
Original Research Article

Evaluation of collateral pathways in patients with extracranial carotid occlusion using transcranial color-coded sonography compared to digital subtraction angiography

Abstract

Background: Cerebrovascular diseases are the leading cause of global mortality. Carotid occlusion is a severe condition closely associated with ischemic stroke. The objective of our study was to assess the concordance between ultrasound combined with Transcranial color-coded duplex sonography (TCCS) and digital subtraction angiography (DSA) in evaluating extracranial carotid occlusion and intracranial collateral circulation.

Methods: Patients with severe stenosis in the extracranial carotid artery were recruited for our study. All patients suspected of having occlusion in the extracranial carotid arteries underwent ultrasound, transcranial color-coded sonography (TCCS), and digital subtraction angiography (DSA). Sensitivity, specificity, positive predictive value, negative predictive value, overall accuracy, and kappa value were employed to assess the effectiveness and consistency of ultrasound and TCCS compared to DSA.

Results: Ultrasound demonstrated a sensitivity of 85.4%, specificity of 100%, positive predictive value of 100%, negative predictive value of 90.4%, and overall accuracy of 93.9% in the diagnosis of extracranial artery occlusion. The kappa value was calculated as 0.87 ($P < 0.001$), indicating substantial agreement between ultrasound and DSA measurements for consistency assessment. Transcranial color-coded sonography (TCCS) exhibited a sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of 97.6%, 100%, 100%, 66.7%, and 97.7% respectively in evaluating collateral circulation in patients with carotid artery occlusion. The kappa value was 0.79 ($P < 0.001$) in assessing the collateral circulation in patients with occluded carotid arteries.

Conclusions: Ultrasound proved to be a valuable tool for evaluating patients with occluded carotid arteries, while TCCS emerged as a reliable approach for assessing collateral pathways in individuals with extracranial carotid artery occlusion.

Key words: extracranial carotid occlusion; Transcranial color-coded duplex sonography; collateral pathways

Introduction

A severely stenosed carotid artery is largely associated with ischemic stroke [1]. Carotid occlusion and near occlusion are severe conditions in carotid stenosis. Traditional angiography is considered the "gold standard" among many diagnostic methods [2,3], but it has several limitations in clinical practice. Due to the risk of death and a higher incidence of allergic reactions and renal toxicity from contrast

agents, some patients are disqualified for DSA [4].

Noninvasive ultrasound has been identified to be a preferred effective tool for assessing plaque formation in carotid artery. And ultrasound duplex is also an ideal technique to determine the degree of lumen stenosis in atherosclerotic carotid artery. Spectral Doppler has a sensitivity and specificity of 90% and 85% respectively in diagnosing of carotid stenosis $\geq 70\%$ that was verified by DSA[5].

In recent years, transcranial color-coded sonography (TCCS) has emerged as a reliable modality for the detection of narrow and occluded intracranial arteries, making it an ideal noninvasive approach to assess the hemodynamic status within the cranium [6]. Furthermore, TCCS allows for visualization of collateral blood flow in cases of extracranial artery occlusion or near-occlusion.

In cases of ipsilateral occlusion of the internal carotid artery or common carotid artery, compensatory activation of the Willis circle or collateral pathways occurs to maintain cerebral blood supply. While angiography is considered the gold standard for evaluating collateral circulation, transcranial color-coded duplex sonography (TCCS) can serve as a non-invasive alternative to effectively assess the compensatory capacity of collateral pathways.

To the best of our knowledge, limited research has been conducted comparing the diagnostic capabilities of ultrasound combined with transcranial color-coded sonography (TCCS) to digital subtraction angiography (DSA) in patients with extracranial carotid occlusion. In this study, we aimed to evaluate the diagnostic efficacy of ultrasound combined with TCCS in patients presenting extracranial carotid occlusion.

Materials and Methods

We retrospectively enrolled patients with severe stenosis in the extracranial carotid artery at our hospital. Severe stenosis was defined as a diameter stenosis rate exceeding 70%. These patients underwent consecutive ultrasound, TCCS, and DSA examinations. Only those patients confirmed to have occlusion of the extracranial carotid artery by DSA were included in our study. The research protocol was approved by the Medical Ethics Committee of Beijing Anzhen Hospital affiliated with Capital Medical University, and informed consent was obtained from all enrolled patients.

