What is the Optimal Imaging Modality to Detect Endoleaks following Elective Endovascular Repair of Abdominal Aortic Aneurysm

Amer Harky1, Darab Khan2, Vineshwar Pal Singh1, Muhammad Maaz Sajid1, and Ewa Zywicka1

1Department of Vascular Surgery, Countess of Chester, UK
2School of Medicine, University of Liverpool, UK

Abstract

Endovascular repair of abdominal aortic aneurysm (AAA), now a day, is the main treatment method which has replaced the traditional open repair for elective AAA in majority of cases. Such endovascular stenting has proven to provide satisfactory early and mid-term outcomes. However, to provide a long-term benefit and ensure the appropriate quality of life is gained from such intervention, a regular follow up with imaging studies are required to detect any early stent-graft issues and plan re-intervention, if required. For this purpose, several imaging techniques have evolved overtime and different modalities have been investigated to provide highest rate of sensitivity and specificity for early detection of endoleaks. In this review article, we outline current literature behind the use of each imaging modalities and its implications on follow up method.

INTRODUCTION

An abdominal aortic aneurysm (AAA) is local expansion of the abdominal aorta with an additional 50% of its normal diameter [1]. In most of patients, such aneurysm remains asymptomatic and some of them are detected during routine assessment for other pathologies or routine national screening program. However, the life-threatening risk is occurring when it ruptures and that is a surgical emergency which needs immediate intervention. Rupture of AAA requires emergency surgery either through open or endovascular repair (EVAR). Open surgery is more invasive and requires an incision into the abdomen to repair the rupture. EVAR however, is less invasive and the stent-graft can be deployed through percutaneous access. The risk of death after elective AAA surgery is estimated to be 4% for open surgery and less than 1% following endovascular repair [1].

After endovascular aneurysm repair, complications may occur which can be life threatening and therefore it requires prompt diagnosis and intervention. The rate of complications after open repair is less than 10%, while it is reported to be 20% following EVAR [1]. Some of these complications in duode, but are not limited to, endoleaks, new aneurysm formation, graft thrombosis and infection. Lifelong imaging surveillance is the current method to monitor these adverse outcomes, as early intervention allows for the complication to progress, prevent aneurysm growth and rupture [2]. There is much debate on which imaging modality is best to use [3], the key studies are listed below:

1) Computed tomography angiography (CTA) – is effective in the detections of migration, kinking, structural failure, endoleaks, infection, and aneurysm growth. It is more sensitive than conventional angiography for detecting endoleaks and their types. However, this is an expensive method and has exposure to ionizing radiation.

2) Ultrasound imaging – In most cases this can accurately determine aneurysm sac size and location, but this can be challenging in obese patients and those with extensive arterial wall calcification. It is; however, a more none invasive method and its use don’t involve utilization of ionized radiation. This enhanced with contrast (CEUS) which is as effective as CT for identifying endoleaks as it allows a dynamic scan time of several minutes compared with static CT images [2].

3) Magnetic resonance angiogram (MRA) – is an effective method to detect luminal patency, device positioning and residual sac flow. It is useful in detection type II endoleaks that may otherwise be classified as endotension or not detected at all by the other modalities. This also avoids exposure to ionizing radiation, but it is ineffective in detecting the integrity of the stent graft.

Another method of non-imaging follow-up will be the utilization of certain biomarkers. One of the key biomarkers is matrix metalloproteinase (MMP)-9. MMP-9 has been reported...
to have a key role in post-myocardial infarction remodelling and mortality and the evidence in literature is widely reported; however the evidence behind its significance to detect endoleak following EVAR or open repair is limited and yet to be established [4].

This article focuses in more details on the different methods of imaging and surveillance for of the major potential complications of EVAR as endoleaks.

