Original Article

Feasibility of contrast-enhanced ultrasound in the detection and classification of endoleaks after endovascular aneurysm repair

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Background: Endoleaks are common complications after endovascular aneurysm repair (EVAR) for abdominal aortic aneurysm (AAA). Computed tomographic angiography (CTA)/digital subtraction angiography (DSA) is considered the gold standard for evaluating contrast-enhanced ultrasound (CEUS) accuracy in the detection and classification of endoleaks. In recent years, CEUS has been widely used in this field. This study aimed to analyze the accuracy of CEUS in the detection and classification of endoleaks after EVAR.

Methods: The data of 98 patients who underwent abdominal aorta CEUS from November 2017 to September 2023 in the ultrasound (US) department of Beijing Hospital were retrospectively analyzed. All the patients underwent EVAR of AAA before CEUS and CTA/DSA, and had complete clinical data. The CEUS and CTA/DSA results were compared to detect endoleaks and categorize the specific types of endoleaks.

Results: Among the 98 patients, 74 were male and 24 were female. The patients had an average age of 74.8±9.8 years (range, 43–90 years). Among the 98 patients, 37 (37.8%) endoleaks were detected by CEUS, of which 8 were type Ia, 2 were type Ib, 15 were type II, 7 were type III, 2 were type IV, 2 were type Ia combined with type III, and 1 was type II combined with type III. In addition, among these 98 patients, 39 (39.8%) endoleaks were detected by CTA/DSA, of which 8 were type Ia, 3 were type Ib, 18 were type II, 6 were type III, 2 were type Ia combined with type III, 1 was type II combined with type III, and 1 was type Ib combined with type II. The sensitivity and specificity of CEUS in the detection of endoleaks were 92.3% and 98.3%, respectively. CEUS and CTA/DSA had similar diagnostic efficacy and good consistency in the detection and classification of endoleaks (Kappa value: 0.914, P<0.01).

Conclusions: CEUS has high sensitivity and specificity in the detection and classification of endoleaks following EVAR, and its diagnostic efficacy is similar to that of CTA/DSA. In addition, US is safe, non-invasive and repeatable, and thus is worthy of extensive clinical application.

Keywords: Abdominal aortic aneurysm (AAA); endovascular aneurysm repair (EVAR); complications; endoleaks; contrast-enhanced ultrasound (CEUS)

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Introduction

Abdominal aortic aneurysm (AAA) is a serious vascular disease (1,2). The risk of rupture of AAA increases as the diameter of the aneurysm sac increases. Once ruptured, the mortality rate is as high as 90% (3). There are two main types of clinical treatment for AAA: open aneurysm repair (OAR); and endovascular aneurysm repair (EVAR), which was approved in 1999. Compared with OAR, EVAR has obvious advantages, including less trauma, faster postoperative recovery, and lower short-term mortality (4-6). The EVAR surgical method is suitable for about 60% of AAA cases (7). However, EVAR also has its own limitations and complexities (8), including many postoperative complications, such as leading artery injury (e.g., perforation, rupture, dissection, and pseudoaneurysm), stent displacement, deformation, fracture, compression, endoleaks, allergy, and renal failure caused by contrast agent, infection. The most common complication is endoleaks (9,10).

An endoleak is a basic and unique complication following EVAR, and it is a main contributor to aneurysm enlargement and potential rupture. Endoleaks are classified into five types (i.e., types I to V). Early postoperative detection and intervention may reduce the rupture rate of AAA.

The imaging methods commonly used to detect endoleaks include computed tomographic angiography (CTA), magnetic resonance angiography (MRA), digital subtraction angiography (DSA), and ultrasound (US). The disadvantages of CTA include radiation exposure and contrast agent nephrotoxicity (11). MRA does not expose patients to ionizing radiation, but contraindications need to be considered (12). DSA is the gold standard for the diagnosis of endoleaks after EVAR, but it is relatively expensive, invasive, and radiative, and it is not used as a routine and first-line screening method for endoleaks. Contrast-enhanced ultrasound (CEUS) uses US contrast agent to enhance the display of the blood flow signal, which is helpful in the detection and classification of endoleaks after EVAR (13). Additionally, CEUS is non-invasive and non-radiative, and thus has great advantages in the detection and classification of endoleaks (14-18).

