



Ultrasound diagnosis of carotid artery stenosis and occlusion

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Abstract

Carotid artery ultrasonography is capable of diagnosing or inferring the presence or absence of stenosis or occlusion of the internal carotid artery (ICA) and vertebral artery (VA), as well as the not directly observable distal ICA, middle cerebral artery (MCA), and basilar artery (BA). Stenosis at the origin of the ICA is mainly evaluated using the parameter peak systolic velocity (PSV), with values of ≥ 200 – 230 cm/s indicating severe stenosis. Recently, the acceleration time ratio has been reported for diagnosis of ICA origin stenosis. An indicator called the end-diastolic (ED) ratio can be used for diagnosing occlusion of the distal ICA or the M1 segment of the MCA. The PSV of stenosis can be used to diagnose stenosis at the beginning of the VA or V1, and mean flow velocity, mean ratio, and diameter ratio can be used to diagnose distal VA occlusion. Furthermore, the usefulness of the VA pulsatility index and resistance index has been suggested for diagnosing stenosis or occlusion of the BA. This review outlines diagnostic sonography criteria for stenosis and occlusion of extracranial and intracranial arteries.

Keywords Pulsed-wave Doppler · Internal carotid artery · Middle cerebral artery · Vertebral artery · Basilar artery

Introduction

In the general population, the prevalence of asymptomatic extracranial internal carotid artery (ICA) stenosis is 0–7.5% for moderate stenosis of $\geq 50\%$ and 0–3.1% for severe stenosis of $\geq 70\%$ [1, 2]. In patients with moderate stenosis of $\geq 50\%$, 0.5–2% develop ischemic stroke on the side with stenosis [3–6], leading to a mortality rate of 7.7% per year in a survey with a follow-up period of about 2.8 years [7]. Mild carotid artery stenosis is not an indication for carotid endarterectomy (CEA) or carotid artery stenting (CAS), but these procedures should be considered in patients with moderate and especially severe stenosis [8]. Moreover, CEA or CAS

can be considered in ischemic stroke patients with $\geq 50\%$ stenosis of the carotid artery [9].

Carotid artery stenosis screening can be performed with magnetic resonance angiography (MRA), contrast-enhanced MRA, contrast-enhanced computed tomography (CT), and carotid artery ultrasonography. However, MRA findings may overestimate the frequency of moderate stenosis, and unwanted effects may occur when using contrast agents for contrast-enhanced CT angiography, although not very often [10]. By contrast, carotid artery ultrasonography is a non-invasive method that is useful for diagnosing carotid artery stenosis and occlusion. It correlates particularly well with digital subtraction angiography (DSA) for carotid artery stenosis [11]. This review describes the use of carotid artery ultrasonography in the diagnosis of carotid artery stenosis and occlusion.

Diagnosis of stenosis at the origin of the ICA

Due to hemodynamic factors, plaque tends to form between the origin of the ICA and the carotid sinus [12], and stenotic lesions are likely to appear. Therefore, this region needs to be examined in detail.

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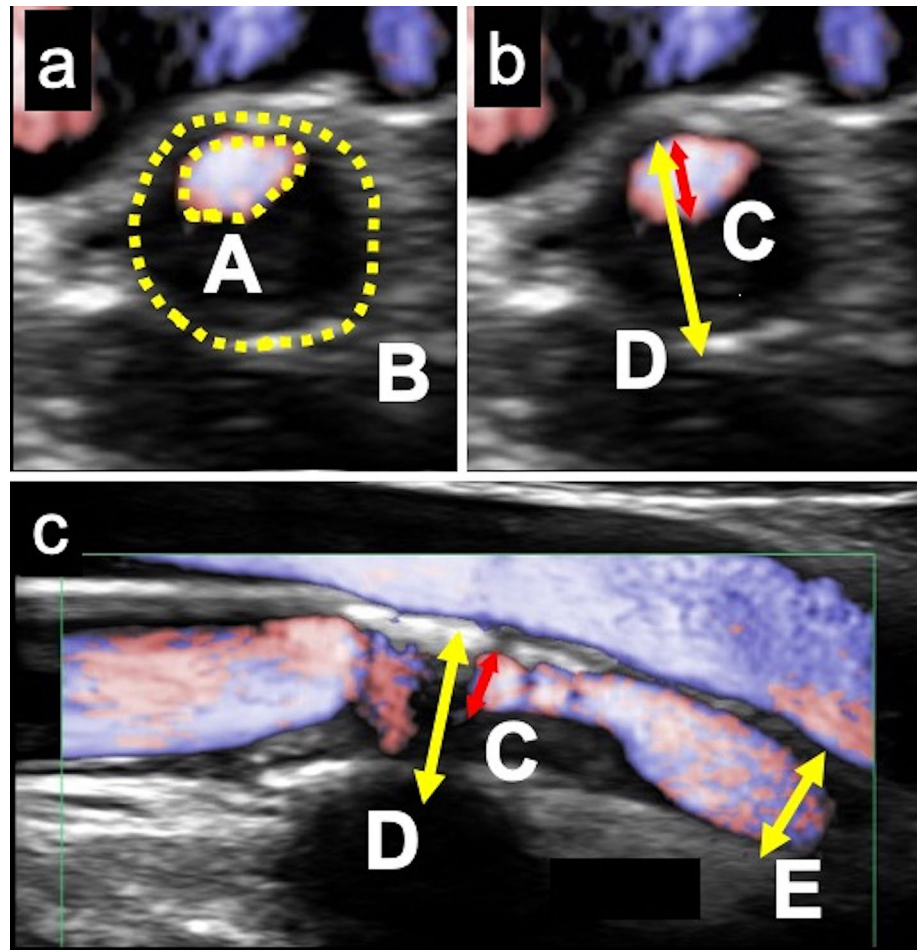
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B-mode and color Doppler imaging can be used to calculate the area stenosis rate from the short-axis view, as well as the diameter stenosis rate from the long- and short-axis views. Two methods have been suggested for measuring the diameter stenosis rate [13], i.e., the European Carotid Surgery Trial (ECST) method [14] and the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method [15] (Fig. 1). Although both use the same DSA measurement approach, with carotid artery ultrasonography, it is often difficult to determine the diameter of the distal ICA; thus, it is easier to assess the diameter stenosis rate using the ECST method. However, for individual cases, the area stenosis rate, diameter stenosis rate using the ECST method, and diameter stenosis rate using the NASCET method are not consistent. Generally, the area stenosis rate leads to the highest stenosis rate, whereas the NASCET method leads to the lowest rate [11]. Therefore, the method used for stenosis rate assessment should always be included in the report. As the DSA-based NASCET stenosis rate is used to determine whether CEA or CAS is indicated, it is best to assess the stenosis rate using the NASCET method whenever possible. The stenosis rate can also be calculated

based on the parameter peak systolic velocity (PSV) determined using pulsed-wave Doppler (PWD) measurements.

