Use of three-dimensional contrast-enhanced duplex ultrasound imaging during endovascular aneurysm repair

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Background: **Iodinated contrast during endovascular aneurysm repair (EVAR) is used with caution in patients with chronic kidney disease. Contrast-enhanced ultrasound (CEUS) imaging using nonnephrotoxic sulphur hexafluoride microbubble contrast is a novel imaging modality that accurately identifies and characterizes endoleaks during EVAR follow-up. We report our initial experience of using three-dimensional (3D) CEUS imaging intraoperatively as completion imaging after endograft deployment. Our aim was to compare intraoperative 3D CEUS against uniplanar angiography in the detection of endoleak, stent deformity, and renal artery perfusion during EVAR.**

Methods: **The study enrolled 20 patients undergoing elective conventional infrarenal EVAR, after which a completion angiogram was performed and the presence of endoleak, renal artery perfusion, or device deformity were recorded. With the patient still under anesthetic, a vascular scientist blinded to angiographic findings performed 3D CEUS and reported on the same parameters.**

Results: **Three endoleaks, one type I and two type II, were detected on uniplanar angiography and 13 endoleaks, 11 type II and two type I, were found using 3D CEUS imaging. Of note, one of these type I endoleaks was not seen on angiography, and this patient underwent balloon moulding of the neck with resolution of the endoleak on repeat imaging. Of the 11 type II endoleaks seen with 3D CEUS imaging, the inflow vessel was identified in nine cases. No graft deformity or limb kinking was seen in any patient. Both renal arteries could be visualized in 10 patients, whereas the target renal artery was seen in 11 patients. In the remaining patients, the renal arteries could not be visualized, mainly due to intra-abdominal gas or patient body habitus.**

Conclusions: **3D CEUS imaging detected endoleaks not seen on uniplanar digital subtraction angiography, including a clinically important type I endoleak, and was also more sensitive than 2D CEUS imaging for the detection of the source of endoleak. This technology has the potential to supplement or replace digital subtraction angiography for completion imaging to reduce the use of x-ray contrast. Intraoperative 3D CEUS has been applied to allow safe EVAR with ultralow or no iodinated contrast usage in selected cases, without compromising completion imaging. (J Vasc Surg 2014;60:1468-72.)**

Endovascular aneurysm repair (EVAR) has reduced the incidence of postoperative mortality compared with open repair,[1] although EVAR may be complicated by acute kidney injury due to maldeployment, renal microembolization, or the use of iodinated contrast (IC) media. IC can result in short-term and long-term contrast-induced nephropathy, particularly in patients with underlying chronic kidney disease (CKD), and is contraindicated in those who are allergic to iodine.[2,3]

Standard endograft deployment technique uses digital subtraction angiography (DSA) with IC media to aid intra-arterial navigation and to provide quality-assurance completion imaging to examine for the presence of endoleaks, visceral vessel patency, and endograft integrity. Although an essential element of safe endograft deployment, completion imaging significantly contributes to the total IC load, especially if several angiographic runs are required. Carbon dioxide (CO_2) has been used as a non-nephrotoxic alternative to IC,[4] but its utility is limited to endograft deployment because CO_2 does not provide adequate image quality for completion quality control.[5]

The role of contrast-enhanced ultrasound (CEUS) imaging in the context of post-EVAR surveillance has gained acceptability in recent years[6-9] because it presents a cost-effective alternative to computed tomography (CT) that does not necessitate nephrotoxic IC or ionizing radiation. CEUS imaging uses non-nephrotoxic sulphur hexafluoride microbubbles as contrast, which are completely eliminated through the lungs. Three-dimensional (3D) CEUS is an evolution of this technology that uses positional information from magnetic field emitters to place and orientate the ultrasound transducer probe precisely in space to allow dynamic interrogation of an endograft from any angle within the aneurysm. A pilot study from our institution showed that 3D CEUS has accuracy comparable to or better than CT to detect endoleaks during post-EVAR follow-up.[10]

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Table I. Patient demographics