This study collected the imaging data of 98 patients who underwent abdominal aorta CEUS in the US department of Beijing Hospital from November 2017 to September 2023. All the patients underwent CEUS and CTA/DSA examinations and had complete clinical data. The CEUS and CTA/DSA results of the patients were compared and analyzed. The aim of this study was to compare the diagnostic accuracy of CEUS to the CTA/DSA reference standard. We present this article in accordance with the STARD reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-24-758/rc).

Methods

Patients

The data of 98 patients who underwent abdominal aortic CEUS in the US department of Beijing Hospital from November 2017 to September 2023 were retrospectively analyzed. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Beijing Hospital (No. 2023BJYYEC-023-02), and the requirement of individual consent for this retrospective analysis was waived.

To be eligible for inclusion in this study, the patients had to meet the following inclusion criteria: (I) have undergone EVAR; and (II) have undergone CTA/DSA examinations after CEUS. Patients were excluded from the study if they met any of the following exclusion criteria: (I) had undergone EVAR to treat an isolated iliac aneurysm, abdominal aortic ulcer, or pseudoaneurysm. (II) had CEUS contraindications or a contrast agent allergy; and/or (III) had incomplete clinical data.

The following data were collected: (I) general information data: gender, age, body mass index, blood pressure, blood lipid, and other results data; (II) abdominal aorta CEUS data; and (III) other examination data (i.e., CTA/DSA examination results data).

US instruments and contrast agent

The contrast agent used in the renal artery CEUS was SonoVue (Bracco Company, Italy). Three types of ultrasonic instruments were used for the CEUS examination: (I) the CA1–7 convex array probe of the Samsung RS80A ultrasonic instrument (probe frequency: 2–5 MHz); (II) the C1 probe of the GE LOGIQ E8 color Doppler US instrument (probe frequency: 3.5–5 MHz); and (III) the i8CX convex array probe of Canon Aplio i800 ultrasonic instrument (probe frequency: 1–8 MHz).

US examination methods

The patient was placed in the supine position, and the AAA was scanned from top to bottom in the cross-section, and

from left to right or right to left in the longitudinal section. Two-dimensional US was used to measure the size of the aneurysm, the position of the stent, the internal location of the stent, and the thrombus between the stent and the aneurysm wall, focusing on whether there was non-echo zone and the location of the non-echo zone. Color Doppler was used to display blood flow in and around the stent. It was important to observe whether there was blood flow signal between the stent and the aneurysm wall to determine whether there were endoleaks. The abnormal blood flow beam was measured with spectral Doppler, and the type of endoleak was determined according to the direction, velocity, and position of the blood flow. When the spectrum was taken, the angle between the blood flow and the sound beam had to be less than 60°. The CEUS mode was then used to observe whether there was contrast agent between the stent and the aneurysm wall, record the time, position, direction and source, and determine the type of endoleak.

This study collected the imaging data of 98 patients who underwent abdominal aorta CEUS in the US department of Beijing Hospital from November 2017 to September 2023. All the patients underwent CEUS and CTA/DSA examinations, and had complete clinical data. If the CEUS results showed endoleaks, DSA examination was performed for confirmation. If endoleaks were not detected by CEUS, a CTA or DSA examination was performed for confirmation. Of the 98 patients, 69 had DSA results but only 29 had CTA results. The CEUS examination was performed within one month of the CTA/DSA examination.

White *et al.* defined an endoleak as the incomplete exclusion of the aneurysm sac by the graft (19). The endoleaks were classified into five types as follows (20): type I: A leak caused by the incomplete attachment of the graft to the aortic lumen, leading to a pressure increase in the aneurysm sac. (The type I endoleaks were further classified as follows: type Ia: proximal; type Ib: distal, and type Ic: iliac occluder, which was related to the inadequate sealing of the iliac artery occluder); type II: a leak caused by the branch arteries of the aorta or iliac artery filling the aneurysm sac. (The type II endoleaks were further classified into two subtypes: type IIa: single vessel, and type IIb: two vessels or more); type III: a leak caused by EVAR graft mechanical failure. (The type III endoleaks were further classified into two subtypes: type IIIa: graft rupture; and type IIIb: fabric disruption); type IV: a leak caused by porous flow through the fabric of the graft; and type V: an endotension leak, which occurs when there is no evidence of a leak site but the aneurysmal sac continues to expand.