Koga et al. [16] evaluated carotid artery echocardiography and DSA in 75 patients with cerebrovascular disease. The results revealed that the PSV of ICA stenosis (ICA_{PSV}) greater than 200 cm/s was the most reliable predictor of ICA stenosis greater than 70% according to the NASCET criteria using DSA findings. In another study of 376 carotid arteries, AbuRahma et al. [17] conclude that when the PSV of ICA_{PSV} is ≥ 125 cm/s or the ratio of the ICA_{PSV} to the common carotid artery (CCA) PSV (CCA_{PSV} ; ICA_{PSV}/CCA_{PSV}) is ≥ 2 , and the ICA end-diastolic velocity (EDV) (ICA_{EDV}) is < 40 cm/s, a stenosis of $\geq 50\%$ according to the NASCET criteria using DSA findings can be assumed. Moreover, they report that for stenosis of $\geq 70\%$ according to the NASCET method, the ICA_{PSV} is > 230 cm/s or the ratio ICA_{PSV}/CCA_{PSV} is > 4 , and the ICA_{EDV} value is ≥ 40 cm/s. The parameter ICA_{PSV} was particularly useful, with an area under the receiver operating characteristic curve (AUC) of 0.97 for stenosis of $\geq 50\%$ and 0.97 for stenosis of $\geq 70\%$ according to the NASCET method. Diagnosing stenoses of $\geq 50\%$ and $\geq 70\%$ based on the NASCET method had sensitivity

Fig. 1 Measurement of the area stenosis rate and diameter stenosis rate. Using conventional B-mode ultrasound with superb microvascular imaging, the short-axis view (a, b) and long-axis view (c) are shown. The area stenosis (a) is calculated by $(B - A)/B \times 100$ (%), the stenosis rate according to the ECST method (b, c) is calculated by $(D - C)/D \times 100$ (%), and the stenosis rate based on the NASCET method (c) is calculated by $(E - C)/E \times 100$ (%). *ECST* European Carotid Surgery Trial, *NASCET* North American Symptomatic Carotid Endarterectomy Trial. Reprinted from reference [13]



values of 96% and 99%, specificity values of 82% and 96%, positive predictive values (PPVs) of 93% and 98%, negative predictive values (NPVs) of 90% and 97%, and accuracy of 92% and 98%, respectively. Tokunaga et al. [18] conducted a retrospective analysis of 127 blood vessels and found that when the ICA_{PSV} was ≥ 130 cm/s, diagnosing stenosis of $\geq 50\%$ based on the NASCET method had 95% sensitivity, 85% specificity, 75% PPV, 97% NPV, and 88% accuracy. When the ICA_{PSV} was ≥ 200 cm/s, diagnosing stenosis of $\geq 70\%$ using the NASCET method had 96% sensitivity, 95% specificity, 83% PPV, 99% NPV, and 95% accuracy. However, another study that compared CT angiography with carotid artery ultrasonography showed little correlation between the stenosis rate determined by the CT angiography-based NASCET method and that determined by ultrasound-based PWD. For NASCET-based stenosis of $\geq 70\%$, the AUC was only 0.51 with an ICA_{PSV} cutoff value of 230 cm/s [19].

According to these studies, the carotid artery ultrasonography-based diagnosis of the stenosis rate in Japan is as follows: When the ICA_{PSV} is ≥ 125 or 130 cm/s, or when the ratio ICA_{PSV}/CCA_{PSV} is ≥ 2 , the stenosis rate based on the NASCET method using DSA is $\geq 50\%$; when the ICA_{PSV} is ≥ 200 or 230 cm/s, or when the PSA_{ICA}/PSV_{CCA} ratio is ≥ 4 , the stenosis rate with the NASCET method is $\geq 70\%$ [11, 13] (Fig. 2).

PSV has also been reported to be useful for predicting asymptomatic carotid artery stenosis. Hicks et al. [20] followed 282 patients with moderate asymptomatic carotid artery stenosis $\geq 50\%$ and $< 70\%$ for about 2 years. They found that the ratio ICA_{PSV}/CCA_{PSV} was the most useful

indicator for predicting stenosis progression. When the ICA_{PSV}/CCA_{PSV} ratio was > 2.5 , > 3.3 , and > 3.8 , the risk of stenosis progression was $\geq 10\%$, $\geq 20\%$, and $\geq 30\%$, respectively. The diagnosis of moderate stenosis in their study was not based on DSA findings but was assessed using PWD carotid artery ultrasonography as $ICA_{PSV} > 125$ cm/s and < 230 cm/s, $ICA_{EDV} > 40$ cm/s and < 100 cm/s, and $ICA_{PSV}/CCA_{PSV} > 2.0$ and < 4.0 . In addition to the lack of a DSA-based diagnosis, the exact stenosis rate remains unknown in this study because an ICA_{PSV} value ≥ 200 cm/s may represent stenosis of $\geq 70\%$ with the NASCET method according to the diagnostic criteria of Tokunaga et al. [18]. However, ICA_{PSV} is a useful indicator for detecting the risk of stenosis progression and for the screening of patients who need careful follow-up.

When diagnosing stenosis with PWD, it is important to accurately measure PSV with an insonation angle of $< 60^\circ$ [11]. The insonation angle is the angle between the direction of the ultrasound beam and the direction of the blood flow. When the direction of the blood flow at the stenosis site is parallel to the vessel wall, correction of the insonation angle is easy, but when the blood flow at the stenosis site is not parallel to the vessel wall, PSV differs when the angle is corrected to be parallel to the vessel wall and when it is aligned with the direction of the blood flow. In a study of 50 cases by Igarashi et al., diagnosing a stenosis rate of $\geq 70\%$ based on the NASCET method using DSA, PWD sonography with the insonation angle being parallel to the vessel wall had an AUC of 0.765, and with a cutoff value of $ICA_{PSV} \geq 256.9$ cm/s, the sensitivity was 70.0% and the specificity was 80.0%. By contrast, when the angle was

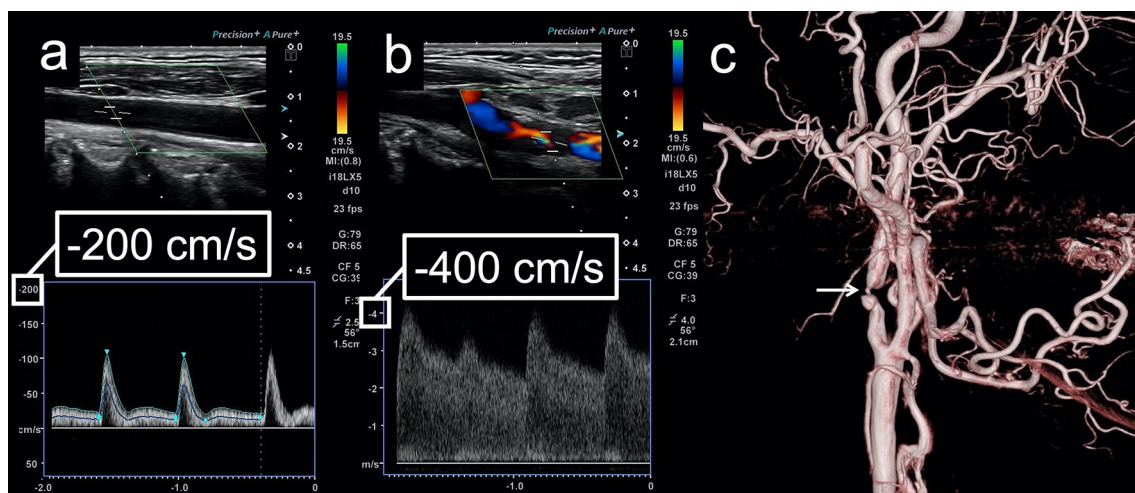


Fig. 2 NASCET stenosis rate using the peak systolic velocity. PWD (a, b) and DSA (c) measurements are shown. PSV in the CCA (a) is 100.7 cm/s, and PSV and EDV at the ICA stenosis (b) are 422.8 cm/s and 237.9 cm/s, respectively. Thus, the ratio PSV_{ICA}/PSV_{CCA} is 4.20. DSA (c) reveals stenosis of $> 70\%$ according to the NASCET method

(arrow). PWD pulsed-wave Doppler, DSA digital subtraction angiography, CCA common carotid artery, PSV peak systolic velocity, EDV end-diastolic velocity, ICA internal carotid artery, NASCET North American Symptomatic Carotid Endarterectomy Trial

aligned with the blood flow direction, the AUC was 0.973, and with a cutoff value of 203.5 cm/s, the sensitivity was 100% and the specificity was 85.7% [21]. Therefore, the stenosis diagnosis seems to be more accurate when the insonation angle is aligned with the direction of the blood flow.

On the other hand, Tola et al. [22] examined the NASCET stenosis rate with DSA and according to the insonation angle in 87 patients with an ICA_{PSV} value of > 125 cm/s. Their results indicate that an insonation angle of 45° may underestimate the stenosis rate. Therefore, the guidelines of the Society for Vascular Ultrasound [23] recommend setting the insonation angle to 60° .