The ultrasound and transcranial color-coded sonography (TCCS) examinations were conducted using a multifrequency linear array transducer (4-18 MHz) and a phased array transducer (1-5 MHz), respectively. These assessments were performed with the Philips EPIQ7 system (Philips co. Ltd), which allowed for intracranial and extracranial evaluation. Both ultrasound and TCCS examinations were carried out by two experienced senior physicians, capturing B-mode grayscale, color flow, spectral Doppler images, as well as utilizing power Doppler to assess carotid artery stenosis. In cases where temporal windows were insufficient, the ultrasound contrast agent SonoVue was administered to facilitate conclusive evaluations.

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Results

We recruited a total of 114 patients with severe stenosis in the extracranial carotid artery, among whom 48 were diagnosed with occlusion in the same artery through DSA examination. The age range of the participants was between 52 and 81 years (mean age, 66.7 ± 7.4), with males accounting for 41% of the sample. Regarding risk factors associated with carotid occlusion due to atherosclerosis, hypertension was present in 87.5% of cases, diabetes in 77.1%, and hyperlipidemia in 81.3%.

Table 1 Characteristics of 48 patients with occlusion in extracranial carotid artery

Median age, years (range)	66.7 (52 to 81)
Male (%)	41(85.4%)
Female (%)	7(14.6%)
Hypertension (%)	42(87.5%)
Diabetes (%)	37(77.1%)
Hyperlipidemia (%)	39(81.3%)
Ipsilateral occlusion in extracranial carotid artery (%)	46(95.8%)
Bilateral occlusion in extracranial carotid artery (%)	2(4.2%)
Internal carotid artery occlusion (%)	46(95.8%)
External carotid artery occlusion (%)	0
Common carotid artery occlusion (%)	5(10.4%)

Among the 48 patients with confirmed complete occlusion based on angiographies, ultrasound misdiagnosed 7 cases as near-occlusion. Ultrasound demonstrated a sensitivity of 85.4%, specificity of 100%, positive predictive value of 100%, negative predictive value of 90.4%, and overall accuracy of 93.9% in diagnosing extracranial artery occlusion. The agreement between ultrasound and DSA was assessed using kappa statistics, yielding a kappa value of 0.87 ($P < 0.001$).

For the assessment of intracranial collateral pathways in patients with extracranial

artery occlusion, four patients still presented suboptimal temporal windows even after administration of ultrasound contrast agent. Among the remaining 44 patients evaluated by transcranial color-coded sonography (TCCS), 63.6% exhibited patency in the anterior communicating artery. The rates of collateral circulation blood flow determined in the posterior communicating artery, ophthalmic artery, and lateral branches of the pia mater were 79.5%, 20.5%, and 34.1%, respectively. TCCS demonstrated a sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of 97.6%, 100%, 100%, 66.7%, and 97.7% respectively. There was a significant concordance between ultrasound findings and digital subtraction angiography (DSA). Compared to DSA, TCCS showed substantial agreement with a kappa value of 0.79 ($P < 0.001$). There was high consistency observed between TCCS and DSA.

Discussion

Atherosclerotic stenosis of the carotid artery is a primary cause of stroke. The occlusion of the carotid arteries represents an extremely critical stage of stenosis. Carotid occlusion can lead to severe cerebral hypoxia and disruption in cerebral hemodynamics [7]. Carotid endarterectomy and endovascular stent placement are effective therapeutic approaches for enhancing cerebral blood supply. Duplex ultrasound examination can be utilized for preoperative assessment to visualize the carotid artery.

Although duplex ultrasound is considered a safe, cost-effective, and morphologically visible technique, its successful implementation requires the expertise of well-trained sonographers. To ensure accurate results for our patients' tests, we have carefully selected experienced ultrasound specialists and utilized standardized equipment. The assessment of carotid artery stenosis involves the utilization of peak systolic velocity (PSV), end-diastolic velocity (EDV), and spectrum analysis. When employing PSV for carotid stenosis estimation, it is crucial to exercise heightened caution due to potential pitfalls. The presence of a contralateral carotid occlusion can lead to elevated PSV values [8]. Ultrasound accuracy may be compromised in cases involving tortuous carotid arteries, obese patients, excessive calcification, and high bifurcations.