DSA examination

DSA examination was performed by angiography machine (GE, USA). The Seldinger cannula technique was used to intubate above the celiac trunk through the femoral artery. The contrast agent (Ultravist, Bayer, Germany) was injected to perform abdominal aortography. Finally, the DSA image was reconstructed by anterior side and double oblique projection, and the data were processed by digital silhouette technology and intelligent software.

CTA examination

Scanning was performed using a 640-row spiral computed tomography (CT) machine (Toshiba, Japan).

The patient was placed in the supine position with both hands raised above their heads, and their head first entering the machine. The scanning range ranged from the diaphragmatic muscle level to the pubic symphysis level. A high-pressure syringe was used to inject 90 mL of contrast agent iopromide (370 mgI/mL, Shanghai Bracco Sine Pharmaceutical Corp. Ltd., Shanghai, China) through the elbow median vein of the patient at a flow rate of 4.0 mL/s. Using intelligent trigger scanning, the triggering layer was the abdominal trunk level abdominal aorta (triggering threshold: 100 HU). After triggering, the arterial phase image was immediately scanned, and the portal vein phase image was collected 25 seconds later. After scanning was completed, the obtained data were transmitted to the post-processing workstation (AW4.2 workstation) for data measurement.

Statistical methods

The data were analyzed using SPSS Statistics 23.0 (IBM Corporation, Armonk, NY, USA). The measurement data with a normal distribution are expressed as the mean ± standard deviation. The count data are expressed as the number of cases (percentage), and were compared between groups using the chi-squared test. Kappa tests were used for the consistency analyses; a Kappa value ≥0.75 indicated that the consistency was satisfactory, and a Kappa value ≥0.4 but <0.75 indicated that the consistency was barely acceptable. A P value <0.05 indicated a statistically significant difference.

Results

General data of 98 patients with EVAR

Among the 98 patients, 74 were male and 24 were

Table 1 General data of 98 patients undergoing EVAR surgery

Characteristics	Value (n=98)
Gender	
Male	74 (75.5)
Female	24 (24.5)
Age (years)	74.8±9.8
BMI (kg/m^2)	24.1±2.8
Coronary heart disease	48 (49.0)
Hypertension	86 (87.8)
Dyslipidemia	66 (67.3)
Smoking	62 (63.3)
Diabetes	37 (37.8)
COPD	34 (34.7)
PAD	29 (29.6)
Aneurysm diameter (cm)	6.2±1.4
Median time (months after EVAR)	21
Renal artery insufficiency (stage 3 or above CKD)	39 (39.8)

Data are presented as mean ± standard deviation or number (%). EVAR, endovascular aneurysm repair; BMI, body mass index; COPD, chronic obstructive pulmonary disease; PAD, peripheral arterial disease; CKD, chronic kidney disease.

female. The patients had an average age of 74.8±9.8 years (range, 43–90 years). The general data of the 98 patients undergoing EVAR surgery is set out in *Table 1*. No adverse events were observed during the CEUS and CTA/DSA examinations.

Comparison of the CEUS and CTA/DSA results for different types of endoleaks

Among the 98 patients, 37 endoleaks were detected by CEUS, of which 8 were type Ia, 2 were type Ib, 15 were type II (*Figure 1*), 7 were type III, 2 were type IV, 2 were type Ia combined with type III (*Figure 2*), and 1 was type II combined with type III. The endoleak detection rate of CEUS was 37.8% (37/98). A total of 39 endoleaks were detected by CTA/DSA, of which 8 were type Ia, 3 were type Ib, 18 were type II, 6 were type III, 2 were type Ia combined with type III, 1 was type II combined with type III, and 1 was type Ib combined with type II. The endoleak detection rate of CTA/DSA was 39.8% (39/98) (*Table 2*, *Figure 3*). The sensitivity and specificity of CEUS in the detection of endoleaks were 92.3% and 98.3%, respectively. CEUS and CTA/DSA had similar diagnostic efficacy and good consistency in the detection and classification of endoleaks

