# Diagnostic vascular ultrasonography with the help of color Doppler and contrast-enhanced ultrasonography



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#### Johannes Rübenthaler, Maximilian Reiser, Dirk-André Clevert

Department of Clinical Radiology, Ludwig-Maximilians-University of Munich-Grosshadern Campus, Munich, Germany

The use of ultrasonography and especially of contrast-enhanced ultrasonography (CEUS) in the diagnosis of vascular pathologies before and after interventions has significantly increased over the past years due to the broader availability of modern ultrasound systems with CEUS capabilities and more trained user experience in this imaging modality. For the preinterventional and postinterventional work-up of carotid diseases, duplex ultrasound as well as CEUS have been established as the standard-of-care examination procedures for diagnosis, evaluation, and follow-up. In addition to its use for carotid arterial diseases, ultrasonography has also become the primary modality for the screening of vascular pathologies. This review describes the most common pathologies found in ultrasonography of the carotid arteries, the abdominal aorta, and the femoral arteries.

Keywords: Contrast media; Ultrasonography, contrast-enhanced; Carotid stenosis; Arteriovenous fistula; Dissection; Plaque, atherosclerotic

## **REVIEW ARTICLE**

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#### Correspondence to:

Dirk-André Clevert, MD, Department of Clinical Radiology, Munich University Hospital, Marchioninistr. 15, 81377 Munich, Germany

Tel. +49-89-44007-3620 Fax. +49-89-44007-8832 E-mail: Dirk.Clevert@med.unimuenchen.de

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## Introduction

The initial diagnostic workup of patients suspected of suffering from carotid artery disease is duplex ultrasonography of the carotid vessels (Fig. 1) [1-7]. Duplex ultrasonography is also the preferred imaging modality for the follow-up of patients after stent implantation or endarterectomy [8,9]. Among patients showing amaurosis fugax or hemispheric transient ischemic attacks, 88% reveal atherosclerotic plaques at the carotid bifurcation [10] and about 25%–50% of all strokes are a result of ruptured atherosclerotic plaques; in addition, about 80% of all strokes are of ischemic origin [11–13]. Internal carotid artery (ICA) stenosis quantification is essential for the clinical management of patients, since several trials have concluded that symptomatic patients with high-grade stenosis (70%–90%) of the ICA, as well as asymptomatic patients with high-grade stenosis, benefit from carotid endarterectomy (CEA) [14–18].

In abdominal ultrasonography, abdominal aortic aneurysms (AAAs) are found in 2% to 8% of men over the age of 65 years, with incidence in women that is lower by a factor of 4 [19]. All AAAs are defined as an enlargement of the abdominal aorta greater than 3.0 cm or greater than 50% of normal size [19]. About 85% of all AAAs are detected below the origin of the kidney vessels [19].



#### Fig. 1. Ultrasonography of a carotid bulb.

A, B. B-Scan (A) and color Doppler (B) sonograms of the carotid bulb demonstrate the distal common carotid artery (asterisk), the proximal internal carotid artery (ICA) (arrow) and external carotid artery (ECA) (arrowhead). C. Contrast-enhanced ultrasonography of the carotid bulb demonstrates the perfused lumen of distal common carotid artery, the proximal ICA and ECA.

Surgical intervention is recommended at any diameter greater than 5.5 cm in men or 5.0 cm in women [19]. The main risk is a rupture, with a risk of less than 1% for aneurysms with a size of less than 5.5 cm, 10% for aneurysms with a diameter between 5.5 cm and 7.0 cm, and 33% for aneurysms larger than 7.0 cm [19]. A ruptured AAA shows a mortality rate of 85% to 90% [19]. Clinical management includes conservative treatment with follow-up ultrasonography for asymptomatic AAAs with a diameter less than 5.5 cm, as there is a higher risk of peri-interventional complications than of rupture and surgical repair for AAAs above that size, with contrast-enhanced ultrasonography (CEUS) follow-up examinations after endovascular aneurysm repair (EVAR) [20–28].