Diagnosis of an ICA origin stenosis using the acceleration time (AcT) ratio

In cases of plaque with an acoustic shadow, especially circumferential calcified plaque, the parameter ICA_{PSV} sometimes cannot be measured at the region of greatest stenosis. In such cases, the pulse Doppler waveform after the stenosis shows a turbulent flow or the AcT on the distal side is prolonged [11] (Fig. 3). However, there are no clear AcT-based criteria for diagnosis of the stenosis rate.

Takekawa et al. [24] measured acceleration times to examine the usefulness of the AcT ratio, calculated as the ratio AcT at the distal ICA/AcT at the ipsilateral CCA. In 127 vessels, the parameters AcT ratio and ICA_{PSV} had a correlation coefficient of 0.82 ($p < 0.0001$). With a cutoff value of 1.75, diagnosing $ICA_{PSV} \geq 150$ cm/s had a sensitivity of 92.3% and a specificity of 97.4%. When the cutoff value was 2.0, diagnosing $ICA_{PSV} \geq 200$ cm/s had a sensitivity of 90.0% and a specificity of 96.6%. In a study of 265 vessels [25], the correlation coefficient between the AcT ratio and the diameter stenosis rate based on the ECST method using carotid artery ultrasonography was 0.60 ($p < 0.00001$). Using a cutoff value of 1.5, diagnosing a stenosis rate of $> 65\%$ had a sensitivity of 90.0% and a specificity of 93.5% (odds ratio [OR] 128.8). Nishihira et al. [26] examined the relationship

between the NASCET stenosis rate using DSA and the AcT ratio in 177 blood vessels. Their results showed that the AcT ratio had the highest correlation with stenosis rate, with the correlation coefficient for ICA_{PSV} being 0.647, that for the ratio ICA_{PSV}/CCA_{PSV} being 0.670, and that for the AcT ratio being 0.744 (all $p < 0.0001$). When the cutoff value of the AcT ratio was 1.31, diagnosing stenosis of $\geq 50\%$ had 94.5% sensitivity, 91.0% specificity, 82.6% PPV, 97.4% NPV, and 92.1% accuracy. With an AcT ratio cutoff of 1.35, diagnosing stenosis of $\geq 70\%$ had 97.1% sensitivity, 83.2% specificity, 99.2% NPV, and 85.9% accuracy, while the PPV was low at 57.9%.

In these studies, the AcT of the distal ICA was measured at about 3 cm distal to the carotid bulb with a convex array probe, and that of the CCA at about 2 cm proximal to the carotid bulb with a linear array probe. In general, AcT is the time from the minimum flow rate to the maximum flow rate, i.e., the time from EDV to PSV. However, the methods described by Takekawa et al. [24, 25] and Nishihira et al. [26] measure the time to PSV as the time until the inflection point when the pulse Doppler waveform is a mono-modal peak pattern with a distinct inflection point, and in cases with a bimodal peak pattern, the time to the first peak is measured. Iizuka et al. [27] compared the methods of Takekawa et al. and Nishihira et al. with a method of measuring the time from EDV to PSV for measuring the AcT. The NASCET stenosis rate using DSA exhibited significant positive correlations with the AcT ratios calculated based on the method by Takekawa et al. and Nishihira et al., as well as with the AT ratio defined as the ratio distal ICA AcT/ipsilateral CCA AcT calculated using the time from EDV to PSV (Fig. 4). The AUC for the diagnosis of stenosis of $\geq 50\%$ was 0.971 for the AcT ratio, whereas the AT ratio was not useful, with an AUC of 0.572. Likewise, the AUC for stenosis of $\geq 70\%$ was 0.621 for the AT ratio, compared to an AUC of 0.920 for the AcT ratio. These findings indicate that the method used by Takekawa et al. and Nishihira et al. to measure AcT is more useful, i.e., measuring the time to the inflection point in the mono-modal peak pattern with a distinct

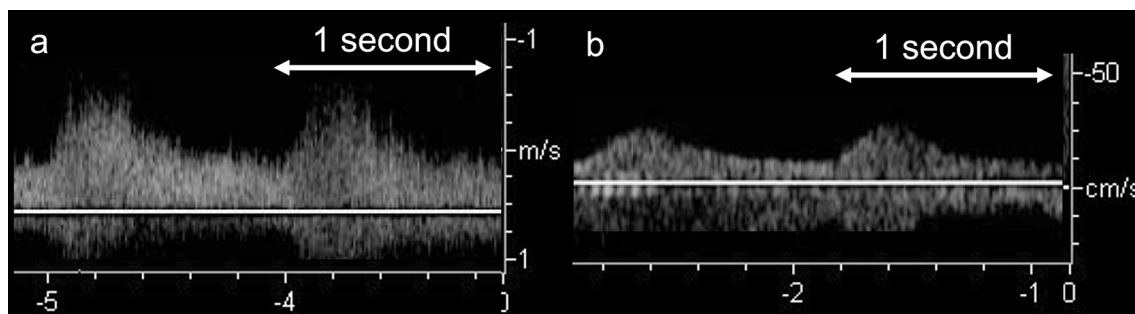
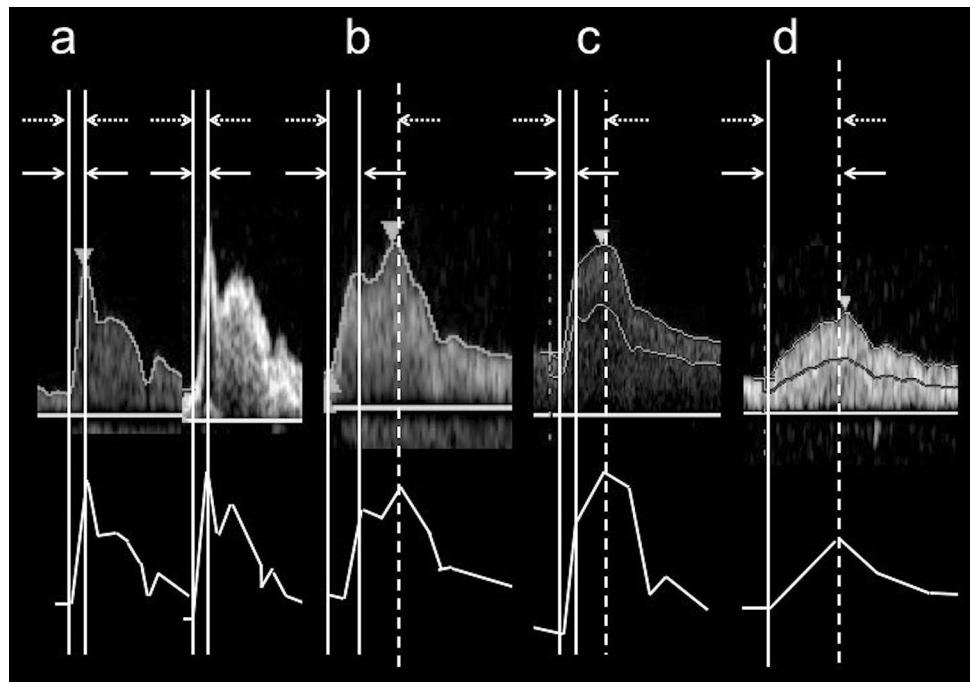


Fig. 3 Pulse Doppler waveform changes distal to the stenosis. When the stenosis is moderate or severe, the pulse Doppler waveform distal to the stenosis shows a turbulent flow (a) and prolonged acceleration time (b)

Fig. 4 Measurements of the AcT ratio and AT ratio. The AcT ratio measures the time to the inflection point, if an obvious one exists, before reaching PSV, or the time to the first peak in bimodal cases (time between solid lines). The AT ratio measures the time to PSV (time between dotted lines). **a** Type A: This is a bimodal peak pattern; the initial peak of the waveform is consistent with PSV. **b** Type B: This is a bimodal peak pattern; the second peak of the waveform is consistent with PSV. **c** Type C: This is a monomodal peak pattern; the waveform has a clear inflection point. **d** Type D: This is a monomodal peak pattern, where the inflection point is unclear. *AcT* and *AT* acceleration time, *PSV* peak systolic velocity. Reprinted from reference [27]



