

Diagnostic imaging methods applied in long-term surveillance after EVAR. Will computed tomography angiography be replaced by other methods?

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Abstract

Endovascular implantation of a stent graft in the abdominal aorta (endovascular aneurysm repair – EVAR) is a widely accepted alternative to open surgery in treatment of abdominal aortic aneurysms. Although EVAR is connected with a significant reduction in the risk of peri- and post-operative complications, it does not eliminate them totally. Long-term surveillance of post-EVAR patients is aimed at early detection of and fast reaction to a group of complications called endovascular leaks. Currently, the gold standard in leak diagnostics is computed tomography angiography (CTA). The other methods are ultrasonography, magnetic resonance (MR) angiography, intra-aneurysm sac pressure measurement, X-ray, and digital subtraction angiography (DSA). Despite many analyses based on long-term research, emphasising the high value and competitiveness of less invasive tests such as US or X-ray compared to CTA, it is still difficult for them to win the trust and acceptance of clinicians. The persisting view is that computed tomography is the test that finally resolves any inaccuracies. Consequently, a patient with a number of concurrent diseases is subject to absurdly high radiation exposure and effects of a radiocontrast agent within a short time. It is therefore logical to acknowledge that the EVAR-related risk is catching up with the open surgery risk, while the endovascular procedure is much more costly. Nevertheless, the status of CTA as the gold standard ultimately seems to be unthreatened. This paper presents a description of the diagnostic imaging tests that make it possible to detect any vascular leaks and to develop strategies for therapeutic processes.

Key words: aortic aneurysm, stent graft, endoleak, computed tomography, ultrasonography, angiography, magnetic resonance imaging.

Introduction

Endovascular techniques have opened a number of possibilities in treating abdominal aortic (EVAR) and thoracic (TEVAR) aneurysms. In the late 1980s and early 1990s, Parodi and Volodos independently described the possibility of providing an aneurysm sac with an implanted endovascular prosthesis [1, 2], whereas in 1998 Dake implanted a stent graft in a thoracic aortic aneurysm. Since that time EVAR/TEVAR has been considered an effective alternative to open surgery, and therefore the number of EVAR procedures performed worldwide has been rising. The procedure consists in implanting a stent graft into an aneurysm sac and sealing its proximal and distal part within the healthy aortic walls. Incomplete elimination of the aneurysm sac from the blood circulation is defined as an endoleak, which is the most frequent complication observed for this method, concerning

from 10% to 45% cases [3]. Endoleaks lead to increasing the aneurysm diameter and a risk of rupture. Therefore, it is obligatory to monitor post-EVAR patients in order to detect any endoleaks or other complications [4].

The classification of endoleaks is based on locating the source of blood inflow into the aneurysm sac. The estimated frequency of endoleaks is up to 45% [3, 5]. The most frequently occurring type II leak is found in 6–30% of post-EVAR patients, most of which subside spontaneously within 6 months from the moment of detection [5–8]. Type I and III leaks, although relatively rare, are connected with a very high risk of aneurysm rupture, which indicates the need for urgent interventional treatment [5–8].

The aim of the present review is to show the relevance of different imaging techniques applied in surveillance and monitoring EVAR-treated patients. The

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review of the evidence-based literature was performed in accordance with specificity, sensitivity, safety and economical justification of available methods of post-EVAR follow-up

Computed tomography angiography

Computed tomography angiography (CTA) is an invasive diagnostic test, which the EUROSTAR and UK EVAR trials consider to be the gold standard in post-EVAR patient diagnostics [9] (Figure 1). Computed tomography has a stable position in abdominal aortic aneurysm (AAA) monitoring. Due to its high diagnostic value it is still considered decisive in determining existence of leaks and aneurysm growth, and consequently in formulating indications for treatment. The advantages of CTA include easy availability, short test time, repeatability and easy storage of the results, which facilitates comparing subsequent images. The major drawbacks of this method include exposure to radiation and contrast agent administration. Repeated doses of radiation considerably increase the risk of cancerogenesis [10, 11]. The estimated dose of acquired radiation is approximately 10–12 mSv per study [12]. The dose of 10 mSv is estimated to provoke one case of cancer in 2000 [13]. The risk of complications is increased by administration of an intravenous radiocontrast agent, which may lead to allergic reactions and cause renal failure. Cyclically applied CTA leads to progressing renal impairment, even in patients without any clinical signs of contrast-induced renal failure [13, 14]. On average, 11% of patients undergoing CTA suffer irreversible renal damage, while 0.6% of them die as a result of that condition [15]. In the economic aspect, regular reapplication of the test in the patient surveillance process considerably increases the costs connected with EVAR [9]. All the benefits and limitations of computed tomography have contributed to a worldwide discussion questioning the legitimacy of applying CTA in routine surveillance of patients. Some publications question the dominating role of computed tomography as the most sensitive and specific method for aneurysm diameter monitoring as well as endoleak detection and classification. Han *et al.* [16] proved that measurements in transverse scans may misestimate the aorta diameter, in particular when the vessel is bent, which may imitate the aneurysm sac widening. 3D computed tomography makes it possible to correct any potential errors due to making the measurements perpendicularly to the longitudinal axis of the aorta. The difference between the diameter measured in the transverse projection and in the 3D reconstruction may be up to 4.36 mm [17]. Applying CTA, Schmieder *et al.* detected only 58% of leaks, of which only 42% were confirmed during reintervention [18]. Limited sensitivity of the method concerns mainly detection of type II leaks; CTA enabled detection of only 66 out of 123 cases. This result makes computed tomog-

