III endoleaks, graft dislocation, and a large preoperative aneurysm diameter. Ruptures were observed after implantation of first-generation stent grafts.[5] The current incidence of stent graft migration, thrombosis, and occlusion is relatively low and reaches 4% during the first year of follow-up. A notable reduction in the occurrence of complications is due to common access to the new generation of more technically advanced stent grafts with suprarenal fixation.[11] Dislocation exceeding 10 mm with respect to renal arteries is considered as stent graft migration. The underlying causes include unstable fixation of the main body of the prosthesis, intramural abnormalities of the adjacent parent vessel, and enlargement of the aneurysm neck.[12] Stent graft thrombosis usually develops as a result of severe iliac angulation, and its incidence ranges between 2.4% and 11.7%. In the majority of cases, it affects the iliac limb of aortic endograft unilaterally and occurs during the first year after treatment. Aortic main body or iliac limb stenosis usually develops in the setting of tortuous iliac and femoral arteries.[5,8]

One of the most common complications of AAAs are endoleaks, which result from incomplete aneurysm exclusion by an endoluminal graft.[13,14] They are classified according to the source of blood flow, and 5 types of endoleaks are currently distinguished (FIGURE 1A–1E).

Type I endoleak refers to the blood leakage at proximal (infrarenal aneurysm neck, type IA) or distal (iliac arteries, type IB; iliac occluder, type IC) graft ends. It is observed in 4% to 7% of patients after stent graft implantation.

Type II endoleak results from retrograde aneurysm perfusion via aortic side branches, for example, single or multiple lumbar arteries, inferior mesenteric artery, or other collateral vessels. It is relatively common, with the incidence rate of 27% to 37%.[15,16] Some authors distinguish 2 subtypes of type II endoleaks: IIA with a single supplying vessel and IIB with 2 or more delivery vessels. According to other sources, type IIA and IIB endoleaks are defined as originating from the inferior mesenteric artery or lumbar arteries, respectively. The latter definition was used for the purpose of this analysis.

Type III endoleak is related to the structural defect, namely, a fabric tear or junction separation of the modular components of the endograft. It affects less than 3% of patients.[16,17] The following subtypes of type III endoleaks are recognized: IIIA, which arises from the separation of modular devices and junctions, and IIIB, which is due to disruptions or holes involving the fabric of the device.[16,18]

Type IV endoleaks develop due to endograft porosity. The incidence rate is around 5%.[19] The condition is principally self-limiting due to rapid endograft sealing with fibrin. This type of endoleak is rarely seen with the newer generation of stent grafts, which are composed of less porous fabrics.

Endotension is classified by some authors as type V endoleak.[16,18,20] It is defined as increased intra-aneurysmal pressure that results in the expansion of the aneurysm sac, without radiographic evidence of a leak site. In some cases, this may occur due to presence of an endoleak whose source could not be detected using available imaging studies. The less probable causes of endotension include a seroma generating increased pressure within the aneurysm sac, pressure transmission from a thrombus surrounding the endograft, or prosthesis infection.[20] The classification of endoleak types and subtypes is presented in TABLE 1.

Patients undergoing EVAR require follow-up imaging examinations for early detection of potential complications. Multidetector or multislice computed tomography, regarded as a gold standard in monitoring of this population, is usually performed at 3, 6, and 12 months, and then every year after stent graft implantation.

The main objective of this study was to determine the efficacy of distinct ultrasound techniques in detecting endoleaks, with special focus on contrast-enhanced ultrasound (CEUS) and with regard to the gold standard method of coronary CTA.