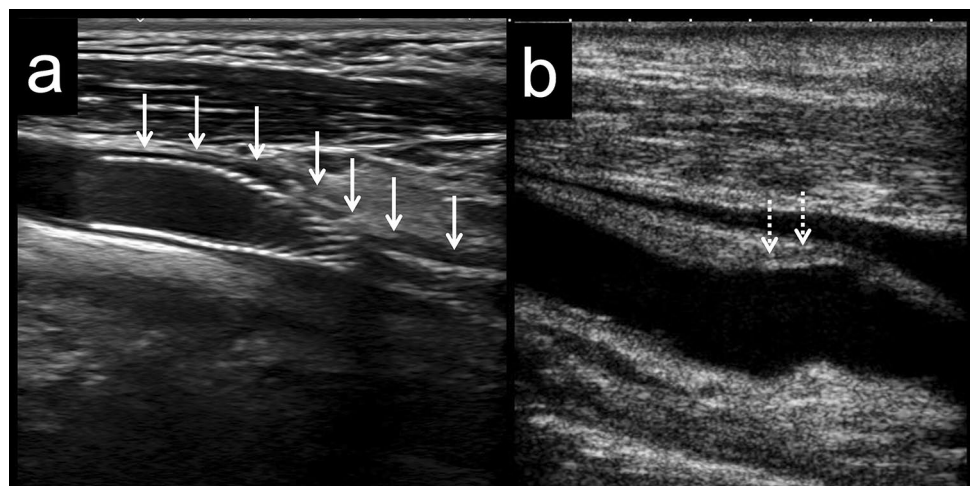
flexion point, and the time to the first peak is measured in the bimodal peak pattern.

It should be noted that, when the AcT is prolonged in the bilateral CCAs, ICAs, and external carotid arteries, aortic stenosis might be a differential diagnosis [28]. However, Okamura et al. [29] examined the correlation between aortic stenosis and the AcT ratio in 60 cases and found that the AcT ratio was not affected by aortic stenosis.

Carotid artery ultrasonography in patients with carotid artery stenting (CAS)

CEA and CAS are recommended for severe symptomatic extracranial ICA stenosis of $\geq 70\%$ in patients with ischemic stroke, whereas CEA is recommended for moderate stenosis of $\geq 50\%$ [9]. Even in cases of asymptomatic extracranial ICA stenosis without ischemic stroke, CEA or CAS should be considered in patients with moderate-to-severe stenosis, especially those with severe stenosis [8] (Fig. 5). Although the choice between CEA and CAS is based on the patient's condition and other factors, preoperative carotid artery ultrasonography plays an important role.

Fig. 5 B-mode imaging of CAS and CEA. Conventional B-mode ultrasound images of the carotid artery in CAS (**a**) and CEA (**b**) are shown. Stent struts (solid line arrows) and sutures (dotted line arrows) are observed. CAS and CEA are recommended for severe stenosis, especially for severe symptomatic stenosis of the extracranial internal carotid artery. *CAS* carotid artery stenting, *CEA* carotid endarterectomy



Preoperative assessments include measurements of the stenosis rate, plaque properties, stenosis length, degree of flexion of the ICA distal to the stenosis, vessel diameter, and internal diameter [11]. In particular in patients scheduled for CAS, it is important to identify cases of poor dilatation and reduced blood pressure during diastole when calcified plaque is $\geq 3/4$ of the circumference. Echolucent plaque increases the risk of distal emboli or filter cloggings during distal filter protection. Data on stenosis length, internal diameter, and flexion are also important factors when choosing the stent. Carotid artery ultrasonography is useful for these assessments, and stenosis length and internal diameter correlate well with corresponding DSA findings [30]. Carotid artery ultrasonography is also useful in cases of postoperative restenosis, dissection, fluid collections, thromboembolism, and stent deformation [31].

Furthermore, while the incidence of restenosis $\geq 70\%$ does not differ between CEA and CAS, restenosis $\geq 50\%$ or occlusion is more common with CEA than with CAS (OR 2.00, 95% confidence interval 1.12–3.60) [32]. The rate of restenosis $\geq 50\%$ was 3.9% after 6 months and 5.7% after 12 months [33], with a cumulative 5-year risk of 40.7% [34]. PSV at the stenosis site can be used to diagnose restenosis with carotid artery ultrasonography, but the PSV cut-off value differs between surgical and nonsurgical cases. Setacci et al. [35] evaluated restenosis in 814 patients who underwent CAS. They found that ICA_{PSV} at the stenosis site was ≤ 174 cm/s for 30–50% restenosis and ≤ 299 cm/s for moderate restenosis of 50–70%. In addition, restenosis of more than 70% was defined as $ICAPSV \geq 300$ cm/s, $ICA_{EDV} \geq 140$ cm/s, and ICA_{PSV}/CCA_{PSV} ratio ≥ 3.8 . The AUC values were 0.99 for ICA_{PSV} , 0.98 for ICA_{EDV} , and 0.99 for ICA_{PSV}/CCA_{PSV} , demonstrating high reliability. Several other studies have shown that in severe stenosis of 70% or 80% after CAS, ICA_{PSV} at the stenosis site is ≥ 300 –330 cm/s, ICA_{EDV} is ≥ 120 –140 cm/s, and ICA_{PSV}/CCA_{PSV} is ≥ 3.2 –4.0 [36]. AbuRahma et al. [37] examined 200 patients who underwent CEA. They found that the sensitivity, specificity, PPV, NPV, and accuracy were all 98% for diagnosing restenosis $\geq 30\%$ when the ICA_{PSV} was ≥ 155 cm/s at the site of restenosis after CEA. The sensitivity, specificity, PPV, NPV, and accuracy were 99%, 100%, 100%, 98%, and 99%, respectively, for $\geq 50\%$ restenosis when the ICA_{PSV} was ≥ 213 cm/s. Furthermore, when ICA_{PSV} was ≥ 274 cm/s, severe restenosis of $\geq 70\%$ could be diagnosed with a sensitivity of 99%, specificity of 91%, PPV of 99%, NPV of 91%, and accuracy of 98%. However, limited research exists on the use of carotid artery ultrasonography for diagnosing restenosis after CEA, and there are no clear diagnostic criteria. Recently, the usefulness of transoral carotid ultrasonography has been demonstrated, with contrast-enhanced transoral carotid ultrasonography being especially useful for assessments before and after CAS [38].

Diagnosing ICA and middle cerebral artery (MCA) occlusion

In the acute phase of cerebral infarction, the indications for intravenous recombinant tissue plasminogen activator or mechanical thrombectomy must be determined based on the time of onset or discovery, clinical symptoms, and imaging findings [39]. Mechanical thrombectomy is a particularly good indication for occlusion of the M1 or M2 segment of the MCA, and acute cerebral infarction requires a rapid diagnosis of the occluded vessel.

Yasaka et al. [40] examined whether the occlusion site could be inferred from the EDV of the CCA in 46 patients with acute cardioembolic cerebral infarction. Their results demonstrated the usefulness of the ED ratio, i.e., the ratio of the EDV of the CCA of the nonaffected side divided by that of the affected side. The ED ratio was ≥ 4.0 for ICA occlusion, 1.3–4.0 for M1 segment occlusion, and < 1.3 for MCA occlusion distal to M1. The accuracy was 97% for ICA occlusion and 93% for M1 occlusion, and the ED ratio is now widely used for occlusion diagnosis (Fig. 6). Kimura et al. [41] examined the usefulness of EDV and ED ratio of the CCA for diagnosing ICA occlusion. Their results showed that in acute atherothrombotic cerebral infarction, the ED ratio was ≥ 1.4 and EDV was 10.9 ± 6.1 cm/s. The ED ratio was ≥ 1.4 in cardioembolic cerebral infarction with ICA occlusion, but the EDV was 1.8 ± 3.4 cm/s, which was significantly lower than in atherothrombotic cerebral infarction. In 25 healthy participants, the ED ratio was < 1.4 and EDV was 20.3 ± 6.0 cm/s. These findings show that the ED ratio is ≥ 1.4 in acute cerebral infarction with ICA occlusion, that EDV is significantly lower in patients with occlusion than in healthy individuals, and that EDV is significantly lower in patients with acute cardioembolic cerebral infarction than in those with atherothrombotic cerebral infarction [13] (Fig. 7). Some patients with ICA occlusions have mobile thrombi that quickly move to the cranial side in the systolic phase with relatively uniform echogenicity, then slowly return to the original position during the diastolic phase. This type of mobile thrombus is also called an oscillating thrombus (Fig. 8) and tends to appear in ICA occlusion due to acute cardioembolic cerebral infarction [13, 42].