raphy no better than ultrasonography. Therefore, it is suggested that the number of CT tests per patient should be reduced. Go undermined the legitimacy of applying check-up CTA every 3–6 months in the first year following EVAR, showing that among the patients without post-operative complications (no leaks in CTA 1 month after the procedure), repeating the test after 6 months does not provide any clinically relevant data [19]. None of the patients who skipped the test experienced any incidents that jeopardised their life or health, or required urgent reintervention. Similar conclusions were drawn by Dias *et al.*, who pointed out that fewer than 10% of post-EVAR patients benefit from frequent monitoring by means of CTA [20]. In recent years the standard procedure for endoleak detection is multiphase CTA, allowing more accurate type II endoleak detection [21]. However, the radiation dose in this case is higher, which makes repeated multiphase CTA problematic due to the probability of a stochastic radiation effect [13, 22]. The effect of radiation may be reduced by low voltage dual energy CTA, but this methodology needs additional studies [22]. Multiphase CTA is especially effective in the case of planning of the intervention and together with contrast-enhanced ultrasonography (CEUS) allows assessment of flow direction in the endoleak area. Nevertheless, it must be stressed that performing CTA is absolutely indispensable for planning a reintervention procedure.

Duplex ultrasonography

Duplex ultrasonography (DUS) is a basic method in monitoring patients with aneurysms in the infrarenal aorta [23]. As the endovascular procedure (EVAR) became more and more popular, which was followed by the



Figure 1. Type II endoleak in cross-sectional CTA scan

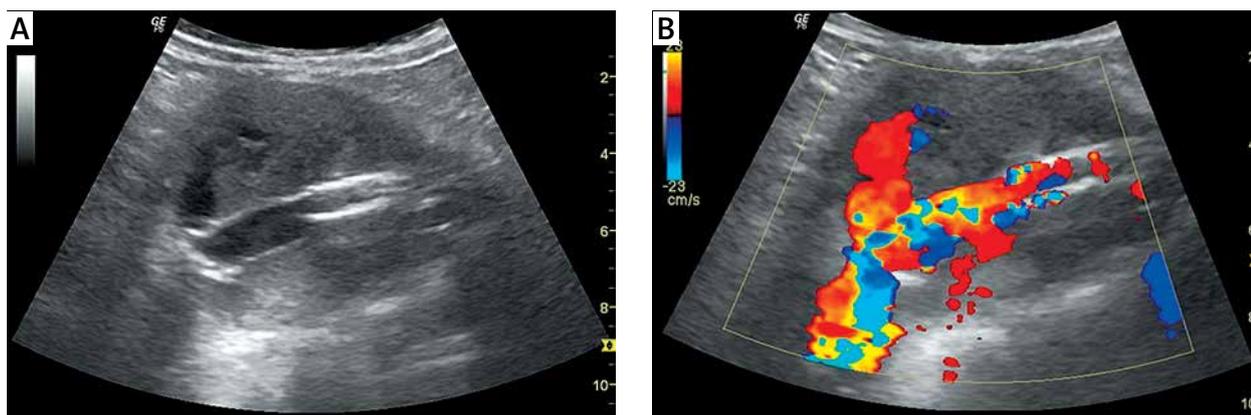


Figure 2. A – B-mode image of stent graft and aneurysmal sac. B – Type I A endoleak in DUS