Age, years	*Sex*	*BMI, kg/m²*	*Aneurysm size, cm*	*Current smoker*	*Diabetes*	*SBP, mm Hg*	*DBP, mm Hg*	*Creatinine, μmol/L*	*EVAR device*
70	M	33.6	7.2	No	No	128	79	175	Cook LP[a]
86	M	27.8	6	No	No	160	80	109	Endurant II[b]
74	M	26.1	7.8	No	No	171	74	118	Zenith[a]
72	M	30.5	5.6	No	No	130	90	115	Endurant II[b]
77	M	25.2	6.1	Yes	No	161	95	213	Ovation[c]
66	M	32.7	5.5	No	No	124	83	71	Endurant II
75	M	30.4	5.7	No	No	127	72	120	Endurant II
68	M	23.1	8.4	No	No	150	70	83	Endurant II
79	M	29.8	6.4	No	No	193	93	102	Ovation
79	M	24.0	5.7	No	No	142	65	59	Endurant II
64	M	30.0	6.7	No	No	151	80	66	Aorfix[d]
86	F	26.4	5.5	No	No	131	63	83	Ovation
84	M	30.1	5.5	No	No	118	68	84	Endurant II
88	F	28.3	5.8	No	Yes	110	40	72	Endurant II
74	M	32.2	7.1	No	No	137	68	83	Endurant II
81	M	20.0	4.2 (iliac)	Yes	Yes	128	64	66	Endurant II
72	M	26.0	5.3	No	No	162	80	129	Endurant II
83	M	27.2	5.7	No	No	165	74	69	Endurant II
86	M	29.0	6.1	No	No	128	61	102	Anaconda[e]
75	M	29.0	9.5	No	No	142	48	107	Endurant II

BMI, Body mass index; *DBP,* diastolic blood pressure; *F,* female; *M,* male; *SBP,* systolic blood pressure.
[a]Cook, Bloomington, Ind.
[b]Medtronic, Minneapolis, Minn.
[c]TriVascular, Santa Rosa, Calif.
[d]Lombard Medical Technologies PLC, Oxfordshire, UK.
[e]Sulzer Vascutech, Bad Soden, Germany.

Intraoperative use of this technology gives the potential to visualize stent graft positioning and endoleak immediately after deployment while reducing the overall requirement of IC media. Thus, intraoperative CEUS potentially has clinical utility in patients with chronic renal impairment or when CO_2 is used the primary contrast medium. The aim of this feasibility study was to assess the clinical utility of 3D CEUS for intraoperative completion imaging after EVAR as an alternative to conventional uniplanar catheter angiography for the detection of endoleak, endograft deformity, and renal artery patency.

METHODS

The study prospectively enrolled 20 patients undergoing elective infrarenal EVAR under the care of a single surgeon. The local ethics committee approved the project, and the patients gave informed consent. All patients were initially seen in the clinic and reviewed by a consultant vascular surgeon. Suitability for EVAR was determined from an initial CT scan using IC. The morphologic characteristics of the aneurysm and access vessels were reviewed at a multidisciplinary team meeting.

All patients underwent EVAR deployment while under general anesthesia in a vascular operating theater with mobile C-arm imaging. After endograft deployment, a standard completion uniplanar DSA was done using 20 mL full-strength iodixanol contrast (Visipaque 270; GE Healthcare, Hertfordshire, UK) injected at 10 to 15 mL/s. The presence of endoleak, renal artery perfusion, and device deformity were recorded. Endoleaks were characterized by type and source. Renal artery perfusion and presence of graft deformity were also noted. With the patient still anesthetized, an accredited vascular scientist with specific training in 3D CEUS attended the theater. This individual, who was blinded to the angiographic findings, performed conventional 2D and 3D CEUS imaging to measure the same parameters.