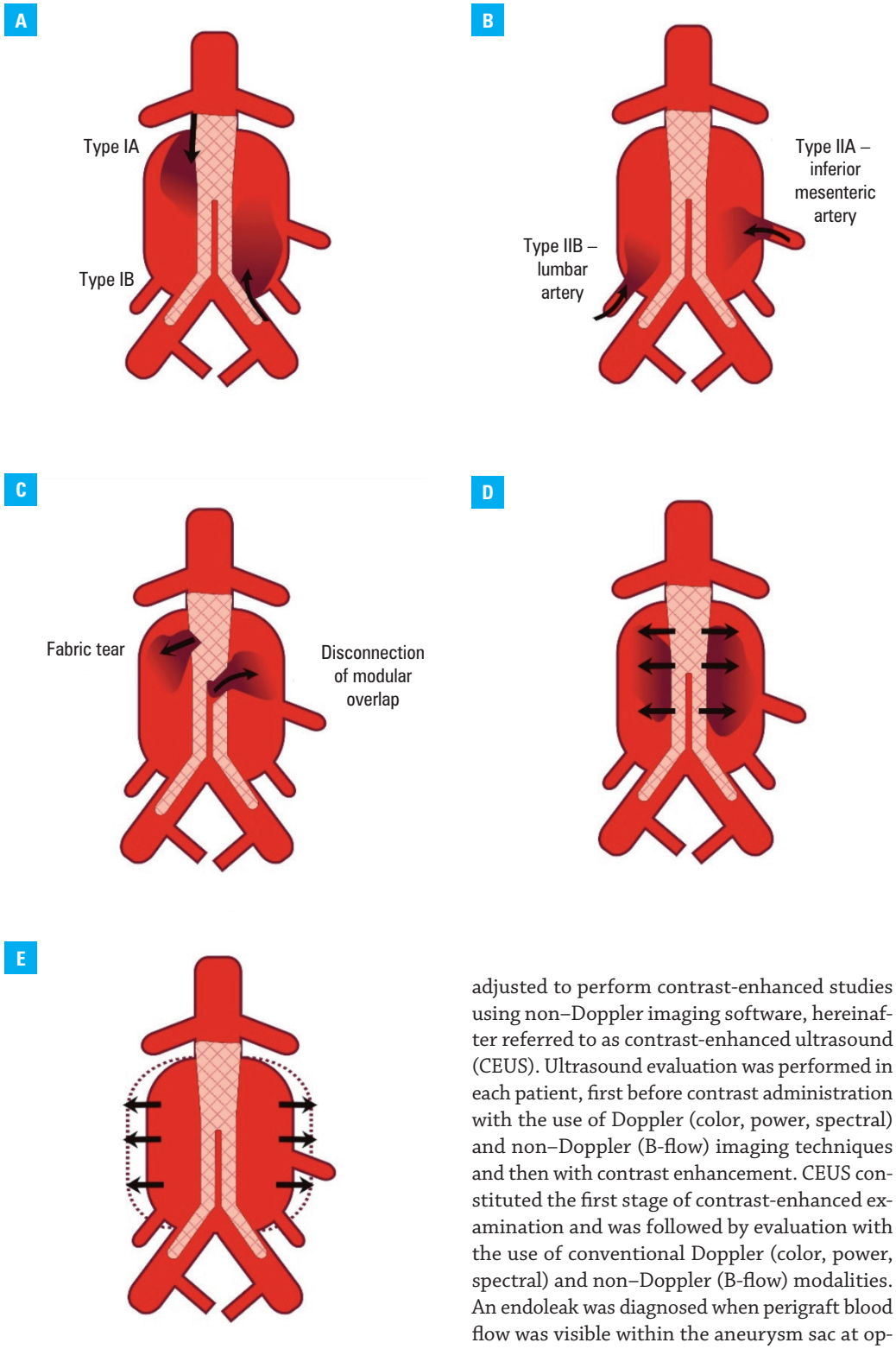

FIGURE 1 Endoleak types I–V: **A** – type I endoleak; **B** – type II endoleak; **C** – type III endoleak; **D** – type IV endoleak; **E** – type V endoleak

PATIENTS AND METHODS The study cohort included 198 patients (166 men and 32 women; age, 46–90 years) who underwent EVAR for AAA. Follow-up examinations were performed in each patient at 6 and 12 months after the procedure, using the same study protocol. Ultrasound scans before and after contrast administration were done first, followed by abdominal CTA.

All ultrasound examinations were performed with 3.5-MHz convex-arrayed transducer of LOGIQ 7 ultrasound setup (GE Healthcare, Milwaukee, Wisconsin, United States). The system was equipped with harmonic imaging and adjusted to perform contrast-enhanced studies using non–Doppler imaging software, hereinafter referred to as contrast-enhanced ultrasound (CEUS). Ultrasound evaluation was performed in each patient, first before contrast administration with the use of Doppler (color, power, spectral) and non–Doppler (B-flow) imaging techniques and then with contrast enhancement. CEUS constituted the first stage of contrast-enhanced examination and was followed by evaluation with the use of conventional Doppler (color, power, spectral) and non–Doppler (B-flow) modalities. An endoleak was diagnosed when perigraft blood flow was visible within the aneurysm sac at optimal ultrasound settings (pulse repetition frequency, gain, filter, focus). Abdominal CTA was performed within 5 to 7 days from ultrasound examination with 64 row CT (GE LightSpeed Ultra; GE Healthcare). Abdominal aortic and peripheral arterial images were acquired from the level of the celiac trunk to femoral bifurcation at the peak saturation point, 30 seconds after contrast administration (5-mm nominal slice thickness, 7.5-mm/s table feed, 1.5-mm pitch, 2-mm effective slice thickness). An automatic injector was used to inject 100 to 120 ml of iodinated contrast medium (Ultravist 370 mg I/ml, Schering, Germany) at a speed of 2.5 ml/s.

