The role of contrast-enhanced ultrasound imaging in the follow-up of patients post-endovascular aneurysm repair

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Abstract

Endovascular aneurysm repair is a minimally invasive technique for the treatment of abdominal aortic aneurysms. Patients who undergo endovascular aneurysm repair are potentially at risk of developing problems related to the graft such as the development of endoleaks. Endoleaks can cause expansion of the aneurysmal sac, which can potentially lead to rupture. It is for this reason that lifelong surveillance of patients is required to assess the graft and the aneurysmal sac. This article discusses the role of contrast-enhanced ultrasound in the follow-up of patients post-endovascular aneurysm repair. Contrast-enhanced ultrasound is rapidly becoming a powerful, accurate and cost-effective tool to complement computed tomography in the follow-up of endovascular aneurysm repair patients. Real-time imaging of contrast filling into the arterial system means that contrast-enhanced ultrasound is an excellent problem-solving tool, particularly when assessing for the type and anatomy of endoleaks. In some instances, contrast-enhanced ultrasound can detect endoleaks when other modalities are equivocal.

Keywords

Contrast-enhanced ultrasound, Doppler ultrasound, vascular

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Introduction

Endovascular aneurysm repair (EVAR) is a minimally invasive technique that is used for the treatment of abdominal aortic aneurysms (AAA) owing to its proven decrease in operative mortality at 30 days after the procedure.^{1,2} It is only considered in patients where the morphology of the aneurysm is amenable to EVAR.

EVAR has several other advantages over the conventional open repair of AAAs. Being a minimally invasive technique, it means that inpatient stay is greatly reduced, as well as patient morbidity and mortality.¹ However, the need to follow up these patients post-procedure is greater when compared with patients undergoing open repair. Patients who undergo EVAR are at risk of developing endoleaks. An endoleak occurs when there is filling of the aneurysm sac outside the aortic stent graft.³ Consequently, patients are regularly imaged to review the graft. This article discusses the

role of contrast-enhanced ultrasound (CEUS) in the follow-up of patients following EVAR. Its use and application as a problem-solving tool are explored with case examples, and its drawbacks and limitations are discussed. Future considerations and technological developments are also considered with regard to the future role of ultrasound in vascular imaging.

The follow-up protocol post-EVAR is extremely varied. Many modalities, including computed tomography (CT), plain radiographs, duplex ultrasound and magnetic resonance angiography (MRA) are used at different stages post-EVAR.⁴ Most institutions utilise CT as the main tool for assessing aortic grafts post-EVAR.⁵ A

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typical review includes assessing the graft 1 to 3 months post-procedure and then further assessments at 6 and 12 months.⁶ Following this, the graft and aneurysm sac are assessed annually using duplex ultrasound. The burden of radiation dose to the patient, as well as additional hospital visits and potentially the need for re-intervention, is a disadvantage when compared with open repair after which no routine follow-up imaging is arranged.

CEUS is rapidly becoming a powerful tool to complement CT and has the potential to reduce the frequency of performing CT scans, thereby reducing the radiation burden to the patient. Real-time imaging of contrast filling into the arterial system means that CEUS is an excellent problem-solving tool, particularly when evaluating for endoleaks. In some cases, CEUS may demonstrate an endoleak that is not identified on CT scans.⁷

CEUS

SonoVue is the most commonly used second-generation contrast agent. It contains sulphur hexafluoride microbubbles stabilised in a phospholipid shell.^{8,9} This is different from first-generation contrast agents, which contain air. First-generation ultrasound agents are no longer used owing to the high solubility of air in blood.