The 3D CEUS was undertaken with a Phillips IU22 ultrasound console (Phillips, Amsterdam, Netherlands) using a C5 2-MHz curved array probe. Then, 1-mL boluses of sodium hexafluoride (SonoVue, Bracco, Italy) were administered intravenously to a maximum of 5 mL. The images acquired were processed using a Curefab CS 3D system (Curefab, Munich, Germany) and were replayed and manipulated to identify endoleaks. The 3D CEUS findings were then verbally relayed to the team performing the EVAR and recorded. If necessary, any interventions based on the 3D CEUS findings were then undertaken.

The recorded outcome measures were presence of an endoleak, type of endoleak, inflow vessel of endoleak, renal artery visualization and patency, and evidence of limb kinking.

RESULTS

The study included 20 consenting patients, and their demographics are given in Table I. Of these patients, 19 underwent EVAR for infrarenal abdominal aortic aneurysm, including 18 bifurcated stent grafts and one aortouniiliac

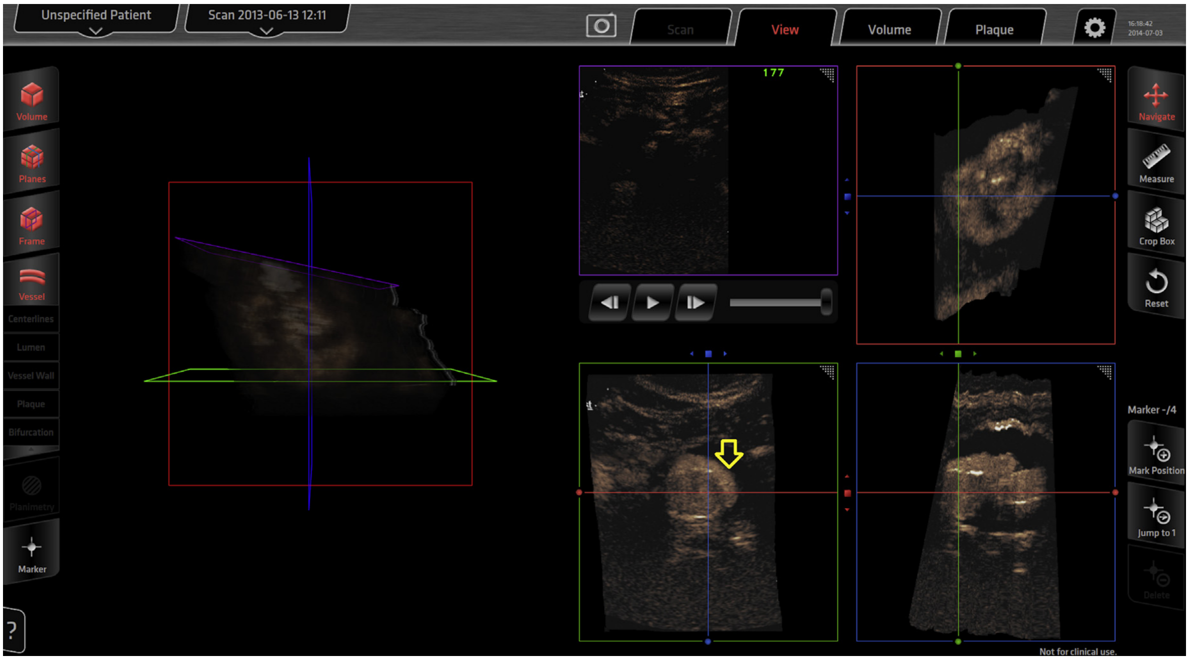

Fig. A type I endoleak (*arrow*) as seen on the Curefab CS system workstation (Curefab, Munich, Germany) that was not identified on uniplanar angiography.

device. One patient had EVAR with a bifurcated graft for a common iliac aneurysm that could not be treated with a straight stent graft. The choice of stent graft was determined by aneurysm anatomy and was within the manufacturer's instructions for use in all cases.