TABLE 1 Summary of endoleak classification

Type I	Leakage at graft ends	A	Proximal
		B	Distal
		C	Iliac occluder
Type II	Aneurysm filling via side branches	A	Single vessel / IMA
		B	Two and more vessels / lumbar artery
Type III	Mechanical failure of graft components	A	Separation of modular devices and junctions
		B	Tear in a fabric
Type IV			Endograft porosity (intentional)
Type V			Endotension

Abbreviations: IMA, inferior mesenteric artery

TABLE 2 Endoleaks diagnosed at 6 and 12 months of follow-up (by type and modality)

	Follow-up							
	6 months				12 months			
Endoleak type	Pre-CE	Post-CE	CEUS	CTA	Pre-CE	Post-CE	CEUS	CTA
IA	6 (37.5)	6 (27.3)	6 (23.1)	6 (27.3)	2 (28.6)	2 (15.4)	2 (11.8)	2 (13.3)
IB	4 (25.0)	5 (22.7)	5 (19.2)	5 (22.7)	1 (14.3)	2 (15.4)	2 (11.8)	2 (13.3)
IIA	2 (12.5)	4 (18.2)	6 (23.1)	4 (18.2)	2 (28.6)	4 (30.8)	5 (29.4)	5 (33.3)
IIB	4 (25.0)	7 (31.8)	9 (34.6)	7 (31.8)	2 (28.6)	5 (38.5)	8 (47.1)	6 (40.0)

Data are presented as number (percentage) of endoleaks.

Abbreviations: CEUS, contrast-enhanced (non–Doppler) ultrasound; CTA, computed tomography angiography; Post-CE, Doppler ultrasound with contrast enhancement; Pre-CE, Doppler ultrasound prior to contrast enhancement

A detailed evaluation of stent graft deployment and integrity was possible with the use of multiplanar and curved reconstructions, minimum and maximum intensity projections, and 3-dimensional volume rendering. The results of pre- and postcontrast ultrasound were then compared with the outcomes of CTA to determine the efficacy of ultrasound modalities in endoleak identification.

RESULTS **Follow-up at 6 months** The ultrasound examination prior to contrast administration revealed 16 endoleaks. The next step of evaluation was CEUS, which enabled visualization of 26 endoleaks, including 10 (1 type I and 9 type II) that were previously missed in the precontrast scan. Further ultrasonographic assessment in postcontrast Doppler and B-flow techniques led to detection of 22 endoleaks: 6 new and 16 previously diagnosed in the precontrast scan. The primary subdivision of these 16 endoleaks was confirmed by the postcontrast scan. In the second phase, CTA revealed 22 endoleaks to the aneurysm sac.

Detailed data regarding the number and type of endoleaks detected by distinct techniques are presented in TABLE 2. At 6-month follow-up, the highest number (ie, 26) of endoleaks was visualized by CEUS, and this was considered as 100% (FIGURE 2).

Follow-up at 12 months Precontrast ultrasound imaging led to detection of endoleaks in 7 patients. The to-and-fro waveform was observed in 1 patient with type II endoleak, indicating that the entry and exit of blood is through the same vessel. Such a type of endoleak is classified as "simple" as opposed to "complex" endoleak.

Endoleak presence was detected by CEUS in 17 patients.

Two type IA and one type IB endoleaks were detected in patients who previously underwent endovascular treatment due to identical findings on precontrast ultrasound at 6-month follow-up (FIGURE 3). Endoleak presence at 12 months indicated that the procedure was ineffective. In another patient diagnosed with type IB endoleak at 6-month follow-up, no signs of perigraft blood flow were seen in any of the imaging methods.

Type IIA endoleak was detected in 5 patients. In 1 patient, persistent type IIA endoleak was observed that was previously diagnosed by precontrast ultrasound. In another patient, persistent type IIA endoleak was detected at 6 months by CEUS only (FIGURE 4). In the remaining 3 patients, type IIA endoleaks were diagnosed for the first time at 12-month follow-up.

