



Cohort Study

Comparison of Doppler Ultrasound and Digital Subtraction Angiography in extracranial stenosis

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ABSTRACT

Objective: Evaluating the degree of extracranial stenosis is important in predicting the risk of cerebrovascular events and to assess if the patient can benefit from any intervention. Non-invasive methods, like Doppler Ultrasonography (DUS) are preferred to invasive methods such as Digital Subtraction Angiography (DSA).

Methods: In this retrospective study, the level of agreement between DUS and DSA regarding the degree of stenosis of Internal Carotid Arteries (ICAs) and Vertebral Arteries (VAs) was assessed. The degree of ICA stenosis was classified into 5 groups. DSA was assumed as the gold standard. VA stenosis was classified into two groups of more or less than 50% stenosis.

Results: A total of 428 ICAs were assessed. Based on DSA results, DUS could estimate the degree of arterial stenosis in groups of 0–15% stenosis and 100% stenosis most accurately, and the least accuracy was in groups of 50–69% and 70–99% stenosis. The overall agreement between DUS and DSA in the classified ICA stenosis was moderate (Weighted Kappa = 0.565, $P < 0.001$). Also, the agreement of DUS and DSA when classifying ICA stenosis into two groups of above and below 50%, was moderate (Kappa = 0.583, $P < 0.001$). DUS was most sensitive and specific in the group of 100% stenosis (Sensitivity: 0.75 Specificity: 0.99) as well as the group of 1–15% stenosis (Sensitivity: 0.80 Specificity: 0.76). Also, DUS was least sensitive in group of 50–69% stenosis (Sensitivity: 0.11 Specificity: 0.94). Regarding VAS, 108 arteries were assessed and the agreement between DUS and DSA was fair (Kappa = 0.248, CI95 = -0.013 - 0.509, $P < 0.01$).

Conclusions: DUS can be used as the first-line screening tool for detecting extra cranial arteries stenosis. The practicality of the DUS as a screening tool for extracranial VAs stenosis appears to be limited.

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1. Introduction

Stroke is one of the major leading causes of disability and death and has a high value of attributable disability-adjusted life years (DALYs) [1]. An important and common etiology of ischemic stroke is extra cranial vascular stenosis [2,3]. Carotid stenosis is primarily due to formation of atherosclerotic plaques at carotid bifurcation and the initial portion of the internal carotid artery. Patients who are diagnosed with carotid stenosis, the degree of occlusion needs to be assessed in order to determine the risk of stroke and to evaluate if the patient benefits from interventions [4].

Determining the level of stenosis plays a crucial role in choosing the best treatment strategy for these patients. Those with over 50% stenosis benefit significantly from endarterectomy to decrease their susceptibility to ischemic stroke [5,6]. Although the gold standard for detecting the stenosis level is digital subtraction angiography (DSA), it tends to have a few disadvantages including invasiveness and the need for an experienced operator, which limits its safety and availability [7,8].

Most recently, non-invasive techniques have also been suggested for assessing the luminal stenosis such as Duplex Ultrasound Sonography (DUS), Magnetic Resonance Angiography (MRA), and Computed Tomography Angiography (CTA) [9–11]. Among these, DUS serves as primary screening tool for carotid stenosis, as it is available and cost-effective in most healthcare centers including ours. Occasionally the results of DUS are rechecked with the Gold Standard (i.e., DSA) for the final decision. This is because the accuracy of the Doppler ultrasound is not certain and DUS might have some pitfalls including technical errors, missing additional stenotic lesions or tandem lesions, inability to distinguish pseudo-occlusion from true total occlusion or pseudo-normalization of velocities in cases of extremely severe stenosis, underestimating severe stenosis due to calcified plaques, and a number of other issues [12].

Therefore, it is crucial to know how accurate DUS study is when compared to intra-arterial angiography so that the maximum usefulness of carotid endarterectomy can be achieved. Misdiagnosis of carotid stenosis may result unnecessary exposure of patients to the risk of surgery or patients not being operated and thereby facing otherwise preventable strokes [13].

The aim of this study is to assess the accuracy of DUS for the estimation of Internal Carotid and Vertebral artery stenosis compared to DSA in our center, as one of the main referral stroke centers in the region.

2. Methods

2.1. Study population

In this prospective study, we assessed the integrity between previous reports of ultrasonography and DSA regarding the degree of stenosis of Internal Carotid and Vertebral arteries in patients who had been referred to the multi neurovascular center of (XXX) from September 2019 to June 2020. Inclusion Criteria were patients aged 18–65 years with any clinical suspicion of extra cranial vascular stenosis who were assessed by both Doppler ultrasound and DSA in series. Exclusion criteria were patients <18 or >85 years old, those with intraventricular drainage, hydrocephalus, or hematoma, without temporal bone window and those who had not been assessed by both Doppler and intra-arterial angiography modalities.