SonoVue is presented as a vial containing sulphur hexafluoride gas and phospholipid powder.⁸ This is mixed with a prefilled syringe of saline and reconstituted using the provided transfer and ventilation system, which forms the microbubbles. Following injection of 2.4 ml of SonoVue and 5 ml of a 0.9% saline flush through a peripheral venous cannula into the antecubital fossa, the contrast agent accumulates in the area of interest and resonates when exposed to the ultrasound beam from the transducer.^{7,4} The echogenicity within blood vessels is increased when compared with the background tissues, which improves the signal-to-noise ratio and thus the image quality displayed on the screen.^{10,11} Owing to its low solubility, continuous imaging can occur at a relatively low mechanical index (0.01–0.04).^{7,8} This effectively reduces the background tissue signal and enables one to focus on the area of interest. Imaging with a low mechanical index is crucial to avoid increased tension of the microbubbles, which can subsequently rupture.¹⁰

SonoVue demonstrates a pattern of uptake within blood vessels that is similar to that seen with the contrast agents used in CT and magnetic resonance imaging (MRI).⁸ Similar patterns of uptake enable easy interpretation of abnormalities, which can be directly compared with these other imaging modalities. The advantage of SonoVue in comparison with CT and MRI contrast agents is that there is less likelihood of inducing nephrotoxicity. This is because SonoVue does

not rely on renal excretion, but is instead broken down into sulphur hexafluoride gas, which is exhaled, and the phospholipid microbubble shell, which is metabolised endogenously.

What is an endoleak?

An endoleak is defined as filling of the aneurysmal sac outside the aortic stent graft.³ This is seen in 20–25% of patients following EVAR.^{12,13} It has several causes and their classification system is described below and demonstrated in Figure 1.

Type 1(a) is defined as filling of the aneurysm sac owing to a defect in the proximal attachment of the graft.¹² Type 1(b) endoleaks occur when the distal attachment of the graft is defective. In some patients, only a unilateral iliac graft is inserted and a femoral–femoral bypass is performed.¹⁴ The contralateral common iliac artery is occluded to prevent filling and expansion of the aneurysmal sac. If occlusion of the contralateral common iliac artery fails, this is termed a Type 1(c) endoleak. Filling of the aneurysmal sac owing to retrograde flow in an aneurysmal branch vessel, commonly a lumbar artery or the inferior mesenteric artery, occurs in Type 2 endoleaks, which is the most common type of endoleak.¹² Rarely, a Type 3 endoleak can occur through mechanical graft failure along any portion of the graft resulting in filling of the aneurysmal sac. Porosity of the graft may occur and result in a Type 4 endoleak. Expansion of the aneurysmal sac occurring without any obvious cause is termed a Type 5 endoleak, also referred to as endotension. CEUS has an important role to play in

Figure 1. Types of endoleak following EVAR.

assessing the cause of endotension and in excluding a more common endoleak that may not have been identified through conventional ultrasound or CT scans.^{4,15}

Imaging of endoleaks

Imaging with CT may not be able to differentiate between Type 1 and Type 2 endoleaks. This could be resolved by CEUS based on the timing of arrival at the endoleak. Figure 2 shows early filling of the aneurysmal sac at the superior aspect of the graft with simultaneous filling of contrast into the body of the graft. These features are consistent with a Type 1(a) endoleak, which requires urgent intervention and treatment, as the aneurysm sac is exposed to systemic blood pressure. The source of the endoleak might have been missed had images been acquired later on (as with a CT scan), as the entire sac would have been filled with contrast. The timing of imaging is a recognised and previously described cause of false negative CT scans.¹¹ Continuous imaging with CEUS enables slow flowing endoleaks to be detected.

Figure 3 shows a case of a Type 2 endoleak identified with CEUS. The patient had previously only had imaging with CT that showed a serial increase in aneurysmal sac size without an obvious cause. The sac reached 9.5cm in size and the patient was diagnosed as having endotension. The cause of the serial increase in sac size was, therefore, investigated further using CEUS. This example demonstrates the value of CEUS in investigating the cause of a problem unidentified on CT scans. Filling of contrast within the sac was identified after a delay in scanning, which would explain why the leak was not identified in the snapshot CT image. This is a key differentiator

to Type 1 endoleaks where filling of the aneurysm sac usually occurs much earlier, with simultaneous filling of contrast within the graft. The real-time imaging of CEUS is clearly an advantage over CT without having to be concerned about radiation dose to the patient. Further examples of a Type 2 endoleak are shown in Figures 4 and 5.