Of all type IIB endoleaks, one was detected at 6-month follow-up both by CEUS and by contrast-enhanced Doppler evaluation (FIGURE 5). A single case of persistent type IIB endoleak was detected at 6 months by CEUS only. The remaining 6 endoleaks were first diagnosed at 12-month follow-up.

Contrast enhancement facilitated detection of 13 endoleaks in both Doppler and B-flow ultrasound techniques.

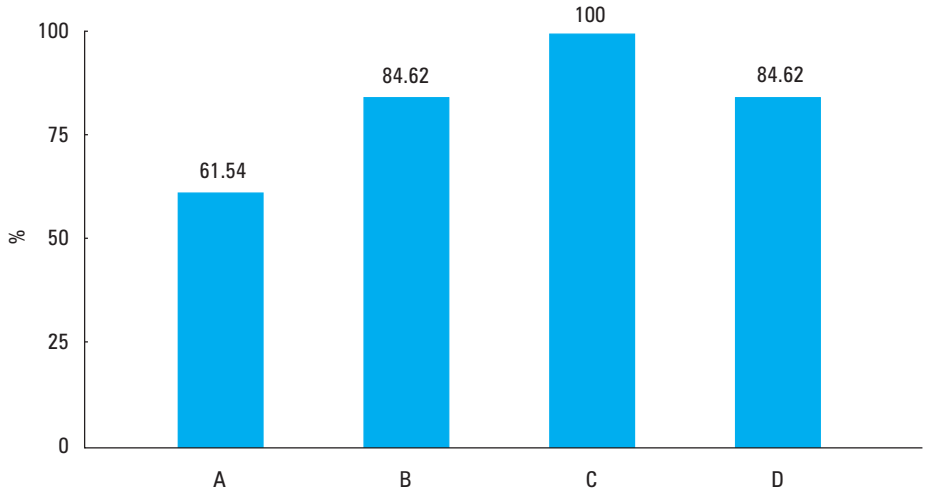

FIGURE 2 Percent of endoleaks detected by precontrast ultrasound (**A**), postcontrast Doppler and B-flow imaging (**B**), contrast-enhanced ultrasound (**C**), and computed tomography angiography (**D**) at 6-month follow-up

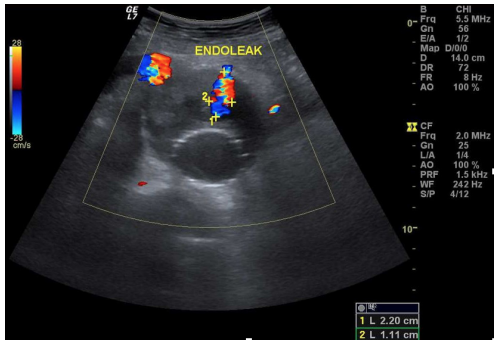

FIGURE 3 Type IIA endoleak to the anterior portion of the aneurysm sac in color-coded Doppler presentation (transverse view); precontrast ultrasound at 6-month follow-up

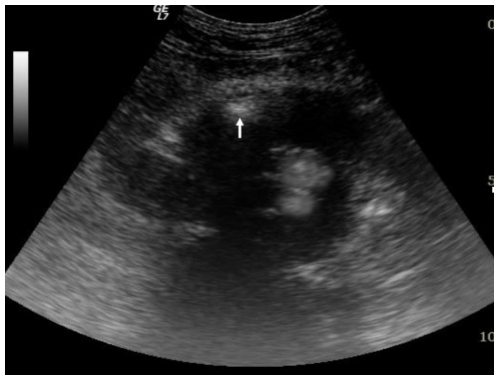

FIGURE 4 Type IIA endoleak (arrow) on contrast-enhanced ultrasound at 6-month follow-up. The endoleak was visible only in this modality.

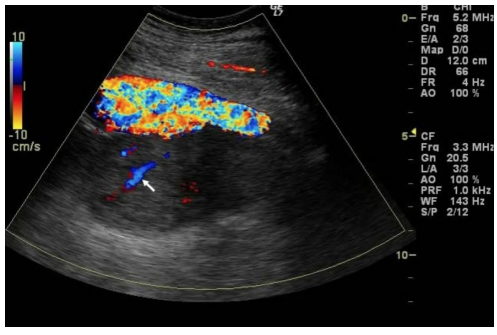

FIGURE 5 Type IIB endoleak to the posterior part of the aneurysm sac (arrow) in color-coded Doppler presentation (longitudinal view). Postcontrast ultrasound at 6-month follow-up. The endoleak was not visible before contrast administration.