The Society of Radiologists established color duplex ultrasound velocity criteria for clinical reference in 2003 [9]. Despite the widespread use and acceptance of duplex ultrasound in clinical practice, there is still significant variation in the threshold for diagnosing carotid stenosis. The PSV range for moderate ($\geq 50\%$) stenosis diagnosis was between 110 and 245 cm/s, while the criteria for severe (70%) stenosis ranged from 175 to 340 cm/s [10]. The sensitivity and specificity of carotid stenosis assessment remain widely varied with estimated values [11]. The sensitivity of stenotic obstruction decreases by two-thirds, transitioning from severe to moderate stenoses; however, the specificity remains constant [12]. Jahromi et al. reported a diagnostic sensitivity and specificity of 90% and 94%, respectively, for carotid stenosis $\geq 70\%$ confirmed by angiography [5]. Rojoa et al demonstrated a diagnostic sensitivity of 97% and specificity of 99% for internal carotid artery occlusion [13].

In our research, ultrasound has demonstrated a sensitivity of 85.4% and a specificity of 100% in the diagnosis of extracranial artery occlusion. Ultrasonic techniques exhibit strong concordance with digital subtraction angiography (DSA). Duplex ultrasound effectively evaluates the extent of stenosis and occlusion in carotid arteries.

The intracranial vascular can be visualized in color Doppler using TCCS, enabling a sonographer to measure flow velocities accurately with angle correction. TCCS is a reliable tool for detecting narrow or occluded intracranial vessels. Additionally, TCCS provides a feasible non-invasive approach to assess intracranial collateral pathways and hemodynamic status. In cases of severe stenosis or occlusion in extracranial carotid arteries, TCCS allows visualization of collateral blood flow through anterior and posterior communicating vessels. The utilization of sonographic contrast agents in patients with poor acoustic windows can significantly enhance the visualization probability of intracranial main vessels [14]. However, despite the administration of SonoVue as a contrast agent, four patients still exhibited inadequate temporal windows in our study.

The intracranial collateral circulation encompasses both main and secondary branches. The anterior communicating artery and posterior communicating artery are classified as primary collaterals, while the secondary branches consist of leptomeningeal vessels and ophthalmic arteries [15]. Abd-Allah et al. have reported that transcranial color-coded sonography (TCCS) is a reliable tool for assessing cerebral perfusion and reserve capacity in patients with symptomatic carotid occlusion [16].

The compensation of intracranial blood flow primarily relies on alternative routes based on arterial anatomy, particularly the integrity of the circle of Willis [17]. Connolly et al. have reported that anterior communicating artery (ACoA) is the most effective blood supplement in patients with internal carotid artery occlusion [18]. In our study, we also found that ACoA was activated in most patients with extracranial carotid artery stenosis. Our results are consistent with Zarrinkoob et al., who reported that ACoA is the primary branch closely related to equalization of blood flow rates in patients with carotid artery stenosis [19].

Our study demonstrated that the sensitivity and specificity were 97.6% and 100%, respectively, when compared to DSA. The ultrasound findings were highly consistent with those of DSA. Abd-Allah et al. utilized a novel TCCS-based collateral grading system in their investigation on patients with carotid occlusion, revealing a significant correlation between the grading system and Single-Photon Emission Tomography (SPECT) for assessing collateral circulation and cerebrovascular reserve capacity [16]. The weighted kappa values of the 3-D TCCS system, as reported by Wessels et al., were found to be 0.56, 0.63, 0.56, and 0.43 for the first auditory area celiac artery, anterior communicating artery, first parental generation celiac artery, and posterior communicating artery respectively when compared with DSA or magnetic resonance (MR) in patients with subarachnoidal hemorrhage [20].

Our study had certain limitations. Despite being a comparative analysis of ultrasound and DSA in evaluating occluded carotid arteries and intracranial collateral

pathways, the sample size of admitted patients was small. Due to unforeseen circumstances, we were unable to gather sufficient subjects for analyzing the disparity between DSA and contrast-enhanced ultrasound using SonoVue in extracranial carotid artery occlusion.