Type 2 endoleaks from stented iliac artery aneurysms can also be well delineated with CEUS. Figure 6 demonstrates the follow-up of a patient with a right common iliac artery aneurysm. EVAR was performed after branches of the right internal iliac artery were prophylactically coiled in order to prevent an endoleak. Figure 6 demonstrates a Type 2 endoleak through a branch of the internal iliac artery that was not initially identified and therefore not prophylactically coiled.

Contrast leaks into the aneurysmal sac can result in increased pressure within the sac, which may increase the size of the sac and, consequently, raise the risk of rupture.^{12,16,17} Type 2 endoleaks do not often carry this risk, so if there is no significant serial increase in sac size (i.e. an increase of less than 5mm), they may require follow-up only, as opposed to urgent intervention.^{12,18} Type 1 and 3 endoleaks result in direct communication with systemic blood flow and thus increase pressure within the sac and require immediate repair to prevent the risk of rupture.^{19,20}

Benefits of CEUS

CEUS is more effective at detecting endoleaks than conventional colour-Doppler ultrasound (CDUS).⁵ Cantisani et al.⁴ reported a sensitivity and a specificity of 58% and 93%, respectively, with CDUS compared to 96% and 100% with CEUS. The presence of

Figure 2. Type 1(a) endoleak. Early contrast filling into the aneurysmal sac (arrow) superior to the graft along with the contrast within the graft. The features are consistent with a Type 1(a) endoleak.

Figure 3. Type 2 endoleak. Contrast filling (arrow) of the aneurysmal sac posterior to the graft.

Figure 4. Type 2 endoleak. A Type 2 endoleak has occurred owing to filling of the aneurysmal sac by the right lumbar artery.

Figure 5. Type 2 endoleak. CEUS and CT performed show that a Type 2 endoleak has occurred owing to filling of the aneurysmal sac by the inferior mesenteric artery.

Figure 6. Type 2 endoleak. (a) Contrast leaking into the aneurysm sac from a branch of the internal iliac artery that was not coiled. (b) The coils (red arrow) that were inserted to prevent an endoleak from occurring. (c) The contrast leak into the sac, which was also identified on CEUS.

Figure 7. (a) CT post-EVAR. This demonstrates a 9.1 cm aneurysmal sac that was persistently increasing in size on follow-up imaging. CT with contrast did not demonstrate an endoleak. (b) CDUS post-EVAR. CDUS performed on a patient previously diagnosed with endotension. There is an area of increased echogenicity (arrow) posterolateral to the graft but no definite leak was demonstrated. (c) CEUS post-EVAR. The CEUS performed clearly demonstrates a Type 2 endoleak posterior to the graft (arrow). (d) Catheter angiography demonstrating a Type 2 endoleak. The patient proceeded to catheter angiography where the endoleak is again demonstrated. The microcatheter is in the left lumbar artery.

real-time contrast filling enables accurate localisation of the source of an endoleak followed by identification of the accumulation of contrast within the sac on delayed imaging. A similar poor sensitivity was reported with CDUS in a meta-analysis involving 21 studies that compared CDUS with contrast-enhanced CT. Mirza et al.⁵ reported a pooled sensitivity of 0.77 in detecting endoleaks with CDUS and a pooled specificity of 0.94.

Figure 7(a) to (d) shows an example of a case that failed to demonstrate an endoleak with CDUS. Figure 7(a) illustrates a surveillance CT scan performed post-EVAR that showed a 9.1 cm aneurysmal sac that had been increasing in size over serial imaging. As no endoleak was demonstrated, the patient was diagnosed as having endotension. However, further investigation and imaging were warranted given the sac size. An endoleak was not demonstrated with CDUS (Figure 7(b)). The patient then underwent a CEUS that clearly demonstrated a Type 2 endoleak posterior to the graft (Figure 7(c)). Catheter angiography

confirmed that this was an endoleak from the left lumbar artery, which was subsequently coiled with a good result (Figure 7(d)).