ENDOLEAK CLASSIFICATION

Endoleaks can be defined, as Guimarães et al. suggest, as "persistent blood flow outside of the lumen of an endoluminal graft but within the aneurysm sac or adjacent vascular segment" [5]. They are complications exclusive to endovascular aneurysm repair (EVAR). Endoleaks occur by the incomplete sealing or exclusion of the aneurysm sac [5]. Blood inflow and reflux into the aneurysm sac causes pressurization of the aneurysm, leaving the patient at risk for rupture; manifestations may be asymptomatic, or as severe as uncontrolled aortic rupture [6].

Veith et al., stated that such complications can occur in up to 25% of patients who undergo EVAR, majorly as type 1 and 2, with the latter predominating; type 2; this typically resolve with no clinical intervention, and no detrimental effects afterwards [7].

Endoleaks can be classified according to the source of the flow of blood. This classification is necessary to determine the patient’s treatment, modes of surveillance, and protocols of follow-up. Shah et al. [8], classified endoleaks into 5 types (Table 1)

<table>
<thead>
<tr>
<th>Type of Endoleak</th>
<th>Location of Leak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>Attachment site</td>
</tr>
<tr>
<td>A</td>
<td>Proximal</td>
</tr>
<tr>
<td>B</td>
<td>Distal</td>
</tr>
<tr>
<td>C</td>
<td>Iliac occluder</td>
</tr>
<tr>
<td>Type 2</td>
<td>Collateral vessel</td>
</tr>
<tr>
<td>A</td>
<td>Single vessel</td>
</tr>
<tr>
<td>B</td>
<td>Multiple vessels</td>
</tr>
<tr>
<td>Type 3</td>
<td>Graft failure</td>
</tr>
<tr>
<td>A</td>
<td>Mid-graft puncture</td>
</tr>
<tr>
<td>B</td>
<td>Junctional</td>
</tr>
<tr>
<td>C</td>
<td>Other (e.g. suture hole)</td>
</tr>
<tr>
<td>Type 4</td>
<td>Porosity of graft wall</td>
</tr>
<tr>
<td>Type 5</td>
<td>Endotension</td>
</tr>
</tbody>
</table>

Type 1 endoleaks usually occurs early in the course of treatment, rarely occurring later. It is associated with increased pressure of the aneurysm sac with a progressive growth risk and therefore, risk of sudden rupture. Type 2 endoleaks are the most common, occurring by retrograde flow from anastomotic connections of aortic or iliac artery branches, most commonly the inferior mesenteric or lumbar artery, into the aneurysm sac [9]. Type 2 endoleaks may further be classified, as transient (spontaneous resolution within 6 months) or persistent (residual endoleak after 6 months of observation) [5]. Type 3 endoleaks results from structural stent-graft failure. Although majorly occurring in the early period due to technical problems, they can occur later due to device component embarrassment or increasing stent-graft age. While type 4 endoleaks result from the wall porosity of the stent graft. They usually resolve once coagulation parameters normalize after EVAR. Due to stent graft fabric improvements, and the improvements in normalizing coagulation parameters post-EVAR, type 4 endoleaks are rare and typically clinically inconsequential. Finally, type 5 endoleaks are known also as ‘endotension’; it is a ‘continued enlargement of the aneurysm sac without evidence of a leak site’ [5]. Persistently elevated pressure, post-EVAR, in the aneurysm sac results in its enlargement [9].

CURRENT GUIDELINES

The current European guidelines suggest that computerized tomography angiogram (CTA) as the prime option for imaging following EVAR. However, due to the ionizing nature of such scans, ultrasounds can be considered if there are contraindications. It is suggested according to NICE guidelines that duplex ultrasound should not be used as the principal modality of imaging due to the high level of false negative results [10]. Recent analysis has found that contrast enhanced Doppler ultrasonography is more specific and sensitive than duplex ultrasound is when looking at type 2 endoleaks [11]. Another option for imaging is the use of Magnetic Resonance Imaging (MRI), which is found to be highly accurate, yet this too is expensive, and is incapable of imaging metal stents, meaning that X-ray has to be used along with this to be able to create a useful image. During research it was found that imaging modalities are very variable, however CTA is seen as the gold standard [3].