Diagnosis of vertebral artery (VA) occlusion

Koch et al. [43] studied VA origin stenoses of $\geq 50\%$ in 386 vessels. The AUC values for diagnosing stenosis based on the parameters VA origin PSV, ratio VA origin PSV/V1

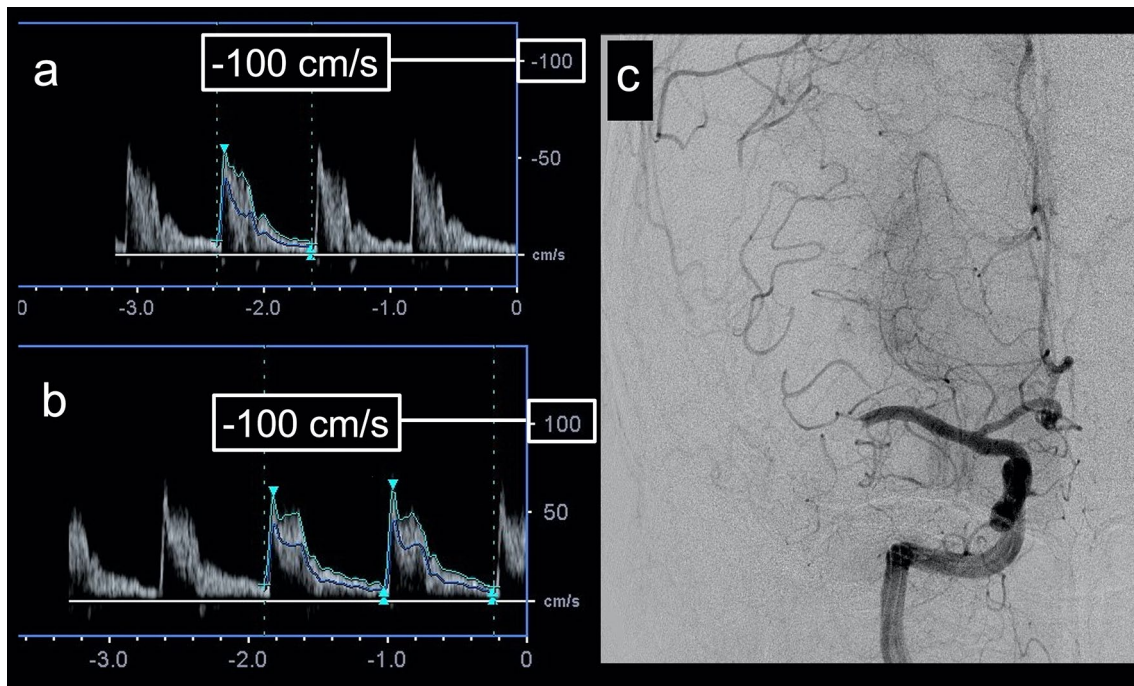


Fig. 6 Ultrasound findings of MCA occlusion in cardioembolic cerebral infarction. PWD (a, b) and DSA (c) measurements are shown. The EDV values of the right (a) and left (b) CCA are 5.4 cm/s and 7.9 cm/s, respectively. Therefore, the ED ratio is 1.46. DSA (c)

revealed an occlusion to the right M1 segment of the MCA (arrow). *MCA* middle cerebral artery, *PWD* pulsed-wave Doppler, *DSA* digital subtraction angiography, *EDV* end-diastolic flow velocity, *CCA* common carotid artery

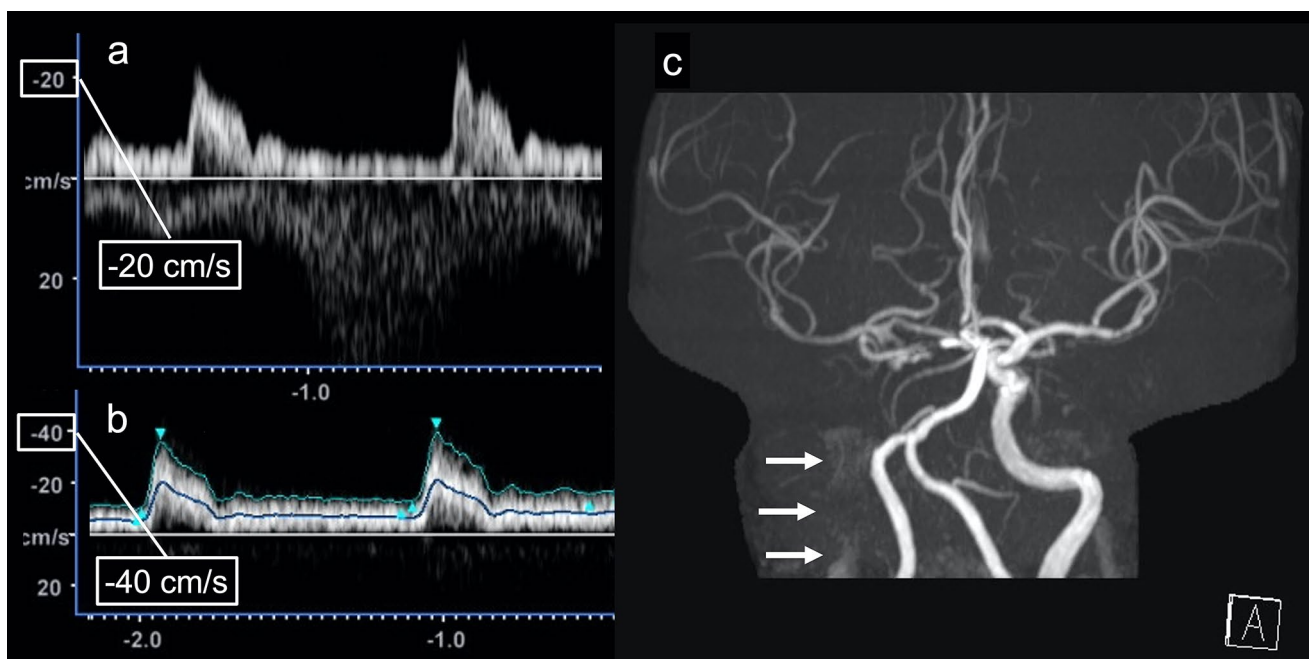


Fig. 7 Ultrasound findings of ICA occlusion. Pulsed-wave Doppler ultrasound (a, b) and MRA (c) are shown. The EDV values of the right (a) and left (b) CCA are 4.8 cm/s and 12.9 cm/s, respectively. Therefore, the ED ratio is 2.7. MRA (c) reveals occlusion of the left

ICA (arrow). *ICA* internal carotid artery, *CCA* common carotid artery, *MRA* magnetic resonance angiography, *EDV* end-diastolic flow velocity. Reprinted from reference [13]