CEUS has a similar sensitivity to CT in detecting endoleaks. Gürtler et al.²¹ reported a sensitivity of 97% and a specificity of 93% with CEUS on a cohort of 132 patients following EVAR. A systematic review by Chung et al.²² included a cohort of 454 patients and reported a pooled sensitivity of 0.914 and a pooled specificity of 0.782 with CEUS. Although it is generally accepted that CT remains the gold standard in assessing for endoleaks, the use of CEUS should be considered, particularly when the CT result is equivocal.^{5,21} Further research is required into the use of CEUS as a primary imaging modality.⁵

The advantage of real-time imaging is that it can help to differentiate Type 1 and Type 2 endoleaks based on the timing of contrast arrival into the sac. CEUS also helps to define the anatomy of the endoleak by demonstrating the inflow and outflow vessels

Figure 8. Occluded limb graft post-EVAR. (a,b) CEUS performed on different patients that demonstrates normal filling into the left limb of the graft. There is no contrast uptake in the right limb of the graft. The appearance is consistent with an occluded limb graft. (c) CT correlation, which again demonstrates an occluded right limb graft (arrow).

from the sac. As stated previously, CT only captures a snapshot image within the arterial phase, so this is therefore a recognised cause of a false negative CT study.¹¹

Although CEUS has not yet been recognised as a substitute for CT, it is an adjunct that is more patient friendly and does not have some of the limiting factors of CT. For instance, patients who have impaired renal function have a cumulative risk of developing worsening renal function when iodinated contrast agents are administered on serial follow-ups. CT carries both the risk of renal impairment and the risk from ionising radiation. When compared with CT, CEUS is a safe modality and is shown to be a more cost-effective problem-solving tool.⁸ Because there is no concern about ionising radiation, real-time imaging can be performed from before the contrast is injected until the contrast is excreted. A longer scanning period provides increased sensitivity in detecting endoleaks, particularly in Type 2 endoleaks where there may be slow flow into the aneurysmal sac.²²

Some patients may have difficulties with the technical factors required for CT imaging. For instance,

some patients have claustrophobia and struggle to lie still during image acquisition. In the acute setting, patients may not be well enough to come to the department for a CT. In such cases, CEUS can be performed as a bedside test.⁴ The use of CEUS in the intraoperative period has also been described, particularly in patients with contraindications to iodinated contrast agents.²³

CEUS also enables accurate assessment of the patency of the graft. The treatment of an occluded limb graft is largely dependent on patient symptoms and findings following clinical assessment. The incidental detection of an occluded graft will prompt further investigation and treatment to avoid limb ischaemia.²⁴ An example of an occluded limb graft is shown in Figure 8(a) to (c).

Patients can have an instant result from the sonographer or vascular radiologist following the procedure. As well as the results of the test, they are informed when their next follow-up scan will be. It is hugely beneficial and reassuring for patients to have an instant diagnosis rather than having the uncertainty of waiting for a report or follow-up appointment.

Figure 9. Aortic calcification producing artefact. Aortic calcification within the aneurysmal sac giving a false positive result for an endoleak. The arrow marks the area of calcification.

Figure 10. Aortic calcification. CT correlation of the same patient as in Figure 9 confirmed that the abnormality identified on CEUS was an area of aortic calcification (see arrow).

Drawbacks of CEUS

The presence of aortic calcification, particularly within the aneurysmal sac, may mimic an endoleak.²⁵ This is particularly the case if the area of calcification was not identified on the pre-contrast images. This is one of the potential drawbacks of CEUS, as it may produce a false positive result. An example of an artefact caused secondary to aortic calcification is shown in Figure 9, where the area of calcification (within the aortic wall thrombus) lies close to the aortic graft and mimics a leak. The location of the artefact was compared with a previous CT. The abnormality was

confirmed to be an area of calcification rather than a leak (Figure 10).

Similarly, artefact and subsequent image degradation can occur secondary to different types of embolic material used in the treatment of a Type 2 endoleak. An example of this is shown in Figure 11(a), where the artefact is produced by the embolic coils used to treat an endoleak caused by the left lumbar artery. Despite intervention, an endoleak persisted, which is clearly demonstrated after delayed imaging (Figure 11(b)).