Similar to Europe, CTA is the preferred method of postoperative imaging in America, but duplex ultrasonography is also commonly used [12]. According to the Society for Vascular Surgery, postoperative imaging is essential, and they recommend using ultrasounds, CT or MRI as part of their long term imaging [13]. In a study looking at the rate of detection of endoleaks, it was found that a combination of imaging modalities is the most effective way of imaging after EVAR [12].

With regards to time frames for imaging, both Europe and America encourage long term imaging, with varying frequencies depending on patient and guidelines that are followed.

ULTRASOUND IMAGING, DUPLEX VS CONTRAST ENHANCED

Although currently the most commonly utilized technique for the follow-up of EVAR is computed tomographic angiography, ultrasound imaging is emerging as a potential alternative with some advantages, such as its non-invasive character, its availability, and its cost-effectiveness [14]. Several studies have offered evidence to conclude that contrast-enhanced ultrasound (CEUS), or simply contrast ultrasound, is far superior, vis-à-vis diagnostic performance, to standard duplex ultrasound. A Millen et al. Study [14] concluded that contrast ultrasound can greatly enhance EVAR surveillance; in all 33 patients evaluated, it was able to detect the rate of endoleaks appropriately.
Bendick et al. [15], studied twenty patients to assess the efficacy of ultrasound imaging against computed tomography. Their study showed that duplex ultrasound with contrast can identify all endoleaks which were seen with CTA, additionally, it was able to differentiate between type 1 and type 2 endoleaks. Contrast ultrasound detected smaller endoleaks that were not seen with CTA. The same study also showed that standard duplex ultrasound failed to identify four out of 10 endoleaks in a particular group of patients. Overall, the authors concluded that contrast ultrasound “appears to provide good sensitivity to the presence and type of endoleaks”.

Bredahl et al. [16], reached a similar conclusion as Bendick et al., from their study of 278 patients. They were able to identify 69 endoleaks by using contrast enhanced ultrasound, while only 68 of them were identified by CTA, and only 46 by standard duplex ultrasound. Contrast imaging is far more sensitive than standard duplex (93% vs. 46%), and significantly more specific (95% vs. 85%). All endoleaks detected by CTA were also detected by contrast ultrasound; 3 patients, however, were missed by standard duplex ultrasound.

Cantisani et al. [17], further supports above conclusions, finding that contrast ultrasound allowed better classification of endoleaks in patients compared to standard duplex, CTA, and MRA. According to their study, contrast ultrasound has a sensitivity of 93% and specificity of 96%, only marginally different to CTA and MRA; standard duplex, which has significantly lower values at 58% and 83% respectively.

In Clevert et al, study [18], contrast ultrasound had a sensitivity and specificity of 100% and 92.8% respectively, as compared to standard duplex values of 33% and 92.8%. Standard duplex was true positive for 11.6% of patients, and false positive for 4.6%. Contrast ultrasound was true positive for 34.9% patients and false positive in 4.6%. Due to the smaller sample size and a comparison of the data with CTA, however, Clevert et al., concluded that contrast ultrasound “does not have sufficient diagnostic accuracy as the results suggested that CEUS is more sensitive than CTA in the detection of endoleaks most probably due to the possibility of dynamic examination.

Iezzi et al. [19], showed that contrast imaging significantly enhanced the diagnostic value of standard duplex ultrasound in the detection of endoleaks. Respectively, sensitivity (97.5% vs. 62.5%), negative predictive value (97.3% vs. 65.1%), accuracy (89.3% vs. 63.1%), and specificity (81.8% vs. 63.6%) which were all significantly improved.

Contrast ultrasound, however, does have its limitations; it is unable to provide information on graft anchoring, integrity, and aneurysm morphology [15]. Although useful in EVAR surveillance programs, it remains limited in its diagnostic scope with respect to more complicated patients.