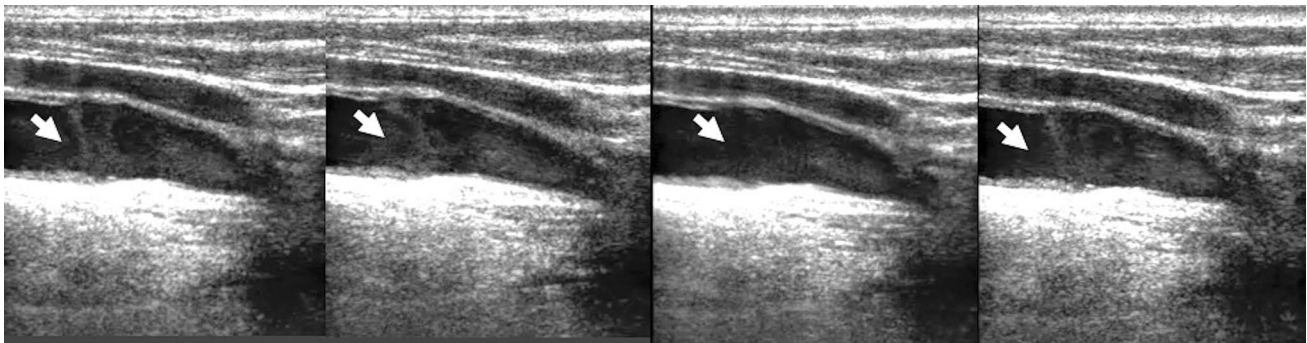


Fig. 8 Oscillating thrombus. An oscillating thrombus is a mobile thrombus with a relatively uniform echo intensity (arrow), particularly evident in patients with ICA occlusion caused by acute cardioembolic cerebral infarction. ICA, internal carotid artery. Reprinted from reference [13]

segment PSV, and ratio VA origin PSV/V2 segment PSV were 0.821, 0.733, and 0.765, respectively, demonstrating VA origin PSV to be the most useful parameter. For diagnosing stenosis of $\geq 50\%$, VA origin PSV ≥ 58 cm/s had 90% sensitivity and 45% specificity, ≥ 77 cm/s had 80% sensitivity and 71% specificity, ≥ 114 cm/s had 70% sensitivity and 90% specificity, and ≥ 129 cm/s had 60% sensitivity and 92% specificity. Hua et al. [44] examined stenoses at the origin of the VA in 247 cases. They found that for mild stenosis ($< 50\%$), the VA origin PSV was ≥ 85 cm/s, the ratio VA origin PSV/V2 segment PSV was ≥ 1.3 , and the VA origin EDV was ≥ 27 cm/s. In moderate stenosis (50–69%), the VA origin PSV was ≥ 140 cm/s, the ratio VA origin PSV/V2 segment PSV was ≥ 2.0 , and the VA origin EDV was ≥ 35 cm/s. For severe stenosis ($\geq 70\%$), the VA origin PSV was ≥ 210 m/s, the ratio VA origin PSV/V2 segment PSV was ≥ 4.0 , and the VA origin EDV was ≥ 50 cm/s. The AUC values were highest for VA origin PSV at 0.974 for $< 50\%$ stenosis, 0.986 for 50–69% stenosis, and 0.950 for $\geq 70\%$ stenosis. For the ratio VA origin PSV/V2 segment PSV, the AUC values were 0.953, 0.972, and 0.907, respectively, confirming it to be almost as useful as VA origin PSV. For VA origin EDV, the AUC values were 0.640, 0.834, and 0.858, respectively, indicating it is less useful than the other assessment parameters. For VA origin PSV, the accuracy was 94.5% for $< 50\%$ stenosis, 96.2% for 50–69% stenosis, and 88.7% for $\geq 70\%$ stenosis.

Rozeman et al. [45] studied 337 cases of vertebrobasilar stroke with $\geq 50\%$ stenosis. They found that for diagnosing V1 segment stenosis of $\geq 50\%$, a PSV ≥ 140 cm/s at the stenosis had 39% sensitivity and 88% specificity, ≥ 130 cm/s had 48% sensitivity and 85% specificity, ≥ 120 cm/s had 61% sensitivity and 78% specificity, ≥ 110 cm/s had 68% sensitivity and 69% specificity, ≥ 100 cm/s had 71% sensitivity and 57% specificity, ≥ 90 cm/s had 84% sensitivity and 47% specificity, ≥ 80 cm/s had 84% sensitivity and 37% specificity, and ≥ 70 cm/s had 87% sensitivity and

25% specificity. They determined the most suitable cutoff value for V1 stenosis as 90 cm/s. However, in many cases, the V1 segment cannot be observed by carotid artery ultrasonography, and the authors concluded that carotid artery ultrasonography was of limited use in the diagnosis of VA stenosis.

Diagnosis of distal VA occlusion has also been studied. Analyzing data from 128 patients, Saito et al. [46] proposed diagnostic criteria for VA occlusion using VA vessel diameter, time-averaged maximum flow velocity (TAMV), PSV, and EDV. These authors suggest that if VA blood flow is completely absent, the VA is occluded at the VA origin. By contrast, if the blood flow in the pulse Doppler waveform is only absent during diastole, the VA is occluded before the branch of the posterior inferior cerebellar artery (PICA). If a diastolic blood flow signal can be identified, TAMV should be evaluated. A TAMV value of ≥ 18 cm/s is considered normal, but if it is < 18 cm/s, the mean ratio, i.e., the ratio between the TAMV value of the higher side and the lower TAMV value of the contralateral side, should be calculated. A mean ratio of < 1.4 is normal, but for a mean ratio ≥ 1.4 , the diameter ratio (i.e., the larger vessel diameter divided by the smaller, contralateral vessel diameter) should be determined. If the diameter ratio is < 1.4 , meaning there is not much of a left–right difference in vessel diameter, the VA is occluded after the PICA bifurcation on the side with the lower velocity. If the diameter ratio is ≥ 1.4 , the diagnosis is asymptomatic VA occlusion or hypoplastic VA (Fig. 9). Although the accuracy of these diagnostic criteria is high at 95%, it should be noted that 65.6% of the patients in the study had acute cerebral infarction. A bow hunter's stroke, in which an ischemic stroke is caused by cervical rotation or other movements, can be diagnosed by observing changes in the VA pulse Doppler waveform during these movements [47]. Therefore, it is important to examine the VA in different neck positions.

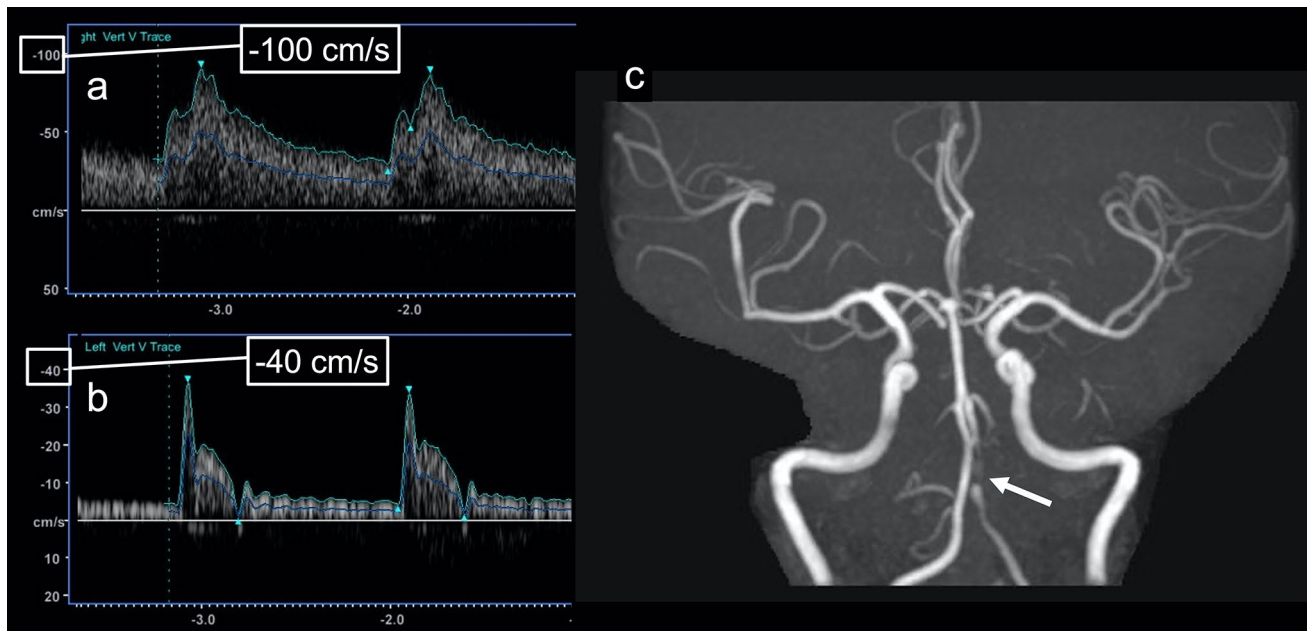


Fig. 9 Diagnosis of the VA occlusion site. Pulsed-wave Doppler ultrasound (a, b), and MRA (c) images are shown. In the right VA of this patient, the vessel diameter is 3.6 mm, EDV is 42.8 cm/s, and TAMV is 49.7 cm/s (a). In the left VA, the vessel diameter is 3.0 mm, EDV is 4.4 cm/s, and TAMV is 9.0 cm/s (b). The MV ratio is 5.5, the

diameter ratio is 1.2, and MR angiography reveals a symptomatic left VA occlusion after the PICA branch (c). VA vertebral artery, MRA magnetic resonance angiography, TAMV time-averaged maximum velocity, PICA posterior inferior cerebellar artery, EDV end-diastolic velocity. Reprinted with modification from reference [13]

