Contrast-enhanced ultrasound in the follow-up of patients after endovascular abdominal aortic aneurysm repair (EVAR): A pictorial review

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Authors: R. Iezzi, F. Pirro, M. Nestola, A. Simeone, L. Bonomo; Rome/IT
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Learning objectives

To review ultrasound contrast agents and contrast-specific imaging characteristics and to learn the CE-US scanning technique.

To describe the normal aspect of stent-graft on CE-US imaging.

To illustrate the aspect of EVAR-correlated complications on CE-US imaging, focusing on detection and classification of endoleaks.
Background

Endovascular abdominal aortic aneurysm repair (EVAR) is today an accepted alternative to open surgery for selected patients with aortic pathology, offering reduced rates of perioperative mortality and procedure-associated complications, and overall reductions in the length of patient hospitalization [1-3].

However, despite these known excellent early results, many patients treated with EVAR require re-intervention during the middle and long term follow-up due to complications related to the procedure. The most common complication is represented by endoleak [4-8], which is the major cause of enlargement and rupture of the aneurysm, and the main indication for surgical late conversion [9, 10]. For this reason, a strictly surveillance of these patients is mandatory to early detect the presence of endoleaks, in order to determine the long-term performance of these devices [11].

The preferred method of follow-up is represented by multidetector-row computed tomography (MDCT) angiography, which allows the detection of endoleaks and other procedure-related complications with high sensitivity [12, 14] . However, the most important disadvantage of CT is represented by the use of ionizing radiation.

The introduction of ultrasound contrast agents and contrast-specific imaging (CE-US) has rekindled interest in the potential of this modality for replacing of CTA in routine post-EVAR surveillance.

The purpose of this review is to highlight the diagnostic value of CEUS in the post-EVAR endoleaks detection.
Imaging findings OR Procedure details

CE-US IMAGING TECHNIQUE

Ultrasound Contrast Agents and Contrast-Specific Imaging

Ultrasound contrast agents are characterized by the capacity to be modified by the process used to image them [15], creating a contrast-specific signals, with the response depending on the insonation power, i.e. the amplitude of the acoustic pressure wave, indicated by the mechanical index (MI).

With the use of an high acoustic powers (high MI) the microbubbles are destroyed producing specific signals, which are of very high intensity over a broad range of frequencies, not requiring contrast-specific imaging software but simply using the normal color Doppler mode.

As a matter of fact, initial CEUS studies were performed by using the first-generation agent SHU 508A in combination with color Doppler or tissue harmonic imaging [16-19]. SHU 508A comprised relatively fragile bubbles of air surrounded by a lipid shell containing palmitic acid and is best imaged with a high MI technique whereby the agent is destroyed as it is imaged. However, signals are only very transient, since the microbubbles are destroyed within a few milliseconds, not allowing a continuous assessment of structures (dynamic imaging). With the use of a low acoustic powers (low MI) the microbubbles remain static, simply resonating when interrogated with sound. The oscillation of the microbubbles results in the emission of specific sound waves, which can be detected by the transducer as contrast-specific signals [20]. In detail, the resulting image has very little signal originating from background tissue and high-intensity depiction of echoes from microbubbles. This produces high image contrast between tissue and the microbubble agents within the blood pool.

Second-generation microbubble contrast agent consist of a perfluorocarbon gas surrounded by a phospholipid shell. When low MI techniques are used, they are relatively robust, allowing real-time detection without significant agent destruction. As a matter of fact, this combination allows to visualize a stent-graft in real time, from many different angles and over several minutes. This enables more practical and reproducible evaluation of these patients in a routine clinical setting. Furthermore, in case of doubts, microbubbles can be instantly destroyed by using a brief pulse of high-intensity (highMI) in order to detect/exclude the presence of subtle endoleaks.
**Scanning Technique**

US-scans are performed by using a last-generation scanner, equipped with a convex multifrequency 5-2 MHz probe, with contrast-specific software using a nonlinear imaging techniques with a low mechanical index of between 0.1 and 0.2.

Fasting patients are scanned in the supine or lateral position with the head slightly elevated at 10°, with grey scale and color Duplex before the intravenous contrast medium injection.

Both pre- and post-contrast US are performed by using transversal and longitudinal scans focused to the abdominal aorta including the origin of the renal arteries, the whole stent graft from the proximal to the distal anastomosis, including both prosthetic branches or, in the case of an aortic monoiliac prosthesis, only the prosthetic branch and the downstream iliac axis.

The required or optimal dosage for administration of contrast agents after EVAR is not yet clearly defined [21-23]. Our recent published experience [24] performed comparing two different doses of CM (1.2 mL and 2.4 mL) with the attempt to define the optimal US CM dose, show that 2.4 mL is preferred to 1.2 mL, as it provides significantly better results in intensity and duration of contrast enhancement and, consequently, in visualization than the low dose. As a matter of fact, we usually inject a bolus of 2.4 mL of CM, followed by flushing with an injection of a 5cc bolus of saline solution through an 18-20 G cannula placed in an arm vein.