**MAGNETIC RESONANCE IMAGING (MRI)**

Magnetic resonance angiogram (MRA) is currently used as the new alternative to CTA for post EVAR imaging and is useful in assessing of stent graft patency, presence of thrombosis, and aortic rupture. MRA is particularly useful in nitinol stent grafts but less effective for stainless steel and nickel alloy grafts which are ferro-magnetic and making it at risk of migration by the strong magnetic fields [17]. With regards to endoleaks detection, studies have shown that MRA is more sensitive than CTA, especially when using gadolinium contrast images. There are several other advantages of MRA over other imaging modalities. This includes, the lack of using ionizing radiation or any iodinated contrast-based nephropathy. While, methods such as computational fluid dynamics and 4D phase-contrast MRA can be used to analyse hemodynamic.

On the other hand, MRA imaging is time consuming, costly and is not universally accepted. In patients with a glomerular filtration rate (GFR) of 30 or less and in dialysis patients, MRA is frowned upon as it significantly increases the risk of nephrogenic systemic fibrosis. MRA scans in comparison to other modalities last longer, have a greater cost and have a lower accessibility in the community setting [20]. Additionally, MRA scans are ineffective in evaluating stent graft integrity which indicates the use of more radiographs to obtain a complete evaluation of the integrity [21]. The dynamic MRA scan can only be used in combination with the other scans due to its moderate resolution outputs.

**8. Computed Tomography Angiogram (CTA)**

In the study by Cantisani et al., they state that CTA is the most commonly used modality for EVAR surveillance as it is highly available and has a great value in diagnostics [17]. It is an ideal modality for visualising graft patency, as well as integrity when conducting imaging. A shortcoming with CTA technique however, is that it cannot visualise the direction of flow and the feeding of arteries [17].

Contrastingly, the study by Bendick et al., suggests that CTA is not always capable of finding the source of the endoleak, hence not always allowing the determination of endoleak type. Therefore, CTA will not give the clear differentiation between type 1 and type 2 endoleaks. However, CTA is more sensitive than conventional duplex ultrasound scan, as it has good technical quality. Its sensitivity was found to be 100%, whereas conventional duplex ultrasound only had a sensitivity of 33% [14].

A further limitation to CTA is the likelihood of contrast induced nephropathy and the amount of radiation exposure from the procedure [16]. Therefore, protecting the kidney’s during such procedures are crucial [22]. Depending on the dose of contrast and duration of exposure, it could precipitate to requirement for dialysis at the time of follow up, especially in patients with end-stage renal failure and very poor renal functions. However, a recent meta-analysis of more than 100,000 patients showed no evidence of contrast induced nephropathy [23]. They compared Contrast CT with non-contrast CT, contrast-enhanced CT was not associated with higher acute kidney injury rates (odds ratio [OR] 0.94; 95% confidence interval [CI] 0.83 to 1.07), requirement for renal replacement therapy (OR 0.83; 95% CI 0.59 to 1.16) or contributing to significantly to all-cause mortality (OR 1.0; 95% CI 0.73 to 1.36).

Furthermore, the procedure has a high cost associated with it. Another drawback to the use of CTA is the reduced sensitivity in detecting type 2 endoleaks. Also, not only CTA can cause contrast induced nephropathy, but can lead to anaphylaxis or patients
allergic to contrast, meaning that CTA would not be possible for such patients, indicating that they would have to use alternative surveillance modalities [24].

The study by Clevert et al. [18], emphasizes on the also suggests that CTA is the gold standard for follow up post EVAR. As it has the speed at which images are produced, the reproducible nature of such imaging and the clarity and spatial resolution of this technique. The combination of the CTA and CEUS can be used to create something known as image fusion. This uses both techniques and uses the advantages of each technique to create a tool with very high detection rates. This three-dimensional technique is merged with the dynamic real time imaging, generating a technique found to have the highest detection rates. The essence of this technique essentially streamlines the procedure of patient follow up as it allows the direct assessment of ultrasound data with CT data. This is vital for visualising progressive enlargement of the aneurysm sac, which is known to be a sign of endoleaks [25].