Three endoleaks—one type I and two type II—were detected on uniplanar angiography. 2D CEUS imaging found 13 endoleaks: 3 type I, 9 type II, and 1 type III. 3D CEUS also demonstrated 13 endoleaks, including both type I endoleaks. Of note, one of these type I endoleaks was not seen on angiography (Fig), and this patient underwent balloon molding of the neck, with resolution of the endoleak on repeat 3D CEUS imaging. Of the 11 type II endoleaks seen with 3D CEUS imaging, the inflow vessel was identified in nine. 3D CEUS imaging reclassified two endoleaks described by 2D CEUS; the type III endoleak was found to be a type II and one type I was found to be a type II. Table II summarizes endoleak detection and classification.

No graft deformity or limb kinking was seen in any patient. Both renal arteries could be visualized in 10 patients, whereas the largest (lowest) renal artery was seen in 11 patients. The renal arteries in the remaining patients could not be visualized due to intra-abdominal gas and patient body habitus. Use of the microbubble contrast did not cause any adverse reactions or complications.

DISCUSSION

Standard uniplanar DSA using IC has been found to miss 4% to 9% of endoleaks.[11,12] This may be mitigated by multiplanar or rotational angiography but at the expense of increased intra-arterial contrast volume and radiation exposure. A retrospective analysis of 615 EVARs found that duplex scanning ≤48 hours of surgery found endoleaks in 53 patients, including 17 type I and eight type III endoleaks, of which 10 of the type I leaks and none of the type III leaks were seen on completion uniplanar angiography.[12]

The Curefab CS system represents an enhancement to standard duplex ultrasound technology by combining contrast-enhanced duplex, a magnetic field emitter, and tracking sensors that can be applied to most standard ultrasound probes. Processing produces a 3D image that can be enlarged and rotated so the aneurysm body and the graft can be identified from all angles. The ability to rotate the 3D reconstruction and scroll through the ultrasound image slice-by-slice, akin to CT images, simultaneously in sagittal, coronal, and transverse planes, allows the operator to ensure that adjacent vessels are not mistaken for endoleaks. An additional benefit of enabling imaging in three planes

Table II. Endoleak detection by imaging modality used

Endoleak type	*Imaging modality*		
	Uniplanar DSA, No.	*2D CEUS, No.*	*3D CEUS, No.*
I	1	3	2
II	2	9	11
III	0	1	0
Total	3	13	13

2D, Two-dimensional; *3D,* three-dimensional; *CEUS,* contrast-enhanced ultrasound; *DSA,* digital subtraction angiography.

simultaneously, without manually rotating the transducer, is that the operator does not lose a small area of interest during manual rotation, thus allowing confident identification of even small leaks.

Because images are acquired in the same way as conventional CEUS, 3D CEUS imaging does not add to the time required for scanning and is completed in ~5 minutes. Imaging processing takes seconds, and the time for interpretation depends on the presence or absence of an endoleak. In our experience, the scanning, interpretation, and communication of results added only 10 minutes to the EVAR procedure. Provided the operator has experience with CEUS, we have found 3D CEUS images are easier to interpret due to the ability to manipulate the images and view them in multiple planes. A pilot study from our institution showed promising results using 3D CEUS for endoleak detection compared with CT as a gold standard, with encouraging inter-rater reliability ($\kappa = 0.88$; 95% confidence interval, 0.718-1.0).[10]

In this series, 3D CEUS imaging detected a type I endoleak that was not seen on angiography. This was treated at the same sitting with balloon molding. We noted that 2D CEUS imaging found the same number of endoleaks as 3D CEUS imaging, although 3D was superior in delineating the inflow vessel and also reclassified two clinically significant endoleaks—one type III and one type Ia—to type II leaks that did not require any immediate treatment. In each of these cases, the ability to manipulate the 3D images allowed for a more detailed interrogation of the ultrasound data and a more accurate diagnosis. Although it is the experience of endovascular therapists that some type I endoleaks will seal in the postoperative period after reversal of anticoagulation, there is currently no way to predict those that will resolve spontaneously.[12,13]

The type I leak seen on CEUS imaging and not on DSA was thought to be significant due to the volume of contrast seen flowing into the sac. We believe that most endovascular specialists would treat an endoleak of this type. Although the renal arteries could not be seen in 50% of cases, in our experience of CEUS imaging, this does not preclude an accurate diagnosis of type I endoleaks due to their characteristic appearance. We previously established that 3D CEUS imaging has high endoleak sensitivity compared with CT scanning.[10] Although the present study is limited by the number of patients, it provides scope for a larger-scale study involving a greater number of patients. A paired analysis of completion 3D CEUS scanning with biplanar angiography in patients with adequate renal function would further assess the sensitivity to detect endoleaks. The results suggest that 3D CEUS imaging is either noninferior or superior to uniplanar angiography in endoleak detection.