Scanning is started at the beginning of contrast agent injection and the sweep is usually completed within 5 minutes. The phases of CEUS are defined as arterial (10-40 seconds after contrast agent injection) and late (90-300 seconds after injection) phases. In case of uncertain enhancement/doubt diagnosis, a destruction-reperfusion technique can be used. For this technique, a brief pulse of high-intensity (high-mechanical-index) sound is used to confirm the presence of contrast material in an endoleak by its complete destruction. Immediately after this, reperfusion of the endoleaks can also be documented in real time.

**CE-US ENDOLEAK DETECTION**

On CE-US images, the endoleak, which is defined as the persistence of peri-graft flow within the aneurismal sac excluded by the stent-graft, appears as a high attenuation area beyond the graft but within the aneurysm sac, absent on the baseline unenhanced phase images, due to the presence of contrast enhancement.
The evaluation is based on visual assessment with particular attention to the endoleaks wash-in and wash-out, origin of the endoleaks, identification of inflow and outflow collateral vessels as well as enhancement morphology.

Recent literature [18,19, 25-27, 28-30] demonstrated that the use of microbubble contrast agents significantly improves the capability of US to detect endoleaks, overcoming its limitations, principally due to echo reflection by the metallic portion of stent-graft, presence of calcifications, and slow endoleak flow, which does not allow distinction of color signals coming from vessel walls and surrounding tissue from those derived from corpuscular haematic components. In detail, in our recent experience performed on 84 consecutive patients treated with EVAR, CE-US significantly improved the visualization of all parts of the endoprosthesis (fig. 1) as well as the diagnostic performance in endoleaks detection, with an obtained sensitivity and negative predictive value similar to MSCT angiography (97.5% and 97.3%, respectively) [24].

Due to the longer duration of enhancement, lack of metallic artifacts and angio-dynamic evaluation of the leak during the dynamic phase, CEUS seems more specific than CTA in detection of small low-flow endoleaks (fig. 2).

On the other hand, CEUS could also allow an easier identification of small endoleaks with simple diffuse spreading of contrast agent into the thrombus in which the lack of concentration in a defined and confined region of the sac could reduce CTA detection capability (fig.3).

**CE-US ENDOLEAK CLASSIFICATION**

The presence of endoleaks means that the attempt to exclude the aneurismal sac has failed, but it does not necessarily imply that the procedure itself has failed. As a matter of fact, although the presence of endoleaks may cause the enlargement of the aneurismal sac with possible caudal migration of the prosthesis or rupture of the aneurysm, a spontaneous solution may also occur. To understand which endoleak needs to be promptly treated, we should consider the following classification based on the etiology of endoleaks, as proposed by White et al [31-33].

Type I endoleak is due to an incomplete attachment of the proximal and/or distal end of the prosthesis to the aortic walls, due to technical (e.g. suboptimal stent-graft diameter) or anatomical (e.g. short, irregular, ulcerated or angulated proximal neck) problems, or to its caudal migration. On CE-US images, it usually appears as a huge high-flow leak, synchronous with respect to graft enhancement, spreading from the proximal or distal end of the prosthesis into the thrombus with a cranial or caudal direction, respectively (fig. 4).
Type II endoleak is due to a retrograde filling via aortic collateral arteries such as lumbar arteries, inferior mesenteric artery, or hypogastric artery, if covered. On CE-US images, type II endoleak is most pronounced at the periphery of the aneurysmal sac, with no or a little delayed contact with prosthesis, commonly located in a posterior or lateral position and usually associated with opacification of collateral arteries. Furthermore, CEUS allows an angiodynamic visualization of the agent flow into the aneurysm sac, recognizing its direction and easier differentiating type II (directed from the periphery to the graft) from type III (directed from the graft to the periphery) endoleaks (fig. 5). With respect to the time of appearance, it is classified as hyperdinamic (fig.6) or hypodinamic (fig.7) endoleak if wash-in is less or higher than 100 seconds, respectively [22]. As a matter of fact, type-II endoleak is never synchronous with respect to graft enhancement; this characteristic allows an easier differentiation between type I and type II endoleaks.

Type III endoleak arises from a defect of the stent-graft membrane itself, or from modular or graft disconnection; this latter is more likely when multiple prostheses with short overlapping areas are used. On CE-US images, the leak is strictly adjacent to prosthesis, with a delayed contact with margins of the aneurysmal sac, without opacification of collateral arteries. This endoleaks is more frequently synchronous with respect to graft enhancement; as previously described, the opposite direction of the contrast flow allows a differentiation with type II endoleaks (fig. 5).

Type IV endoleak is due to a porosity of the prosthesis and is usually only detected on conventional angiograms performed at the end of the procedure or in the first week after procedure. On CE-US images, it is similar to a diffuse type III endoleak, involving all the stent-graft; the diagnosis of a type IV endoleaks should be one of exclusion.

Type I and type III endoleaks may cause a substantial increase in aneurysm size putting patients at high risk for aortic rupture, therefore needing an early re-intervention. However, the most common endoleak founded in endovascular stent-grafting is type II endoleak. The treatment of these endoleaks is a source of continuing discussion and debate: based on literature, type II endoleaks require a treatment only if associated to an increase in size of the sac.