**ANGIOGRAM AND DSA**

Digital subtraction angiography (DSA) is a potential option for the detection of endoleaks. DSA, an interventional fluoroscopy technique, produces images using contrast media. The use of certain contrast media during EVAR and for EVAR surveillance can lead to adverse events in patients allergic to the medium or who have compromised kidney function and so are at risk for nephropathy just like CTA [26].

Gahlen et al. [27], noted that there is a high risk of renal failure after iodinated contrast medium angiography; not only in patients with pre-existing kidney dysfunction, but presence of diabetes mellitus and renovascular arteriosclerosis are established risk factors. Allergic reactions occur in up to 10% of patients; only 2.2%, however, were severe enough to require therapeutic intervention. Although unknown, it can be theorized that there is a significant capacity for harm in patients with chronic or acute heart failure and hyperthyroidism. Although, in the Huang et al., Study [28], iodinated medium DSA has a greater diagnostic performance than carbon dioxide DSA, but it carries a far greater risk.

Sueyoshi et al. [29], performed a prospective study to evaluate carbon dioxide-contrast DSA, which is used due to its non-nephrotoxic and nonallergenic character. No patient, indeed, had any complications due to the carbon dioxide DSA. The study’s results showed that 40% of patients had a total of 17 endoleaks. Types 1 and 3 endoleaks, carbon dioxide-DSA is shown to have a sensitivity and specificity of 100% and 100%, respectively. For persistent type 2 endoleaks, the sensitivity and specificity are 87% and 97% respectively, which are far more reliable than C-DSA for the detection of direct and persistent endoleaks.

In the earlier study by Huang et al. [28], carbon dioxide DSA had a sensitivity of 84% and a specificity of 72% compared to iodinated contrast angiography; therefore, they concluded that the detection of endoleaks is superior with iodinated contrast medium; however, carbon dioxide-DSA was still feasible for detecting endoleaks. Mendes et al. [30], with a similar group size, noted that the use of carbon dioxide had similar outcomes when compared to iodinated medium DSA; however, due to its inert properties, carbon dioxide is often insufficient, and iodine is required to visualize the lumbar and inferior mesenteric arteries, among others.

**WHAT IS THE OPTIMAL IMAGING METHOD**

As discussed above, there are several advantages and disadvantages to the different imaging modalities. The question still exists as to which imaging technique is optimal to visualising endoleaks. This section of the review focuses on comparative studies that compare CTA, MRI, CEUS and duplex scans. CTA is still the gold standard, hence why we have compared the other imaging techniques to it, weighing up the pros and cons.

**CTA vs CEUS**

A study by Bredahl et al. [16], showed that CTA and CEUS were diagnostically equivalent. However, some endoleaks were missed by CEUS yet were so insignificant that they did not require any further intervention. An advantage of CEUS over CTA is that its dynamic imaging may be used to classify endoleaks into its different types with more certainty than CTA as it shows the direction of flow. Abbas et al., in his article suggested that [31], 3D CEUS has even greater advantage as it allows a reconstruction of the imaging and can be performed in a vascular clinic. Additionally, 3D CEUS is approximately 67% cheaper than CTA for yearly surveillance [31], which questions the cost-effectiveness of CTA. CEUS is more likely to detect type II endoleaks than other imaging modalities. The study by Clevert et al. [18], concluded that the combination of CTA and CEUS is the best for real time dynamic information and detecting endoleaks. Image fusion however, will be a lot more time consuming, more expensive and more difficult to conduct as exact matching can be hindered by temporary movement by the patient due to breathing which leads to a greater exposure time. The study then concludes that such fusion imaging modality should only be used in very complex cases where no other alternative is found[5]. CTA is preferred over CEUS when considering factors such as graft integrity, graft anchorage and changes in the morphology of the aneurysm [32]. Theoretically, CEUS is better at identifying the classification of endoleaks as the longevity of contrast circulation allows for patients in the late phase to be studied too. In our experience and the practice in our centre, CTA is the method of choice for follow up of patients following EVAR. The images and findings will be discussed at local vascular meeting for further follow up. The choice of CTA is purely based on the facility available, however one should mention that our capability for CEUS is limited and we lack the operator experience to provide comparative studies to CTA. Nevertheless, in the nearest two regional centers there are trials currently running comparing paired studies of CTA and CEUS following EVAR and results should be reported soon.