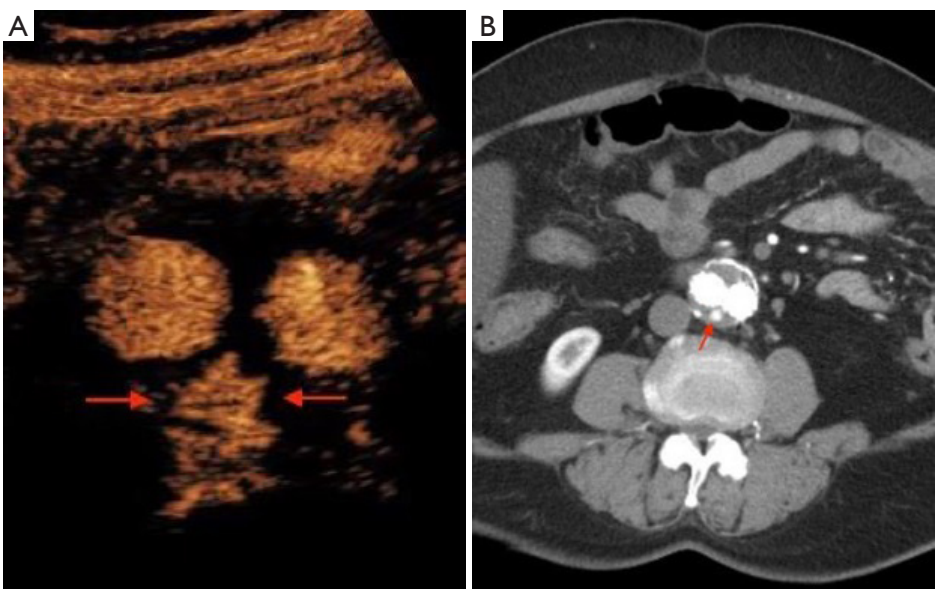

Figure 1 Scans of a 68-year-old female patient. A type II endoleak was found 13 months after EVAR surgery. (A) The location of the type II endoleak from the lumbar artery in CEUS (red arrows). (B) The location of the type II endoleak from the lumbar artery in CTA (red arrow). EVAR, endovascular aneurysm repair; CEUS, contrast-enhanced ultrasound; CTA, computed tomographic angiography.