Duplex ultrasonography is also the imaging modality of choice for the detection of complications after puncture of the femoral artery, as they occur in 0.1%-9% of cases with aneurysms, with arteriovenous fistulas, dissections, and hematomas being the most common complications [29–34].

# Contrast-Enhanced Ultrasonography Technique

With the implementation of specific contrast modes in modern ultrasound systems and the broader availability of these systems in the clinical routine, CEUS can be used for the assessment of vascular complications. Modern contrast modes use a low mechanical index mode that processes the non-linear signals emitted by the microbubbles of the contrast agent and separates out the signals of the tissue and the contrast agent [35,36]. The contrast agent is intravenously administered through a needle of at least 18G. The microbubbles oscillate in response to the emitted ultrasound and reflect an echo with an amplified echo intensity of up to 30 dB [35,37]. Major side effects must be taken into consideration, which are comparable to those of contrast agents used for other imaging modalities. The most important possible side effect of an ultrasound contrast agent is an anaphylactic reaction, which is described to occur in one out of 10,000 cases [38,39].

SonoVue (Bracco, Milan, Italy), most commonly used among modern ultrasonography contrast agents, consists of phospholipid shells, which stabilize microbubbles, and their core, containing sulphur hexafluoride (SF6) gas. Once administered, the ultrasound contrast agent is quickly eliminated. The phospholipids are metabolized endogenously and the SF6 gas is exhaled via the lungs within a time period of up to 8 minutes. At 2–10  $\mu$ m, a single microbubble is about the size of an average erythrocyte. For diagnostic views of the vessels, 1.6 to 2.4 mL of contrast agent should be intravenously administered as a bolus injection, followed by a flush of 5–10 mL of saline solution (0.9% NaCl) in order to achieve good contrast [40].

## **Carotid Arterial Diseases**

#### Stenosis

About 10%–15% of all strokes and transitory attacks of ischemic origin are the consequence of an atherosclerotic stenosis of the ICA, especially of the proximal part [41]. Most important in the initial workup of ICA stenosis is the differentiation between a total occlusion of the ICA or a preocclusive stenosis that is characterized as a stenosis of at least 90% [42–47]. Preocclusive symptomatic stenosis can be treated with surgical intervention or

with other interventional measures in order to prevent a threatening hemiparesis [3,6]. With sensitivities between 86% and 98% and specificities between 87% and 100%, vascular ultrasonography of the ICA has a high diagnostic accuracy in the characterization of ICA stenosis and in the differentiation of ICA occlusions, dependent on examiner experience and parameter settings [48–50]. With CEUS, it is even possible to advance the visualization of carotid artery diseases by detecting the blood flow through the stenosis even in elongated vessels, without the disadvantage of an angle dependency or aliasing or blooming flow artifacts (Fig. 2) [51–55].

#### Postinterventional Follow-up

The traditional method of choice for the treatment of symptomatic and asymptomatic patients with ICA stenosis is the CEA [47,56]. Carotid artery stenting (CAS) is an alternative to the traditional CEA, especially in patients with a high risk of complications from undergoing surgery, for example, patients with significant cardiopulmonary disease [57–59]. The use of CEA carries a risk of restenosis of about 25%, whereas the risk of restenosis after CAS is below 5% in most cases in the initial 5 years after stenting [9,60–63]. Duplex ultrasonography and CEUS are the imaging modalities of choice for postinterventional surveillance for restenosis after CAS and for the characterization of in-stent restenosis after stenting, with CEUS providing a reduction of flow artifacts and a better visualization of the morphology of the restenosis compared to color and power Doppler (Fig. 3) [64–66].