Diagnosis of basilar artery (BA) stenosis and occlusion

Cerebral infarction due to BA occlusion can be fatal. Okamura et al. [48] compared PWD findings in the VA with the BA diameter stenosis rate determined by MRA in 122 cases with TAMV values < 18 cm/s in both VAs. Using PWD, they examined EDV and TAMV of the VA with slower velocities (Min EDV and Min MV, respectively), as well as pulsatility index (PI) and resistance index (RI) of the VA with higher values (Max PI and Max RI, respectively) (Fig. 10). The results showed that BAs with stenosis of $\geq 50\%$ or occlusion had significantly lower Min EDVs and Min MVs, as well as significantly higher Max PIs and Max RIs. However, the AUCs for Min EDV (0.321) and Min MV (0.237) indicated that these parameters were not very useful. Likewise, Max RI had a low AUC of 0.662, whereas Max PI had a predictive value of 0.718, which was also low but expected to indicate the usefulness of this parameter. When Max PI was ≥ 2.0 or Max RI was ≥ 0.82 , diagnosis of BA with $\geq 50\%$ stenosis or occlusion had 75.0% sensitivity, 57.0% specificity, 42.2% PPV, and 84.5% NPV. When Max PI was ≥ 2.0 and Max RI was ≥ 0.82 , this diagnosis had 61.1% sensitivity, 68.6% specificity, 44.9% PPV, and 80.8% NPV. It should be mentioned that 77.9% of the study participants had acute strokes.

Other findings

Carotid artery ultrasonography is useful for diagnosing stenosis or occlusion of the subclavian artery proximal site before the VA bifurcation. Sakima et al. [49] compared stenosis rates of the subclavian artery assessed using pulse Doppler waveform and angiography of the left VA in 22 patients. The results showed no changes in VA pulse Doppler waveform in arteries with $< 50\%$ stenosis, but a mild notch appeared in the systole in arteries with 50–59% stenosis, a retrograde flow was observed in arteries with 60–69% stenosis, more antegrade than retrograde flow in arteries with 70–89% stenosis, and only retrograde flow in arteries with $\geq 90\%$ stenosis (Fig. 11). The degree of subclavian artery stenosis was significantly correlated with the change in VA pulse Doppler waveform ($R^2 = 0.646$, $p < 0.0001$).

In moyamoya disease, the ICA diameter declines rapidly after the bifurcation to less than half of that of the CCA diameter, creating the champagne bottle neck sign, or to less than the diameter of the external carotid artery, resulting in the diameter reversal sign [50]. The champagne bottle neck sign is particularly more likely to appear in patients with severe stenosis or occlusion of grade 4 or higher [51] in a major cranial artery [52].

Moreover, Takayasu's arteritis leads to circumferential thickening of the CCA wall—called the macaroni sign—and in advanced cases, the CCA may be occluded [53].

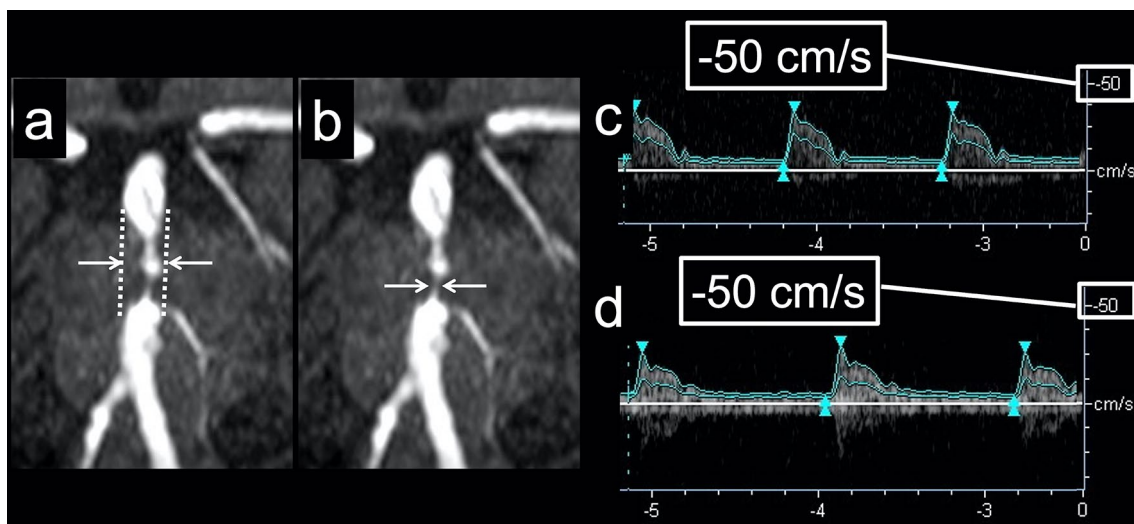
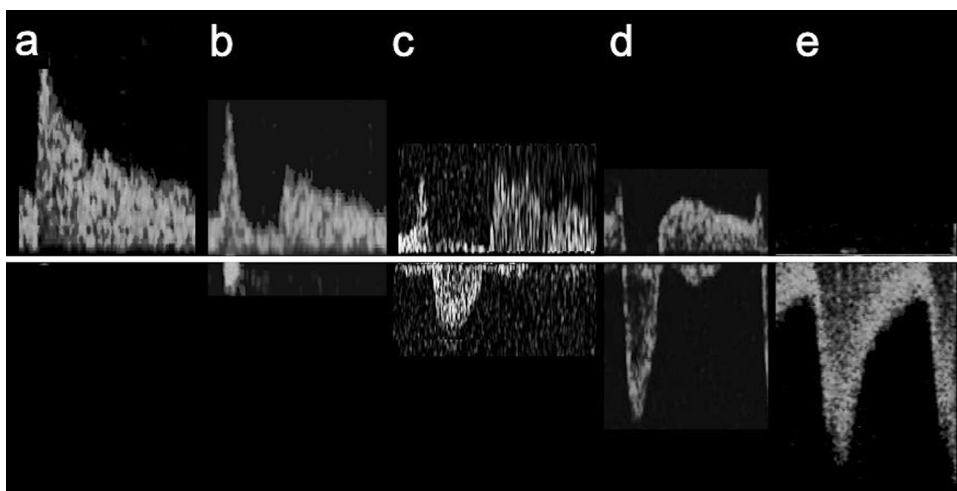


Fig. 10 Ultrasound findings of BA stenosis $\geq 50\%$. MRA (a, b) and PWD (c, d) images are shown. The stenosis rate of the BA calculated based on findings in image b (arrow) and image a (arrow) is $\geq 50\%$. For the right VA (c), the PSV is 33.4 cm/s, EDV is 5.3 cm/s, TAMV is 12.0 cm/s, PI is 2.34, and RI is 0.84. For the left VA (d), the PSV is 26.4 cm/s, EDV is 4.0 cm/s, TAMV is 8.6 cm/s, PI is 2.55, and RI

is 0.83. Thus, the TAMV values are < 18 cm/s in both VAs, Max PI is 2.55, and Max RI is 0.84. BA basilar artery, MRA magnetic resonance angiography, PWD pulsed-wave Doppler, VA vertebral artery, PSV peak systolic velocity, EDV end-diastolic velocity, TAMV time-averaged maximum flow velocity, PI pulsatility index, RI resistance index