**Duplex vs CTA**

Bredahl et al. [16], also highlights that duplex ultrasound (DUS) missed endoleaks in 1/3rd of patients which in CTA were deemed in need of requiring reintervention. Hence making DUS an inadequate for EVAR surveillance within the first year of follow-up in comparison to CTA. Duplex ultrasound is useful in visualising the flow within renal arteries and in identifying any disturbances to blood flow i.e. by stent-graft abnormalities. CTA is a non-invasive technique as discussed above but has its
major drawbacks - it leads to accumulation of nephrotoxic side-effects of contrast media as well as the exposure to radiation. Ultrasound, on the other hand, is also non-invasive and has a lower association with side-effects. The technique is non-ionising, but the aorta is often difficult to visualise in obese patients in those with flatulence. Another disadvantage of DUS is that it has a greater chance of producing false negatives but in this study [33], the findings were suspicious so the significance of these is questionable. Another study found that a total amount of $3000 dollars could be saved if they were to use DUS instead of CTA. However, DUS was found to identify only 65% of patients who had uncomplicated EVAR. This raises the debate of cost vs effectiveness/sensitivity.

**Duplex vs CEUS**

When comparing CEUS with DUS it was found that there was greater tendency to elicit artefacts when coloured contrast was used. Both modalities include the use of contrast, but greater cases of artefacts are found in DUS [33]. A disadvantage of all ultrasound is the limited area that it covers; for example, the inability to view whole thoracic aorta or the whole intracranial area. This may mean that the true extent of the dissection is not appreciated [32]. The main advantage of ultrasound is that it can very easily be used at bed side in a clinical setting and due to the portable nature of the device, it can be used in theatre as well. DUS, as indicated in the study by Millen et al. [34], is limited by factors such as echo reflection by metallic components, calcifications, the amount of experience held by the operator, endoleaks that have a low flow and obesity.

**CTA vs MRI/MRA**

MRA is not commonly used for the detection of endoleaks despite research having shown the MRA has greater sensitivity than CTA [35]. MRA is not the gold standard but is used as an alternative to CTA in centres that lack the technical knowledge and practice of CTA. This method is desirable in certain cases, as it reduces the number of CT scans through integration between different modality of investigations, especially in young patients as it reduces the risk of renal insufficiency and exposure to ionising radiation. However, the key drawback is that it may affect stent-grafts made from nickel and stainless steel as it increases the risk of their migration, which may cause a blockage elsewhere and it could be fatal. Therefore, CTA is deemed safer with regard to this but MRA doesn’t use ionizing radiation and hence will not lead to nephrotoxicity as is the case with CTA. A disadvantage that applies to both techniques is that they are both costly and are both time consuming [19]. Another study concluded that MRI is more sensitive than CTA in the detection of post-EVAR endoleaks. They recommended that MRI should be used in those with continued aortic abdominal aneurysm growth or when findings on CTA are not certain [36-39].

Finally, several studies have been published about utilization of intravascular ultrasound (IVUS) during EVAR. They have demonstrated its role in minimizing radiation and contrast exposure; however, all these studies are intraoperative studies and the use of such technique in postoperative period as follow-up imaging modality is not explored fully and remains debatable [40,41].

**CONCLUSION**

Computerized tomography angiogram remains the most popular imaging method being used as a follow up post EVAR, however contrast enhanced ultrasound is gaining momentum and it is providing high sensitivity and specificity in detecting endoleaks; with additional benefit of lacking the use of contrast and radiation exposure, thus safer profile. Larger randomized studies are required to confirm the superiority of either techniques.

**REFERENCES**

10. Abdominal aortic aneurysm: diagnosis and management. NICE. In development [GID-GGWAVE0769], 2018.