References:

- 1.Chimowitz MI, Lynn MJ, Howlett-Smith H, Stern BJ, Hertzberg VS, Frankel MR, Levine SR, Chaturvedi S, Kasner SE, Benesch CG, Sila CA, Jovin TG, Romano JG, Warfarin-Aspirin Symptomatic Intracranial Disease Trial I. Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis. *N Engl J Med.* 2005,352:1305-1316.
- 2.Sundgren PC, Sunden P, Lindgren A, et al. Carotid artery stenosis: contrast-enhanced MR angiography with two different scan times compared with digital subtraction angiography. *Neuroradiology.* 2002, 44(7):592-9.
- 3.Nguyen-Huynh MN, Wintermark M, English J, Lam J, Vittinghoff E, Smith WS, Johnston SC. How accurate is CT angiography in evaluating intracranial atherosclerotic disease? *Stroke.* 2008,39:1184–1188.
- 4.Adla T, Adlova R. Multimodality Imaging of Carotid Stenosis. *Int J Angiol.* 2015, 24(3): 179–184.
- 5.Jahromi AS, Cina CS, Liu Y, et al. Sensitivity and specificity of color duplexultrasound measurement in the estimation of internal carotid artery stenosis: A systematic review and meta-analysis. *J Vasc Surg.* 2005, 41(6):962-72.
- 6.Valaikiene J, Schuierer, G, Ziemus B, et al. Transcranial Color-Coded Duplex Sonography for Detection of Distal Internal Carotid Artery Stenosis. *AJNR Am J Neuroradiol.* 2008, 29(2):347-353.
- 7.Rafailidis V, Charitanti A, Tegos T, et al. Contrast-enhanced ultrasound of the carotid system: a review of the current literature. *J Ultrasound.* 2017, 20(2):97-109.
- 8.Murray CSG, Nahar T, Kalashyan H, et al. Ultrasound assessment of carotid arteries: Current concepts, methodologies, diagnostic criteria, and technological advancements. *Echocardiography.* 2018;35(12):2079-2091.
- 9.Grant EG, Benson CB, Moneta GL, Alexandrov AV, Baker JD, Bluth EI, et al. Society of Radiologists in Ultrasound Consensus Conference on Ultrasound and Doppler Diagnosis of Carotid Stenosis. *Radiology*2003;229:340-346.
- 10.Columbo JA, Zwolak RM, Arous EJ, et al. Variation in Ultrasound Diagnostic Thresholds for Carotid Stenosis in the United States. *Circulation.* 2020, 141(12):946-953.
- 11.Gokaldas R, Singh M, Lal S, et al. Carotid stenosis: from diagnosis to management, where do we stand? *Curr Atheroscler Rep.* 2015,17(2):480.
- 12.Wardlaw JM, Chappell FM, Stevenson M, et al. Accurate, practical and cost-effective assessment of carotid stenosis in the UK. *Health Technol Assess.* 2006;10(30):iii–iv, ix–x, 1–182.
- 13.Rojoa DM, Lodhi AQD, Kontopodis N. Ultrasonography for the diagnosis of extra-cranial carotid occlusion - diagnostic test accuracy meta-analysis. *Vasa.* 2020,

49(3):195-204.

14.Krejza J, Baumgartner RW. Clinical Applications of Transcranial Color-Coded Duplex Sonography. *J Neuroimaging*. 2004, 14(3):215-25.

15.Liebeskind DS. Collateral circulation. *Stroke*. 2003,34:2279-84.

16.Abd-Allah F, Rizk H, Farrag MA, et al. Assessment of Intracranial Collateral Circulation Using Novel TCCS Grading System in Patients With Symptomatic Carotid Occlusion. *Front Neurol*. 2020,11:666.

17.Kim YS, Meyer JS, Garami Z, Molina CA, Pavlovic AM, Alexandrov AV. Flow diversion in transcranial Doppler ultrasound is associated with better improvement in patients with acute middle cerebral artery occlusion. *Cerebrovasc Dis*. 2006; 21(1-2): 74–8.

18.Connolly F, Rohl JE, Lopez-Prieto, et al. Pattern of Activated Pathways and Quality of Collateral Status in Patients with Symptomatic Internal Carotid Artery Occlusion. *Cerebrovasc Dis*. 2019;48:1–7.

19.Zarrinkoob L, Wahlin A, Ambarki K, et al. Blood flow lateralization and collateral compensatory mechanisms in patients with carotid artery stenosis. *Stroke*. 2019,50:1081-8.

20.Wessels T, Bozzato A, Mull M, et al. Intracranial collateral pathways assessed by contrast-enhanced three-dimensional transcranial color-coded sonography. *Ultrasound Med Biol*. 2004, (11):1435-40.

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