Fig. 11 Pulse Doppler waveform of the VA in subclavian artery stenosis or occlusion. Depending on the presence and degree of subclavian artery stenosis, the pulse Doppler waveform in the VA can show a normal flow pattern (a), a mid-systolic notch (b), a retrograde flow smaller than the antegrade flow (c), a retrograde flow larger than the antegrade flow (d), or a retrograde flow without an antegrade flow (e). VA vertebral artery. Reprinted from reference [13]



Conclusion

This review outlined the diagnosis of stenosis and occlusion in the CCA, ICA, and VA, which can be evaluated with carotid artery ultrasonography. It is also possible to infer stenosis and occlusion in the MCA and BA, which cannot be directly observed with carotid artery ultrasonography (Table 1). These assessments provide essential data for patient risk management. Carotid artery ultrasonography is noninvasive, can be performed repeatedly at the bedside, and can provide rapid assessments and diagnoses

even in emergency rooms. Therefore, in patients with acute ischemic stroke, it can provide important information regarding the pathophysiology, diagnosis, and treatment selection [13].

When a stenotic lesion is found in the extracranial carotid artery, it is important to consider surgical treatment, but the most important thing is to immediately manage the risk of vascular injury and administer antithrombotic drugs as needed, i.e., to provide the best medical treatment. Regular imaging examinations, including carotid artery ultrasonography, should be performed to assess the potential progression of stenotic lesions.

Table 1 Diagnosis of stenosis and occlusion with carotid artery ultrasonography

Diagnosis	Finding	References
ICA stenosis		
NASCET stenosis rate $\geq 50\%$ (DSA)	$ICA_{PSV} \geq 125\text{--}130$ cm/s	[11, 13, 17]
	$ICA_{PSV}/CCA_{PSV} \geq 2$	[11]
	$ICA_{PSV}/CCA_{PSV} \geq 2$ and $ICA_{EDV} < 40$ cm/s	[13]
NASCET stenosis rate $\geq 70\%$ (DSA)	$ICA_{PSV} \geq 200\text{--}230$ cm/s	[11, 13, 16, 17]
	$ICA_{PSV}/CCA_{PSV} \geq 4$	[11]
	$ICA_{PSV}/CCA_{PSV} \geq 4$ and $ICA_{EDV} \geq 40$ cm/s	[13]
	$ICA_{PSV} \geq 200\text{--}230$ cm/s or $ICA_{PSV}/CCA_{PSV} \geq 4$, $ICA_{EDV} \geq 40$ cm/s	[13, 17]
Risk of progression of asymptomatic carotid artery stenosis		
$\geq 10\%$	$ICA_{PSV}/CCA_{PSV} > 2.5$	[20]
$\geq 20\%$	$ICA_{PSV}/CCA_{PSV} > 3.3$	[20]
$\geq 30\%$	$ICA_{PSV}/CCA_{PSV} > 3.8$	[20]
Stenosis of the ICA origin based on the AcT ratio		
$ICA_{PSV} \geq 150$ cm/s	AcT ratio ≥ 1.75	[24]
$ICA_{PSV} \geq 200$ cm/s	AcT ratio ≥ 2.0	[24]
ECST stenosis rate $\geq 65\%$ (US)	AcT ratio ≥ 1.5	[25]
NASCET stenosis rate $\geq 50\%$ (DSA)	AcT ratio ≥ 1.31	[26]
NASCET stenosis rate $\geq 70\%$ (DSA)	AcT ratio ≥ 1.35	[26]
Restenosis after CAS or CEA		
30–50% stenosis (CAS)	ICA_{PSV} 105–174 cm/s	[35]
50–70% stenosis (CAS)	ICA_{PSV} 175–299 cm/s	[35]
$\geq 70\%$ stenosis (CAS)	$ICA_{PSV} \geq 300$ cm/s	[35]
$\geq 70\%$ stenosis (CAS)	$ICA_{EDV} \geq 140$ cm/s	[35]
$\geq 70\%$ stenosis (CAS)	$ICA_{PSV}/CCA_{PSV} \geq 3.8$	[35]
70% or 80% stenosis (CAS)	$ICA_{PSV} \geq 300\text{--}300$ cm/s	[36]
70% or 80% stenosis (CAS)	$ICA_{EDV} \geq 120\text{--}140$ cm/s	[36]
70% or 80% stenosis (CAS)	$ICA_{PSV}/CCA_{PSV} \geq 3.2\text{--}4.0$	[36]
$\geq 30\%$ stenosis (CEA)	$ICA_{PSV} \geq 155$ cm/s	[37]
$\geq 50\%$ stenosis (CEA)	$ICA_{PSV} \geq 213$ cm/s	[37]
$\geq 70\%$ stenosis (CEA)	$ICA_{PSV} \geq 274$ cm/s	[37]
ICA or MCA occlusion		
ICA occlusion (cardioembolic cerebral infarction)	ED ratio ≥ 4.0	[40]
M1 segment occlusion (cardioembolic cerebral infarction)	ED ratio 1.3–4.0	[40]
Peripheral MCA occlusion (cardioembolic cerebral infarction)	ED ratio < 1.3	[40]
ICA occlusion	ED ratio ≥ 1.4	[41]
VA stenosis or occlusion		
$\geq 50\%$ stenosis of the V1 segment from the origin	PSV ≥ 90 cm/s at the stenosis	[45]
$< 50\%$ stenosis at the origin	PSV ≥ 85 cm/s at the origin	[44]
$< 50\%$ stenosis at the origin	Origin PSV/V2 segment PSV ≥ 1.3	[44]
$\geq 50\%$ stenosis at the origin	PSV ≥ 114 cm/s at the origin	[43]
50–69% stenosis at the origin	PSV ≥ 140 cm/s at the origin	[44]
50–69% stenosis at the origin	Origin PSV/V2 segment PSV ≥ 2.0	[44]
$\geq 70\%$ stenosis at the origin	Origin PSV ≥ 210 cm/s	[44]
$\geq 70\%$ stenosis at the origin	Origin PSV/V2 segment PSV ≥ 4.0	[44]
Occlusion at the origin	Loss of blood flow	[46]
Occlusion before the PICA branch	Loss of diastolic blood flow	[46]
Occlusion after the PICA branch	TAMV < 18 cm/s, mean ratio ≥ 1.4 , and diameter ratio < 1.4	[46]
PICAend	TAMV < 18 cm/s, mean ratio ≥ 1.4 , and diameter ratio ≥ 1.4	[46]

Table 1 (continued)

Diagnosis	Finding	References
BA stenosis or occlusion ≥ 50% stenosis or occlusion	TAMV < 18 cm/s in both VAs and PI ≥ 2.0 or RI ≥ 0.82 in the VA with the higher velocity	[48]

AcT acceleration time based on the method of Takekawa et al. [24, 25] and Nishihira et al. [26], *BA* basilar artery, *CAS* carotid artery stenting, *CCA* common carotid artery, *CEA* carotid endarterectomy, *DSA* digital subtraction angiography, *US* ultrasound, *ECST* European Carotid Surgery Trial, *EDV* end-diastolic velocity, *ICA* internal carotid artery, *MCA* middle cerebral artery, *NASCET* North American Symptomatic Carotid Endarterectomy Trial, *PI* pulsatility index, *PICA* posterior inferior cerebellar artery, *PICAend* asymptomatic VA occlusion or hypoplastic VA, *PSV* peak systolic velocity, *RI* resistance index, *TAMV* time-averaged maximum flow velocity, *VA* vertebral artery

Declarations

Conflict of Interest H.T. received lecture fees from Pfizer Japan Inc. and Daiichi Sankyo Co., Ltd. The other authors declare that there are no conflicts of interest.

Ethical approval No ethical statements are required as this review describes the ultrasound diagnosis of carotid artery stenosis and occlusion.

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