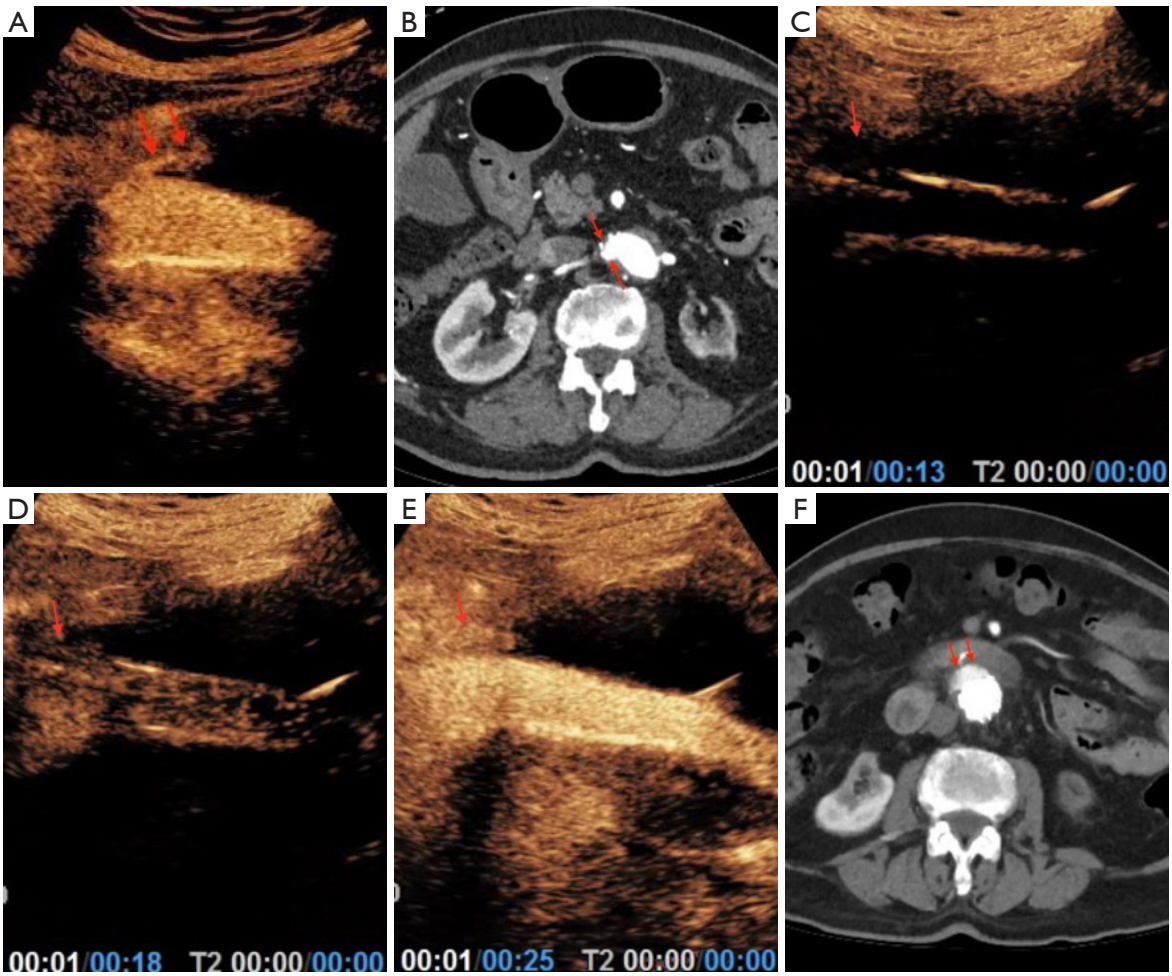

Figure 2 Scans of an 87-year-old male patient. Type Ia with type III endoleaks were found 70 months after EVAR surgery. (A) The position of the type Ia endoleaks near the proximal of the stent in CEUS (red arrows); (B) the position of the type Ia endoleaks near the proximal of the stent in CTA (red arrows); (C-E) the position of the type III endoleaks at the joint of the stent in CEUS (red arrows); (C) no contrast agent was observed in the stent or at the endoleak position when the contrast agent was injected for 13 s; (D) the simultaneous appearance of the arrow position and the contrast agent in the stent at 18 s; (E) the strength of the contrast agent in the endoleaks was the same as that in the stent at 25 s; (F) the position of the type III endoleaks at the stent connection in the CTA (red arrows). EVAR, endovascular aneurysm repair; CEUS, contrast-enhanced ultrasound; CTA, computed tomographic angiography.

(Kappa value: 0.914, P<0.01) (*Table 3*, *Figure 4*).

According to the gold-standard CTA/DSA results, type II was the most common type of endoleak, accounting for 46.2% (18/39) of all endoleaks, while type I accounted for 28.2% (11/39) of all endoleaks, of which 20.5% (8/39) were type Ia and 7.7% (3/39) were type Ib, and type III accounted for 15.4% (6/39) of all endoleaks. Among all the endoleaks, 32 were detected by CEUS and CTA/DSA and classified identically. However, 3 type II endoleaks were not detected by CEUS. A type Ib endoleak was missed in 1 case of a type Ib combined with type II endoleak. Four endoleaks were not correctly classified by CEUS (i.e., a type II endoleak was misclassified as type III, a type II endoleak was misclassified as type IV, a type Ib endoleak was misclassified as type IV, and one patient with no endoleak was misclassified as having a type II endoleak).

Discussion

EVAR is an interventional therapy technique for the isolation of AAAs using coated stents. The stent graft is used to exclude the aneurysm from the blood flow, thereby

reducing the risk for rupture. If it is anatomically feasible, the Society of Vascular Surgery guidelines recommend EVAR over the OAR for the treatment of ruptured AAA (21). The formation of endoleaks is the most common complication of EVAR. If endoleaks occur, hemodynamic changes in the aneurysm and increased pressure can cause aneurysm rupture, which often leads to fatal consequences. It has been reported that endoleaks are a common cause of AAA rupture after EVAR, and most occur within 2–3 years of surgery (22).

Several imaging methods are used to follow up patients after EVAR. CTA is the main reference method for the surveillance of complications after EVAR. The advantages of CTA include its superb spatial resolution and that it is less operator-dependent than US; however, it cannot be

Table 2 The number and positive rate of different types of endoleak detected by CEUS and CTA/DSA

Type of endoleak	CEUS (n=98)	CTA/DSA (n=98)
Type I		
Type Ia	8 (8.2)	8 (8.2)
Type Ib	2 (2.0)	3 (3.1)
Type II	15 (15.3)	18 (18.4)
Type III	7 (7.1)	6 (6.1)
Type IV	2 (2.0)	0
Type V	0	0
Type Ia, III	2 (2.0)	2 (2.0)
Type II, III	1 (1.0)	1 (1.0)
Type Ib, II	0	1 (1.0)
All types	37 (37.8)	39 (39.8)

Data are presented as number (%). CEUS, contrast-enhanced ultrasound; CTA, computed tomographic angiography; DSA, digital subtraction angiography.