#### Fig. 2. Ultrasonography of a 67-year-old woman with recent ischemic neurological symptoms.

A. B-Scan shows a high-degree internal carotid artery (ICA) stenosis with soft plaques (arrow). B, C. Duplex ultrasonography shows a highdegree stenosis of the ICA (arrowhead) with a maximal systolic flow velocity of about 500 cm/sec. D. Contrast-enhanced ultrasonography (CEUS) detects the intrastenotic flow (arrowhead) without overwriting the wall of the vessel and reveals the complete residual lumen and the length of the stenosis. Additionally, CEUS confirms the absence of intraplaque neovascularization (arrow).

#### Dissection

Cervical dissections are rather uncommon and can be divided into spontaneous or traumatic dissections. The annual incidence of dissections is about 1-3 out of 100,000 cases, and they account for 15%-20% of all cerebral infarctions in adolescents [67]. Clinical symptoms of dissections vary acutely from individual to individual [68]. Vascular ultrasonography is the imaging modality of choice for the detection and characterization of acute dissection by imaging the mural hematoma as well as the false and true lumen, along with the normal visualization of a decreased blood volume flow in the false lumen that results in an increased risk for thrombosis, embolization, or even partial or total occlusion of the artery [69–71]. Modern ultrasound probes can even identify a small dissection with very thin membranes of less than 1 mm [4,72,73]. The use of CEUS can aid diagnosis and improve diagnostic accuracy in difficult cases [51,53].

#### **Complications after Intervention**

With an incidence of about 2%–10%, the puncture of the carotid artery is the most common complication after central venous catheterization of the internal jugular vein [74,75]. This intervention is mostly performed at the intensive care unit or for interventional radiological procedures. The most important complication is an arteriovenous fistula that can occasionally be seen clinically as a swelling of the neck, sometimes pulsatile [76]. Duplex ultrasonography and CEUS are the imaging modalities of choice for the detection of arteriovenous fistulae, with CEUS being the superior imaging technique because of its independence from aliasing or overwriting artifacts (Fig. 4) [5,77,78].

#### Plaque Characterization

Ulcerating plaques are thought to be a factor in the aetiology of strokes from carotid arterial diseases [79,80]. The use of CEUS is an imaging modality option for detecting plaque ulceration that might



Fig. 3. Longitudinal ultrasonography after internal carotid artery (ICA) stent insertion.

A. B-Scan shows an ICA stent (arrowheads). B. Power Doppler ultrasonography could not depict any in-stent stenosis. C. Cross-sectional contrast-enhanced ultrasonography (CEUS) image of the ICA stent shows the semi-circular soft plaque (arrow) and the remaining perfused lumen of the ICA stent. According to the criteria of an area stenosis, the degree of the in-stent stenosis will be about 40%–50%. D. CEUS shows some soft plaques (arrow) at the anterior ICA stent wall.

be caused by inflammatory processes and neovascularization inside the plaque; it assesses the contrast uptake in plaques via time-signal intensity curves (Fig. 5) [52,81–84].

## Abdominal Aortic Aneurysm

#### Abdominal Aortic Aneurysm

AAAs are defined as an enlargement of the abdominal aorta greater than 3.0 cm or greater than 50% of normal size [19]. A ruptured AAA shows a mortality rate of 85% to 90% and is the 10th most common cause of death in men over the age of 55 [19,20]. Immediate treatment of a ruptured AAA is essential, as an untreated ruptured AAA is most likely to result in death [20]. About 85% of all AAAs are detected below the origin of the kidney vessels [19]. Surgical intervention is recommended at any diameter greater than 5.5 cm in men or 5.0 cm in women [19]. The main risk is a rupture, with a risk of less than 1% for aneurysms with a diameter of less than 5.5 cm, 10% for aneurysms with a diameter between 5.5 and 7.0 cm and 33% for aneurysms with a diameter greater than 7.0 cm [19]. With a sensitivity of 95%–98%, duplex ultrasonography is the initial imaging method of choice for the diagnosis of AAAs [85]. The use of CEUS can help visualize the direct signs of a rupture (Fig. 6) [86].