need to regularly supervise the post-EVAR patients, ultrasonography was recognised as appropriate for that purpose (Figure 2). Duplex ultrasonography is the first test to be included in the routine follow-up schedule for post-EVAR patients, as it is inexpensive, accessible, as well as easy to perform and interpret. Undoubtedly, DUS is a method whose preciseness depends on the experience of the person performing it [9]. Moreover, DUS is considered less precise in AAA diameter assessment compared to CTA. This is due to the lack of standards in ultrasound measurement techniques, which results in considerable leeway in that regard [24, 25]. In contrast to computed tomography, ultrasonography makes it possible to avoid errors connected with bent aortas, by positioning the transducer probe perpendicularly to the longitudinal axis of the aorta [24–26]. According to Han *et al.*, the compliance of diameter measurements in ultrasonography and 3D CTA reached 92%, while differences in diameter did not exceed 3 mm. Moreover, they showed that to obtain a result that is as much as possible compliant with 3D CT, the longitudinal axis of the diameter must be measured in the DUS, as the difference is then no greater than 0.11 mm [16]. Thus they obtained a very high level of correlation between ultrasonography and CTA, unlike his predecessors who compared aneurysm diameters in the transverse (d’Audiffret *et al.*) and anteroposterior (Manning *et al.*) projection in ultrasonography with the largest dimension of the sac in the CT transverse scan [27, 28]. The research that compares ultrasonography and CT in terms of endoleaks brings various results. The available publications show discrepancies in ultrasonography sensitivity assessment in leak diagnostics within the range from 52% to 81%; nevertheless, they always showed a high negative predictive value of ultrasonography of 86–95%. Sato *et al.* and d’Audiffret *et al.* independently recognised DUS as a promising screening test for endoleaks, showing sensitivity of, respectively, 97% and 96% [26–29]. Elkouri *et al.* obtained weak results in leak detection by means of ultrasonography, showing sensitivity of only 25% and specificity of 89% [30].

The research results of Schmieder *et al.*, on the other hand, were quite astonishing [18]: DUS made it possible to detect 89% of leaks (58% in CT), while the accuracy of endoleak classification was 74% (42% in CT), on the whole, proving impressive usefulness of ultrasonography in detection of leaks requiring reintervention, with sensitivity of 90%, specificity of 81%, negative predictive value (NPV) of 98% and positive predictive value (PPV) of 16% (respective values for CT: 58%, 87%, 98%, 15%). The DUS was found superior to CT in detecting type I and II endoleaks, and results in detecting type III endoleaks were comparable [31]. In an independent study, Sun *et al.* obtained similar results as Schmieder’s, where sensitivity, specificity, PPV and NPV of DUS in endoleak detection were assessed to be 66%, 93%, 76% and 90% respectively [18]. AbuRahma *et al.* proved a high value of ultrasonography in assessing type I and III leaks; however, the results were much worse for detecting type II leaks [32]. It is surprising that most comparative analyses show a greater number of type II leaks found via US compared to CT, which is illustrated by the US : CT ratio 1.5 : 1 [16] and US : CT 2 : 1 [28, 29]. Beeman *et al.* showed that both DUS and CT, to a comparable degree, led to false positive as well as false negative results in leak detection. What is important, by checking up patients only by means of US, they reduced the costs of post-operative patient monitoring by 29% on average [33]. Manning *et al.* found that ultrasonography revealed all the leaks diagnosed by way of CTA, which means the US sensitivity amounted to 86% [28]. Summing up the quoted data, ultrasonography may be considered an attractive alternative to computed tomography in long-term surveillance of patients.

Contrast-enhanced ultrasonography

Contrast-enhanced ultrasonography (CEUS) is an ultrasound test where the echo is enhanced by intravenously administered contrast agent, and it is considered one of the most precise methods of vascular leak detection (Figure 3). The test is done by means of a 3–5 MHz transducer probe and ultrasound contrast agent in the form