CEUS LIMITATIONS

CEUS also has some limitations: patient habitus (obesity) and bowel gas can interfere with imaging and the patient must cooperate. Moreover, sonographic examination results are operator-dependent and obtaining quality images requires training and specific skills.

As reported in our published experience [24], it is mandatory to underline that the "low permeability" design Gore Excluder Endoprosthesis cannot be adequately studied with
sonographic imaging (US as well as CEUS) at 1-month follow-up. As a matter of fact, this innovative device, introduced in the 2002, is composed of a durable, reinforced ePTFE graft, low permeability material layer, electropolished nitinol stent, and bonding film for stent to graft attachment. Its unique graft design reduces the potential for serous fluid movement through the graft wall with consequent endotension. However, the ePTFE graft material produces significant artifacts with echo reflection at 1-month follow-up (fig. 8), not allowing a possible stent-graft evaluation as well as endoleaks detection; these artifacts usually disappear at 6-month follow-up.
Fig. 0: A 75-year-old woman treated with aorto-bisiliac stent-graft implantation (6-month follow-up). CEUS allows an excellent visualization of the stent-graft, recognizing the presence of graft thrombosis (lines in c), as an intraluminal, parietal, concentric not-enhanced area within the stent-graft, as confirmed by CT images (MIP-images: a, b).

Fig. 0: A 85-year-old woman treated with EVAR with increase in size of the aneurysm sac in comparison with previous CT exam. No endoleak was detected on both arterial (a) and 60-seconds delayed (b) phase, with a consequent diagnosis of endotension. However, a small-sized endoleak was detected on contrast-enhanced ultrasonography (c) (arrows). This low-flow endoleak was confirmed by a delayed phase image performed 300 seconds after contrast medium injection (c) (arrows), justifying the increased aneurysmal sac and excluding the previously diagnosis of endotension.

Fig. 0: A 84-year-old man treated with EVAR (12 month follow-up). CEUS allows an easier visualization of a small endoleak with diffuse spreading of contrast agent into the thrombus (arrows in b) in which the lack of concentration in a defined and confined region of the sac could reduce CTA detection capability (arrows in a).

**Fig. 0:** A 79-year-old man treated with EVAR (24-month follow-up). CE-US images (c-d) allow the detection of the right iliac branch angulation with an associated small distal type-I endoleaks (asterisk in d), as confirmed by CT-angiography (arrow in b).

Fig. 0: A 71-year-old man treated with EVAR (1-month follow-up). 3D (a, c) and axial (b) CT images demonstrated a large endoleak located in a postero-lateral position, associated with opacification of a lumbar artery (c), classified as a type-II endoleak. However, the leak is also strictly adjacent to the prosthesis, with a consequent possible diagnosis of a concomitant type-III endoleak. A clearly classification of the endoleak was not clearly performed on the basis of CT images. Dynamic CE-US images (d) evaluation demonstrate the back-filling of the excluded aneurysmal sac via lumbar artery, excluding a concomitant type-III endoleak, as confirmed by DSA (e-g, arrows in f and asterisk in g).


Fig. 0: An hyperdinamic type-II endoleak is detected on both CE-US (wash-in: 35 seconds) and arterial CT images.
Fig. 0: CEUS image (arrows in a) detects a small endoleak with a wash-in higher than 150 seconds, regarded as hypodinamic low-flow leak. CT-images confirm the presence of a small endoleak on the postero-lateral side of the aneurysm, detected only on delayed phase axial CT image (low-flow leak) (arrows in c).

Fig. 0: A 81-year-old woman treated with the implantation of a "low permeability" design Gore Excluder Endoprosthesis (1-month follow-up). At 1-month follow-up (a-b), the ePTFE graft material produces significant artifacts with echo reflection not allowing an adequate stent-graft evaluation as well as endoleaks detection; these artifacts usually disappear at 6-month follow-up.
Conclusion

In conclusion, CEUS is a fast, non-invasive, reliable and valid alternative to MSCT angiography for endoleak detection in endovascular aortic stent graft patients.

However, based on its limitations, in the post-EVAR follow-up, CEUS cannot replace CT-angiography in providing information related to graft anchoring and integrity, aneurysm morphologic changes or visceral vessels patency (renal arteries). As a matter of fact, in our opinion, in the post-EVAR follow-up, CEUS should replace CTA at 6-month follow-up and annually thereafter. On the basis of this opinion, our suggested post-EVAR follow up is based on CTA at 1 and 12 months after EVAR with CEUS performed at 6 months and annually thereafter, if no complications are detected.
Personal Information

Corresponding author:

Roberto Iezzi, M.D.

Department of Bioimaging and Radiological Sciences,

Institute of Radiology,

"A. Gemelli" Hospital -

Catholic University,

L.go A Gemelli 8,

00168 Rome, Italy

Tel.: +39-06-30154977

Fax: +39-06-35501928

e-mail: roberto.iezzi@rm.unicatt.it

iezzir@virgilio.it