### Postinterventional Follow-up

After EVAR of an AAA, the stent needs lifelong imaging surveillance in order to detect complications like endoleaks, fractures, or a progressive enlargement of the AAA [27]. After EVAR, CEUS is the



#### Fig. 4. Ultrasonography after central line placement.

A. Cross-sectional B-scan identifies a hypo-echoic structure suggesting hematoma (arrowheads) without communication between the common carotid artery (asterisk) and the internal jugular vein (arrow). B. The hematoma does not show any perfusion (arrowhead) on color Doppler sonogram. C, D. Contrast-enhanced sonograms of the common carotid artery demonstrate the uptake of contrast inside the hematoma (arrowheads) as the presence of a pseudo-aneurysm after central line placement without aliasing or any overwriting artifacts.



Fig. 5. Ultrasonography of an atheromatous plaque in the carotid artery.

A. B-Scan of show a significant stenosis by atheromatous plaques (arrows). B. Contrast-enhanced ultrasonography shows a neovascularization inside the plaque (arrowhead) as a sign of plaque vulnerability.







## Fig. 6. Ultrasonography of an infrarenal aortic aneurysm.

A, B. B-Scan (A) and color Doppler (B) sonograms demonstrate infra-aortic aneurysm (arrows). C. Real time-resolved 4D contrastenhanced ultrasonography shows the same infrarenal aortic aneurysm in the x-plane (right top), y-plane (right middle), and z-plane (right bottom) with a volume image (left).



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imaging modality of choice, as it allows a fast and noninvasive diagnosis during follow-up. The sensitivity and specificity for the detection of endoleaks is 98%–100% and 82%–93%, respectively (Fig. 7) [21].

## Vascular Complications after Transfemoral Puncture

#### Pseudoaneurysms

False aneurysms or pseudoaneurysms after transfemoral puncture occur in 0.05%–9% of all cases [29,87–89]. They are characterized

as a rupture in the layer of the wall of an artery that does not occlude after puncture. The leaking blood causes a pulsatile hematoma that forms a blood-filled cavity that is fed through a connection between the cavity and the punctured artery. With increasing size there is an increased risk for rupture, making a rapid diagnosis essential [90]. Duplex ultrasonography and CEUS are the imaging modalities of choice for the detection of pseudoaneurysms, with CEUS being the preferred imaging technique because it is independent of aliasing or overwriting artifacts (Fig. 8) [91].



Fig. 7. Ultrasonography of the abdominal aortic aneurysm after endovascular aneurysm repair.

A, B. Cross-sectional B-scan (A) and color Doppler (B) sonograms show aortic aneurysm (crosshairs) with right and left stent graft legs (arrows). No endoleak was detected. C. Contrast-enhanced ultrasonography shows a type II endoleak (arrowheads) over the left lumbar artery.



#### Fig. 8. Ultrasonography of the femoral artery after catheter intervention.

A, B. Cross-sectional B-scan (A) and color Doppler (B) sonograms of femoral artery (asterisks) delineate a pseudoaneurysm (arrowheads) without any discernable flow signal. C. Contrast-enhanced ultrasonography shows a partial perfusion (arrow) of pseudoaneurysm, while the distal part does not show any perfusion (arrowheads).

#### Arteriovenous Fistula

Arteriovenous fistulae occur in 0.1%-3.6% of all cases after transfemoral puncture [29,34,88]. They are described as iatrogenically abnormally connected arteries and veins. If the fistula is large enough, they can be hemodynamically relevant, causing a decrease in peripheral resistance [92]. Arteriovenous fistulae show a tendency to increase in size, making surgical treatment the intervention of choice in many cases. In some cases, the arteriovenous fistula occludes spontaneously or can be compressed via ultrasonography [76]. Duplex ultrasonography and CEUS are the imaging modalities of choice for the detection of arteriovenous fistulae, with CEUS being the superior imaging technique because of its independence from aliasing or overwriting artifacts (Fig. 9) [5.77.78].