Table 3 Comparison of CEUS and CTA/DSA results of endoleak after EVAR of 98 patients

CEUS	CTA/DSA		Total
	(+)	(–)	
(+)	36	1	37
(–)	3	58	61
Total	39	59	98

(+) indicates a positive result (i.e., the presence of an endoleak); (–) indicates a negative result (i.e., no endoleak). CEUS, contrast-enhanced ultrasound; CTA, computed tomographic angiography; DSA, digital subtraction angiography; EVAR, endovascular aneurysm repair.

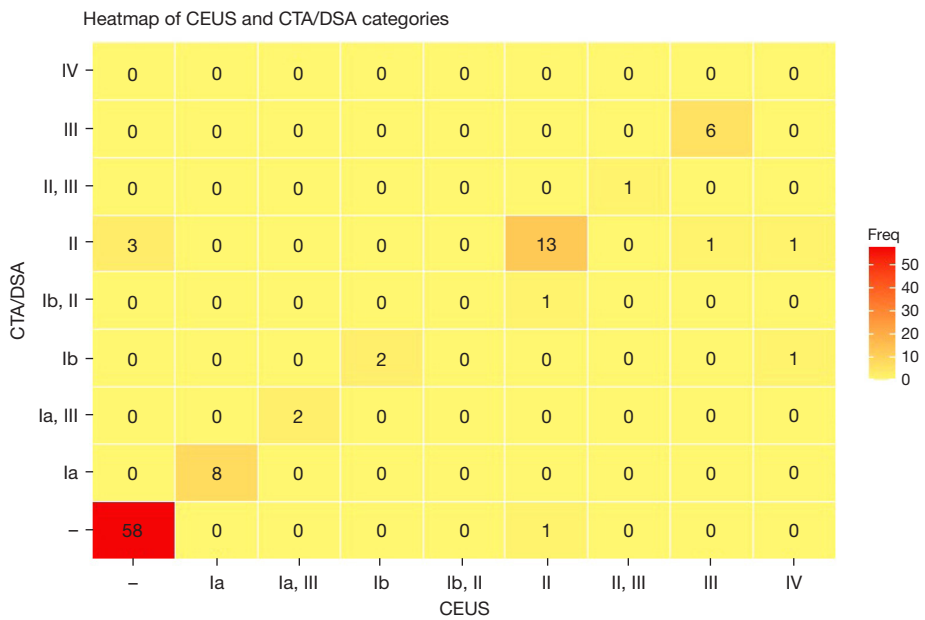

Figure 3 Heatmap of endoleak classification in two imaging modes (i.e., CEUS and CTA/DSA). CEUS, contrast-enhanced ultrasound; CTA, computed tomographic angiography; DSA, digital subtraction angiography.

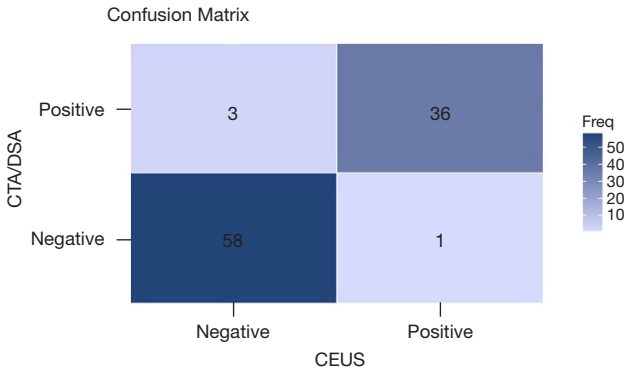

Figure 4 Confusion matrix displaying the number of positive and negative endoleaks for the two imaging modes (i.e., CEUS and CTA/DSA). The color gradient displays different quantities. CEUS, contrast-enhanced ultrasound; CTA, computed tomographic angiography; DSA, digital subtraction angiography.

used to assess the blood flow direction of endoleaks, and thus it has certain limitations in endoleak detection (23). Research has shown that dual-energy CT (DECT) offers advantages over CTA, however, it is worth noting that DECT has a higher sensitivity to iodine and also reduces metal artifacts and beam-hardening, so DECT provides an additional layer of information that cannot be accessed using conventional CT (24). However, the overall quality of DECT images decreases as image noise increases, and the further optimization of images has higher costs and takes a longer time. The advantage of MRA is a lack of exposure to ionizing radiation, but its limitations are high costs and a long scanning time. MRA also has various contraindications, such as ferromagnetic implants and foreign bodies, electronic implants, and claustrophobia (12). As a non-invasive and low-cost imaging method, US is recommended for the routine post EVAR follow up (25). Doppler US and CEUS have advantages in identifying the flow direction of endoleaks (15), which helps in the classification of endoleaks.