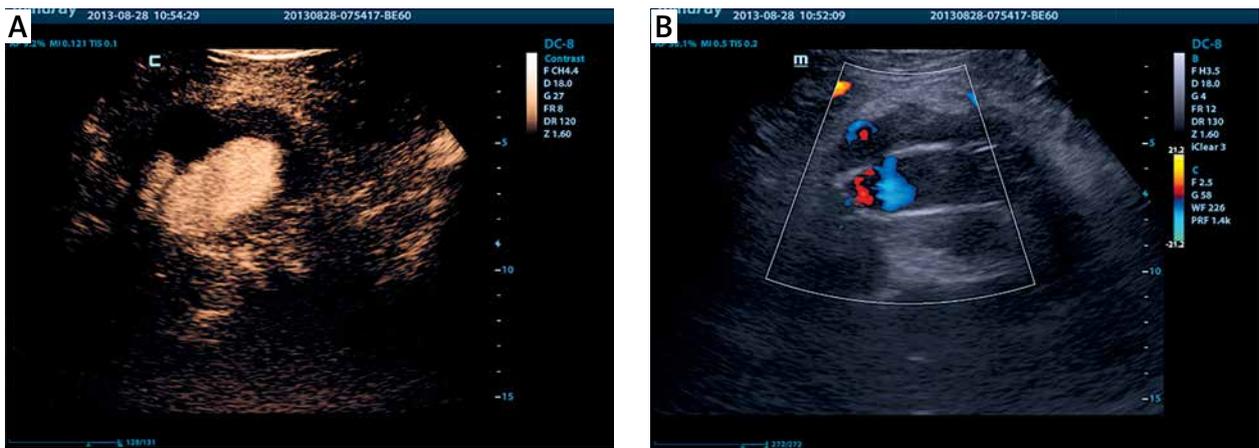


Figure 3. A – Type IA endoleak in CEUS. **B** – Type IA endoleak in DUS

of microbubbles filled with sulphur hexafluoride (SF_6) gas closed in phospholipid capsules. Many research findings have shown that CEUS is a precise test to assess vascular leaks, with considerably higher capabilities than conventional Doppler ultrasonography. Its sensitivity is comparable to that of magnetic resonance, while it does not impose limitations in patient selection as in the case of MR. This is confirmed by the research results obtained by Cantisani *et al.* [34], who proved that CEUS reliably detects leaks, without false positive results (which was verified via DSA). Moreover, CEUS sensitivity is comparable to CT in leak detection [3, 35, 36], while CEUS exceeds CT when it comes to classifying the leaks [37]. This is due to the fact that, as opposed to CT, CEUS provides relevant haemodynamic data on blood flow direction in the leak. The best results, in flow direction assessment, are obtained by 3D CEUS – a technique using positional information from magnetic field emitters and processing it into high-resolution 3D imaging. The results presented by Abbas *et al.* in a pilot study show superiority of 3D CEUS over standard one-phase CT [38]. Despite the poor availability, cost and operator variability, CEUS seems to be one of the safest future developments in endoleak detection.

Digital subtraction angiography (DSA)

Subtraction angiography was previously presumed to be more precise than computed tomography in revealing leak details. Compliance of the results obtained via both methods is evaluated to be 86% [39]. This results from the fact that in computed tomography the radio-contrast agent fills up the lumbar arteries and the lower mesenteric artery, and there is no unambiguous answer whether the blood in the aneurysm sac came from the above-mentioned arteries, as is the case in type II leaks, or whether it is the result of type I or III leak. This doubt can be resolved by DSA, which assesses the blood flow direction, making it possible to precisely classify the endoleak. Performing DSA requires at least one day of hos-

pitalisation, which raises the procedure cost and complication rate. Presently DSA is reserved as a method of intraoperative endoleak assessment during scheduled interventional treatment (Figure 4).

Plain X-ray

A plain X-ray is a simple and cheap diagnostic test which is widely available to all patients. It enables detection of stent deformation, bending or migration more efficiently and with less exposure to radiation compared to CT (Figure 5). Assessing stent graft migration, the position of the prosthesis is compared in relation to specified anatomical features such as the level of renal arteries or vertebrae. Graft migration falling within 5–10 mm is considered as clinically relevant [40, 41]. Standards for correct performance of the test and guidelines for X-ray technicians are specified in the Liverpool/Perth Protocol [42]. It standardises the technical parameters of the test that are necessary to assess the changes of the graft lo-



Figure 4. Type IB endoleak in pre-treatment DSA



Figure 5. Plain abdominal X-ray visualizing correct position of stent graft

cation, an angular bend, distances between the skeletal elements, the stent crown anchoring and mutual mobility of the prosthesis elements. The protocol does not recommend the PA projection due to the inconvenience of the position for elderly patients. It recommends performing X-ray scans in left and right oblique projections, as a supplementation in identifying fractures of metal elements [42, 43]. Hodgson *et al.* proved the value of X-rays compared to CT in diagnosing stent graft migration, involving less exposure to radiation and lower costs [43]. Many researchers prefer X-ray to CT, especially for the purposes of assessing the shape of thoracic stent grafts and abdominal stent graft bends [44, 45].