#### Fig. 9. Ultrasonography of the femoral artery after catheter intervention.

A, B. On cross-sectional B-scan (A) and color Doppler (B) sonograms, arteriovenous fistula with turbulent blood flow in the arteriovenous fistula track (arrowheads) is depicted between the common femoral artery (arrow) and vein (asterisk). The complete extent of the fistulous track is due to aliasing demarcated. C. Contrast-enhanced ultrasonography of the common femoral artery and vein identified the complete extent of the arteriovenous fistulous track (arrowheads) and confirmed the presence of an arteriovenous communication without aliasing or any overwriting artifacts. The distal part of the common femoral vein (asterisk) does not show any contrast uptake due to the arterial scanning.



#### A

#### Fig. 10. Ultrasonography of common femoral artery dissection.

A, B. B-Scan (A) and color Doppler (B) sonograms show the common femoral artery with intimal dissection (arrowheads). Both lumens are perfused in the color Doppler setting (arrows). C. Due to its superior spatial resolution, the dissection membrane (arrowheads) and both perfused lumens are clearly depicted on contrast-enhanced ultrasonography.

## Dissection

Dissections occur in 0.3%–3.6% of all cases after transfemoral puncture [66,93]. Similarly as was described before for the dissection of the carotid arteries, vascular ultrasonography is the imaging modality of choice for the detection and characterization of dissection, by showing the mural hematoma as well as the false and true lumen, and by additionally visualizing any decreased blood volume flow in the false lumen that results in an increased risk for thrombosis, embolization, or even partial or total occlusion of the artery [69–71]. As discussed before, modern ultrasound probes can identify small dissection with very thin membranes of less than 1 mm [4,72,73]. CEUS can help aid diagnosis and improves the diagnostic accuracy in difficult cases (Figs. 10, 11) [51,53].

#### Hematoma

Hematomas occur in 0.4%-11% of all cases after transfemoral

puncture [29,66,94] and are a rather common complication in this circumstance. Normally, hematomas are locally limited and are resorbed within a short period of time. They can be easily depicted using duplex ultrasonography.

## Conclusion

For the detection, characterization, and follow-up of vascular pathologies, duplex ultrasonography is the first choice. However, duplex ultrasonography has technical limitations in diagnostic use, for example, due to aliasing artifacts that can complicate diagnosis. The use of CEUS can increase the diagnostic performance in difficult vascular disorders compared to duplex ultrasonography. Thus, CEUS has become a promising, safe, noninvasive imaging tool in different aortic pathologies, particularly for the detection of endoleaks following endovascular treatment of AAAs. Examinations



#### Fig. 11. Ultrasonography of the common femoral artery with suspicious dissection.

A, B. B-Scan (A) and color Doppler (B) sonograms show incomplete perfusion of the vessel lumen (arrows). C, D. Longitudinal (C) and crosssectional (D) contrast-enhanced images demonstrate a floating embolus (arrowheads) in the center of the common femoral artery (arrow). Due to its superior spatial resolution, contrast-enhanced ultrasonography could be used to exclude the possibility of arterial dissection.

using CEUS of the carotid artery and peripheral vessels improve the delineation of vascular disorders in selected cases. It is a fast, nonionizing, cost effective imaging modality with almost no contraindications. The use of an ultrasound contrast agent increases the sensitivity of ultrasonography in vascular diseases and overcomes some limitations in the detection of blood flow within vascular structures. With the broader availability of contrast modes in modern ultrasound systems and the ongoing distribution of these systems to sonographers, CEUS is an already established, but still emerging imaging technique with a promising future.

ORCID: Johannes Rübenthaler: http://orcid.org/0000-0003-0832-5662; Maximilian Reiser: http://orcid.org/0000-0003-1098-8190; Dirk-André Clevert: http://orcid. org/0000-0003-3889-5447

## **Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

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