CEUS, as with conventional ultrasound, may be limited by patient habitus. Bowel gas may also obscure images of the aorta throughout the length of the graft. The use of the ultrasound machine does require familiarisation and training on the software, so there is an element of operator dependence in order to obtain high-quality real-time images.¹⁹

Current developments and future considerations

Technical advances in ultrasound imaging have enabled the introduction of hybrid imaging techniques. The ability to perform fusion scanning, whereby an abnormality is identified on one modality and used to view with confidence the abnormality on a different modality, is now commonly used, particularly in the context of abdominal imaging.²⁶ This has a valuable role to play in vascular imaging, as shown in Figure 12. The CT scan was performed 12 months following EVAR. The endoleak was followed up using CEUS with CT fusion, which demonstrated the endoleak (arrow) in the same area identified on the previous CT. This enabled the Type 2 endoleak to be diagnosed confidently, as its location was identified clearly on two

Figure 11. (a) Artefact (open arrow) produced by the embolisation coils used to treat a Type 2 endoleak. There was the suspicion of an endoleak anterior to this (closed arrow), which was confirmed on delayed imaging (b). (b) Type 2 endoleak. Filling of contrast into the aneurysmal sac secondary to a persistent endoleak despite embolisation of the left lumbar artery.

imaging modalities. The sac size remained stable, so no intervention was planned and the patient continues to be followed up with ultrasound, thereby reducing the cumulative radiation dose to the patient.

The development of broadband Doppler ultrasound (also known as advanced dynamic flow imaging) addresses the problem of a decreased bandwidth and therefore decreased spatial resolution when using ultrasound with colour Doppler imaging.²⁷ It can be used with or without intravenous contrast. Owing to its wide dynamic range, it can maintain a high spatial resolution similar to B-mode imaging and can visualise resonating microbubbles in real-time when intravenous contrast is administered. It also has good penetration and a high frame rate that enables the detection of smaller bubbles in minute vessels.^{27,28}

More recent developments include that of microvascular flow imaging, also termed superb microvascular imaging (SMI). This uses Doppler ultrasound with a

Figure 12. CT and ultrasound fusion demonstrating a Type 2 endoleak.

built-in algorithm that is more sensitive to low-velocity flow rates, as opposed to CDUS where low-velocity flow signals may be filtered out along with clutter artefacts.²⁸ SMI also offers high resolution and frame rates. Its sensitivity is particularly high when placed in grey-scale/monochromatic mode (mSMI) to enable the detection of minute vessels. Combined colour and B-mode imaging is also available and is termed cSMI. As well as having a role in neoplastic and inflammatory disease processes, it is also more likely to generate a signal from tiny vessels with low velocity and thus detect small endoleaks.²⁹ Its application to post-EVAR surveillance would be less invasive than CEUS, as intravenous contrast would not be required. SMI does currently have limitations, mainly its difficulty in distinguishing between extraneous Doppler signals, because of movement artefacts, from adjacent structures.²⁸ More research is required to determine whether SMI is superior to or comparable with CEUS.²⁹

The ability to detect micro or nanoparticles of contrast agents within blood vessels, i.e. molecular imaging, is still undergoing research. Its use in cardiovascular medicine would be extensive, including detailed assessment of atherosclerotic plaques, angiogenesis and transplant rejection.³⁰ Presently, there is no role for this in surveillance post-EVAR.

Conclusion

CEUS has established its role in surveillance post-EVAR repair. Although not a substitute for CT, it can be used as a valuable adjunct and problem-solving tool, particularly when an abnormality cannot be explained using CT. Technological advances have meant that CT and ultrasound fusion can be performed to confirm any abnormalities identified and define the type and anatomy of endoleaks, thereby increasing diagnostic confidence. Although CEUS has no current role in the routine surveillance programme, it does have the potential to expand into the programme owing to

its lack of the side effects and drawbacks described for CT. Further research is required into future considerations for EVAR surveillance imaging, including the implementation of SMI to detect endoleaks from minute vessels.²⁹

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NJ, PP and RL researched literature and conceived the study. PP and RL provided the case examples. NJ wrote the first draft of the manuscript. NJ, RL and PP reviewed and approved the final version of the manuscript. RL was the project supervisor.

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