The main utility of the addition of a 3D system is the ease of interpretation and image manipulation that is afforded by the volumetric and multiplanar reconstructions. A frequent criticism of US modalities for EVAR surveillance is operator dependency and the difficulties of interpreting 2D images in three dimensions; this may be mitigated by the use of a 3D system. Duplex also affords advantages of hemodynamic measurements to assess for limb kinking that may be missed due to parallax on angiography, although no limb problems were found in this series.

The main application of 3D CEUS imaging in this setting is for patients with impaired renal function where there is a priority to avoid IC volume or in emergency cases with a background of CKD where an additional acute kidney injury is a concern due to repeated contrast loads from CT scanning and to hypotension. Intraoperative 2D or 3D CEUS can provide quality control imaging for EVAR performed using CO_2 angiography. CO_2 angiography is an attractive option for arterial navigation and endograft deployment in patients with poor renal function,[4,14] although it is generally inadequate for completion imaging.[5]

In three cases at our institution, we used CO_2 for navigation and deployment of conventional infrarenal endografts and 3D CEUS for completion imaging, allowing for contrast-free or ultralow-contrast EVAR. In the first case, we treated a patient with stage IV CKD with an estimated glomerular filtration rate (eGFR) of 20 mL/min/1.73 m^2 using a bifurcated Endurant II (Medtronic, Minneapolis, Minn) stent graft. We found that CO_2 provided adequate imaging quality to define the renal arteries and the iliac bifurcation. No endoleaks were seen on uniplanar CO_2 angiography, and this was confirmed with intraoperative 3D CEUS, which also demonstrated renal artery patency.

The second patient also had stage IV CKD (eGFR, 30 mL/min/1.73 m^2) and underwent EVAR using a bifurcated device. In this case, CO_2 failed to adequately demonstrate the target renal artery before deployment and therefore we used a hand-injection of 5 mL contrast to confirm the stent graft position below the renal arteries. Imaging of the iliac system was clear enough to then allow graft deployment, and completion imaging was performed with 3D CEUS.

The third patient presented with a ruptured aortoiliac aneurysm. Intra-arterial contrast was used to define the iliac anatomy and embolize the internal iliac artery; however, graft deployment was performed with CO_2 angiography. Completion imaging with performed with CEUS and limited contrast dose to 25 mL. We obtained full completion imaging in all three patients, and no patient had a postoperative decline in eGFR.

CONCLUSIONS

The results of this feasibility study suggest that intraoperative 3D CEUS imaging accurately identifies and characterizes endoleaks immediately after stent graft deployment. Furthermore, 3D CEUS imaging was able to detect endoleaks not seen on uniplanar DSA, including clinically important type I endoleaks, and has advantages over 2D CEUS imaging in inflow vessel identification and image manipulation. The lowest renal artery could be seen reliably in only 50% of patients; however, by adding CO_2 angiography to guide deployment, this technology has the potential to replace standard completion DSA in patients where renal function is threatened or when the source of an endoleak seen on completion DSA is uncertain. Intraoperative 3D CEUS combined with CO_2 imaging has been applied to allow safe EVAR with ultralow IC or no IC usage in selected patients, without compromising completion imaging.

AUTHOR CONTRIBUTIONS

Conception and design: JG
Analysis and interpretation: DO, CL, JG
Data collection: NS, DO, CL
Writing the article: DO, CL, JG
Critical revision of the article: CM, JG
Final approval of the article: JG
Statistical analysis: Not applicable
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Overall responsibility: JG
DO and CL share first authorship.

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