CTA revealed 15 endoleaks into the aneurysm sac. The use of additional reconstructions enabled further classification of type II endoleaks into 4 simple and 5 complex ones. Unequivocal identification of the endoleak source was not possible in the remaining patients.

Detailed data regarding endoleak detection at 12-month follow-up are presented in **TABLE 2**. The highest number (ie, 17) of endoleaks was visualized by CEUS, and this was considered as 100% (**FIGURE 6**).

None of the imaging modalities revealed the presence of type III or IV endoleaks in the study cohort either at 6 or 12-month follow-up.

DISCUSSION The EVAR procedure substantially differs from the classic surgical approach. Instead of vessel excision, the method aims to reduce intraaneurysmal pressure by excluding the aneurysm from circulation with the resulting blood flow redirection through an endovascular implant, that is, a stent graft. Currently, nearly 50% of patients with AAA are treated endovascularly,[21-23] and in some centers, the percentage reaches 70%.[24] The endovascular procedure enables treatment of high-risk patients who would not meet the criteria for classic surgery due to severe cardiovascular and respiratory problems.[25]

Although the method is growing in popularity, it is not free of complications. Patients with AAA who underwent EVAR require systematic follow-up examinations to assess treatment efficacy and detect potential complications. Despite advancements in stent graft design and increasing experience with deployment techniques, endoleaks remain the weak point of the procedure. About 50% of endoleaks undergo spontaneous thrombosis and do not require any further interventions. Persistent endoleaks may, however, lead to enlargement or even rupture of the aneurysm sac, an effect that is contradictory to the very basic concept of EVAR. Endoleaks are defined as blood leakage into the aneurysm outside the stent graft, and they were first described by White et al.[26,27] They develop in 15% to 32% of patients after EVAR.[15,17,19]

In this study, only type I and II endoleaks were detected. Type II endoleaks arising from lumbar arteries occur substantially more often than the other types.[10,28,29] Baum et al[9] distinguished 2 kinds of type II endoleaks: simple and

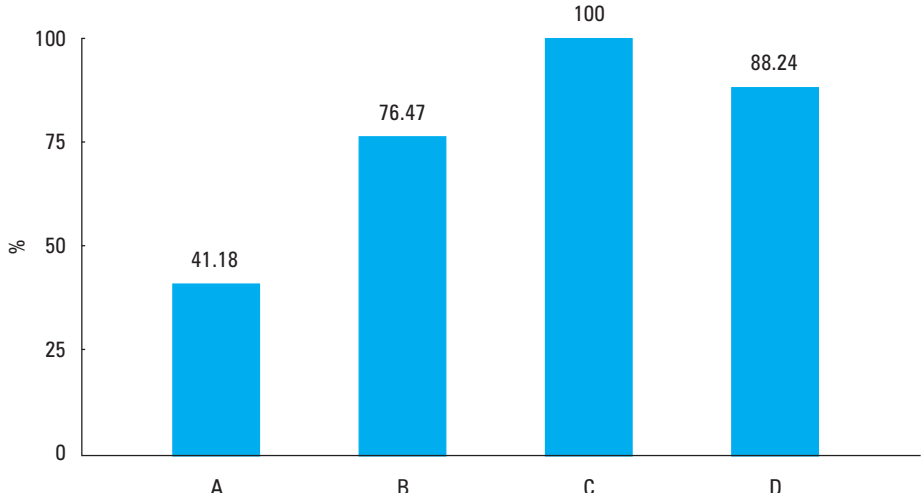

FIGURE 6 Percent of endoleaks detected by precontrast ultrasound (**A**), postcontrast Doppler and B-flow imaging (**B**), contrast-enhanced ultrasound (**C**), and computed tomography angiography (**D**) at 12-month follow-up

complex. The first type is associated with a single vessel serving as both an inflow and outflow for the leak, resulting in an appearance similar to arterial pseudoaneurysm. In the complex endoleak, an ingress from the inferior mesenteric artery with an egress from the lumbar arteries is the most typical pattern.[9] Blood flow associated with an endoleak as assessed by ultrasound is typically uniform, reproducible, and persists into diastole.[28,30]

We aimed to compare the efficacy of the 4 imaging modalities in the detection of endoleaks at 6 and 12 months of follow-up after EVAR. Previously published papers analyzed either pre- and postcontrast ultrasound with CTA or CEUS with precontrast ultrasound and CTA. To our knowledge, this is the first study including direct comparison of all 4 imaging techniques.