The accurate diagnosis of endoleaks in the short term after EVAR is very important to facilitate early interventions for patients. As different types of endoleaks are treated in different ways in the clinic, the imaging examination is very important for the accurate classification of endoleaks. For type I and type III endoleaks, the clinical management approach is either to extend the stent in the appropriate position or to dilate the balloon (20). For type II endoleaks, a wait-and-see approach can be adopted (26), or spring coil embolization or laparoscopic ligation can be performed (27). However, if there are multiple endoleaks or the aneurysm is growing, aggressive surgical intervention is needed. As type IV endoleaks usually resolve on their own after surgery, a wait-and-see approach is usually adopted.

Among the 98 patients included in this study, 37 endoleaks were detected by CEUS, of which only 15 were type II; the remaining 21 (21.4%) endoleaks required clinical re-interventions. Similarly, 39 endoleaks were detected by DSA/CTA, of which only 18 were type II; the remaining 21 (21.4%) (21/98) endoleaks required clinical re-interventions. The proportion reported in this study was significantly higher than those reported other studies (28-31). The main reason is that there is a certain degree of bias in the patients included in this study. In clinical practice, many endoleaks were not found to be abnormal in the CEUS examination, or only type II endoleaks were found, and many of these patients did not undergo CTA/DSA examination, so these patients were not included in this study. This might be the reason for the high proportion of re-interventions required in this study.

It has been reported that type I and type II are the most common types of endoleaks (32). In this study, type II endoleaks were the most common type. Type II endoleaks detected by CEUS accounted for 40.5% (15/37) of all endoleaks, and type II endoleaks detected by CTA/DSA accounted for 46.2% (18/39) of all endoleaks. The CEUS and CTA/DSA results were statistically analyzed, and the consistency test showed that the Kappa value was 0.914, indicating that the two tests had similar diagnostic efficacy. These results are consistent with those reported in previous studies (12,33-35).

Previous studies have also reported that CEUS has also been successfully used for intraoperative completion control after EVAR to verify the absence of endoleaks at the end of the endovascular procedure (36,37). Compared with the CTA examination, CEUS provides more information about blood flow timing and direction, which can assist in determining the type of endoleak. CEUS can identify the type of endoleak by reference to the time and location of the US contrast agent. If the time of appearance of the contrast agent in the aneurysm is consistent with the time in the stent, it indicates a type I or type III endoleak. If the appearance time of the contrast agent is longer than that of the contrast agent in the stent (i.e., if the delay is greater than 5 s), it indicates a type II endoleaks (12).

The ultrasonic contrast agent SonoVue is composed of inert, non-toxic gas sulfur hexafluoride. Microbubbles with a diameter of 2–10 μm can freely pass through capillaries,

which is conducive to the display of endoleaks that are difficult to detect by conventional US. SonoVue is a safe contrast agent with a low incidence of side effects, and no contraindications in the liver or kidney. The adverse reactions reported in the literature are usually non-serious, transient, self-recovering, and have no effects (38-42). The European Federation of Societies for Ultrasound in Medicine and Biology is of the view that US contrast agents are very safe and have a very low incidence of side effects. Compared to the contrast agents used in CT or magnetic resonance imaging, the frequency of allergic reactions is much lower (43). CEUS for EVAR follow up is safe and effective. The use of CEUS reduces the radiation exposure of patients undergoing CTA (44).

Conclusions

The use of CEUS for the postoperative follow up of EVAR is safe and effective. CEUS can accurately detect and classify endoleaks, and its results are highly consistent with CTA/DSA examination results. CEUS is the recommended examination method for routine follow up after EVAR, as it reduces the radiation exposure of patients, and causes no damage to liver and kidney function.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-24-758/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-758/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Beijing Hospital (No. 2023BJYYEC-023-02), and the requirement of individual consent for this retrospective analysis was waived.

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