Nuclear medicine

Compared to celiac artery angiography, static and dynamic scintigraphy applying Tc-99m labelled erythrocytes and Tc-99m sulphide colloids is considered to be a more sensitive and more specific method in diagnosing bleeding into the lower sections of the alimentary tract. On that basis, attempts were made to apply nuclear medicine in detection of post-EVAR vascular leaks. The research done by Stavropoulos *et al.* showed that the nuclear medicine techniques effectively detected leaks; however, compared to CTA their sensitivity was much lower [46]. Hovsepian *et al.* found that scintigraphy applying Tc-99m sulphide colloids is incapable of assessing leaks, whether they are characterised by slow or rapid flow rates [47].

Intra-aneurysm sac pressure measurement

High pressure inside an aneurysm sac is correlated with its augmentation and increased risk of rupture, while low pressure is associated with its shrinkage [48]. With this in mind, two wireless pressure measurement systems were developed and made available: Endosure Sensor (CardioMems, Inc. Atlanta, GA) and Remon (Remon Medical, Tel Aviv, Israel). Both systems are installed during a stent graft implantation procedure and then ac-

tivated by external devices and do not require an internal power supply. The Remon system consists of a piezoelectric membrane actuated by an impulse of ultrasound frequency; it was tested by Ellozy *et al.* [49]. The Endosure system applied in the research conducted by Hoppe *et al.* [50] features two interconnected flexible plates placed in a hermetic capsule. A change in the pressure around the sensor changes the distance between the plates, which induces a change in the volume and acoustic frequency of the whole module. Then the changes in frequency are converted into a pressure graph. Researchers found a considerable intra-aneurysm pressure increase in patients with type I and III leaks confirmed by CTA. In the case of type II leaks, confirmed by CT, pressure measurement turned out to useless, as it showed a decrease or a value comparable to the pressure before the procedure [49, 50]. In 2007, the prospective multicenter APEX (Acute Pressure Measurement to Confirm Aneurysm Sac EXclusion) trial was published, confirming the usefulness, safety and effectiveness of both systems in vascular leak detection [51]. The sensitivity and specificity of the pressure measurement method in detection of type I and III endoleaks is assessed to be 94% and 80%, respectively. The drawbacks of the method include a substantial increase in the cost of the stent graft implantation procedure, and discrepancies in pressure measurements from 5% to even 15%, depending on the structure of the environment in which the sensor was implanted. At the current level of measuring equipment technological progress, this method is useless in detection of type II endoleaks, which are the most frequent complications observed in post-EVAR patients.

Magnetic resonance imaging (MRI)

This is a recognised, valuable test applied in surveillance of post-EVAR patients. Compared to CTA or DSA, its advantage is application of gadolinium as the contrast agent, which has only minor nephrotoxic effects, and, due to its weak affinity for proteins, it is connected with a significantly lower risk of an allergic reaction. Moreover, in the case of magnetic resonance there is no exposure to radiation. Compared to CT, this method was proved to be more sensitive in leak detection. In the research based on observation of patients following implantation of stent grafts, comparable usefulness of MRI and CTA was shown in detection of large leaks. Haulon *et al.* [52] and Alerci *et al.* [53] in two independent studies comparing MRI and CT proved that resonance was definitely more sensitive in diagnosing small-flow leaks. In both studies, the resonance test revealed small type II endoleaks which were not visible in the CT test. The MRI accuracy and lack of false positive results were verified and confirmed by means of angiography [52]. The drawback of MRI angiography (MRA) is that not all patients may undergo it, which is connected with the various materials applied in

stent graft production. Only the prostheses with nitinol (an alloy of nickel and titanium) structure are compatible with the MRI device and do not generate artefacts. Stent grafts made from Elgiloy (an alloy of chromium, nickel and cobalt) may blur in with the surrounding structures in the MRI image, whereas those made from high-grade stainless steel, which has ferromagnetic properties, will be damaged or dislocated when they are placed in a powerful magnetic field [52]. Despite its numerous advantages, resonance is a test which is time-consuming, costly and still hardly available to patients.

Conclusions

Monitoring post-EVAR patients by means of CTA as the gold standard is becoming more and more questionable. Despite many analyses based on long-term research, emphasising the high value and competitiveness of less invasive tests such as US or X-ray compared to CTA, it is still difficult for them to win the trust and acceptance of clinicians. The persisting view that computed tomography is the test that finally resolves any inaccuracies is getting stronger with new tools of low-dose CT, enabling 70% dose reduction [54]. As a result, the patient in the surveillance period undergoes a number of non-invasive tests, which are then verified by tomography, which often is repeated during hospitalisation, and finally undergoes a repair procedure controlled by means of angiography. Taking into consideration presently available data, the status of CTA as the gold standard ultimately seems to be unthreatened.

Conflict of interest

The authors declare no conflict of interest.

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