According to Heilberger et al,[31] color ultrasound allows for detection of endoleaks arising from the lumbar arteries or inferior mesenteric artery, which are not always visible on CTA or conventional angiography. The outcomes of endoleak diagnosis with plain and contrast-enhanced color-coded ultrasonography are subject to debate. AbuRahma et al[32] reported that the estimated sensitivity of the plain Doppler examination reaches only 42%. On the contrary, Sato et al[33] reported that the sensitivity and specificity of Doppler imaging without contrast enhancement in endoleak detection is 97% and 74%, respectively, as compared with CTA.[33] Finally, Wolf et al[34] reported a sensitivity of 81% and a specificity of 95% for endoleak visualization by Doppler ultrasound, compared with CTA.[34]

CEUS was shown to have higher sensitivity rates for detecting the extragraft flow than color Doppler.[13] Contrast-enhanced imaging enables to overcome certain limitations of color-coded Doppler, such as color artifacts and poor ability to demonstrate weak blood flow. Henao et al[35] assessed the efficacy of CTA in endoleak detection in a group of 20 patients. They managed to visualize 9 leakages, most of which were type II endoleaks.[35] They concluded that CTA reveled no additional endoleaks, as compared with CEUS. Clevert et al[36] investigated the incidence of endoleaks in 43 patients by comparing the outcomes of CTA with plain Doppler imaging and CEUS. They used CTA as the gold standard. The sensitivity and specificity of non–contrast Doppler imaging were 33.3% and 92.8%, respectively, whereas for CEUS, they were 100% and 93%, respectively. Additionally, 2 CEUS outcomes primarily considered as false positive turned out to be true positive during further patient surveillance. These results correspond well with our findings. At 6-month follow-up, CEUS indicated the presence of 4 type II endoleaks, which were not confirmed by CTA. However, 2 of these endoleaks were again detected both by ultrasound and CTA at 12 months. Furthermore, 2 more endoleaks missed by CTA were diagnosed with CEUS at 12 months. Our results clearly demonstrate that CEUS revealed the greatest number of endoleaks, both at 6 and 12 months of follow-up. Interestingly, the contrast-enhanced ultrasound examination using Doppler and B-flow options allowed a detection of 4 endoleaks fewer than CEUS. This may result either from the lower sensitivity for detecting low-velocity blood flow or signal deterioration with time from contrast administration. The protocol of our study comprised a single intravenous contrast administration; CEUS evaluation was done first, followed by Doppler and B-flow imaging. Therefore, it would be reasonable to perform a comparative study with the use of continuous contrast infusion, which would prolong the enhancement time. In our study, 3 ultrasound techniques, namely, color-coded, power Doppler, and B-flow, were used for each follow-up examination to screen for potential complications. We observed no significant diagnostic difference between these techniques. At the same time, to our knowledge, there have been no studies directly comparing the performance of these methods in the evaluation of endoleaks or stent graft limb patency.

Our analysis indicates that CEUS has the highest sensitivity for endoleak detection, which is in line with previous studies.[13] Nonetheless,

contrary to Doppler imaging, CEUS does not provide information on blood flow parameters.

Our data demonstrate similar effectiveness of contrast-enhanced ultrasound and CTA in patient surveillance after EVAR, and thus ultrasonography may replace CTA in screening for potential complications. Although CTA is still considered the gold standard, advancements in ultrasound techniques, with special focus on contrast--enhanced studies, may soon lead to a substantial shift in the diagnostic approach and become a new reference method. Contrary to CTA, ultrasound assessment of patients after EVAR is not associated with exposure to ionizing radiation or nephrotoxic contrast media.[37]

In conclusion, contrast agents substantially increase the sensitivity of ultrasound for the diagnosis of endoleaks, particularly type II. However, it is CEUS that presents the highest sensitivity in terms of endoleak detection by revealing abnormalities undetected by other modalities, including CTA. Ultrasound evaluation, particularly contrast-enhanced, may substitute CTA in the surveillance of patients after EVAR.

CONTRIBUTION STATEMENT ADZ conceived the concept of the study. MS, MK, and TJ contributed to the design of the research. All authors were involved in data collection. MK, ŁŚ, EK, and KP analyzed the data. AD-Z, MK, and JS were responsible for the manuscript draft. TJ, EC-C, M. Pech, and M. Powerski revised the manuscript critically for important intellectual content. TJ, EC-C, and AW coordinated funding for the project. All authors edited and approved the final version of the manuscript.

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