2.2. Study design

Doppler ultrasound was performed or supervised by two expert academic neurologists, in the field of Doppler ultrasound, by a 13-6 MHz Linear-array probe (HFL38x, Sonosite M-Turbo, USA). Vascular bed occlusion percentages were divided in five categories, including 0–15%, 16–49%, 50–69%, 70–99%, and 100% stenosis, respectively. This

measurement was made based on North American Symptomatic Carotid Endarterectomy Trial (NASCET) [14] using the formula, percentage of stenosis = $(1 - \text{minimum residual lumen} \div \text{normal distal cervical internal carotid artery diameter}) \times 100$. DSA was performed and interpreted by a 7-year experienced neurologist. Under general anesthesia, catheter was inserted in ICA through femoral method. Angiographic study was performed with C-arm Allura FD20 system (Philips Healthcare, the Netherlands). 3D rotational angiography with infection rate of 3 ml/s for 6 s where projection with the best view was selected. Iopamidol was used as the contrast agent The occlusion percentage of mentioned vascular beds were assessed and documented. The results of each patients' ultrasound for ICA and VA and those of DSA were compared.

2.3. Statistical analysis

Data were analyzed by SPSS software package (SPSS Inc., Chicago, IL, USA). Quantitative data were described statistically by means and standard deviations while qualitative variable are reported by frequencies. The integrity between reports from two diagnostic modalities, DSA and sonography, was assessed by linear weighted kappa. Weighted kappa values $K \leq 0.2$ were interpreted as slight, $K = 0.21-0.4$ fair, $K = 0.41-0.60$ moderate, $K = 0.61-0.80$ good, and $K = 0.81-1.0$ perfect agreement [15].

Unique identifying number is: researchregistry7280.

The methods were written in compliance with STROCSS 2021 guidelines [16].

3. Results

217 patients had both, carotid and vertebral arteries examined. The mean age of patients was 55.6 ± 11.8 years and out of 217 patients, 123 (56.7%) of were males. The mean interval between DSA and DUS was 14 ± 6 days.

3.1. Internal Carotid Arteries (ICA)

Out of Four-hundred and thirty-four ICAs, 6 arteries were excluded, as either DSA results or DUS results were not completed. The remaining 428 arteries were classified into 5 groups based on their level of stenosis diagnosed by DSA. 220 arteries (51.4%) were diagnosed as the group of 0–15% stenosis, 81 (18.9%) as the group of 16–49% stenosis, 36 (8.4%) as the group of 50–69%, 67 (15.7%) as the group of 70–99% stenosis and 24 (5.6%) as the group of 100% stenosis (Table 1).

DUS estimated the level of arterial stenosis in groups 0–15% stenosis and 100% stenosis most accurately, and least accurate in groups of 50–69% and 70–99% stenosis.

The agreement between DUS and DSA in classifying ICAs into five groups was moderate (Weighted Kappa = 0.565, CI95 = 0.498–0.632, $P < 0.001$). Also, we investigated the agreement of DUS and DSA when they were classifying ICAs stenosis into two groups of above and below 50%, the agreement was moderate (Kappa = 0.583, CI95 = 0.497–0.692, $P < 0.001$).

The sensitivity and specificity of DUS estimation of stenosis was calculated in each group (the sensitivity is shown in Fig. 1). Overall, DUS was most sensitive and specific in group of 100% stenosis (sensitivity: 0.75 specificity: 0.99) as well as the group of 1–15% stenosis (sensitivity: 0.80 specificity: 0.76). Also, DUS was least sensitive in group of 50–69% stenosis (sensitivity: 0.11 specificity: 0.94). Moreover, since our output for DUS was ordinal, we were unable to determine specifically if our DUS overestimated or underestimated in any range.

3.2. Vertebral arteries (VA)

From 434 vertebral arteries, 108 arteries were analyzed which were classified into two groups of more than 50% stenosis and less. DSA

Table 1
Cross tabulation of DUS and DSA results of carotid arteries.

		Digital Subtraction Angiography					Total
		0–15%	16–49%	50–69%	70–99%	100%	
Doppler Ultrasound Sonography	0–15%	176	19	3	4	0	202
	16–49%	29	53	18	5	0	105
	50–69%	1	2	4	14	0	21
	70–99%	1	0	2	21	4	28
	100%	0	0	0	1	18	19
Total		207	74	27	45	22	375

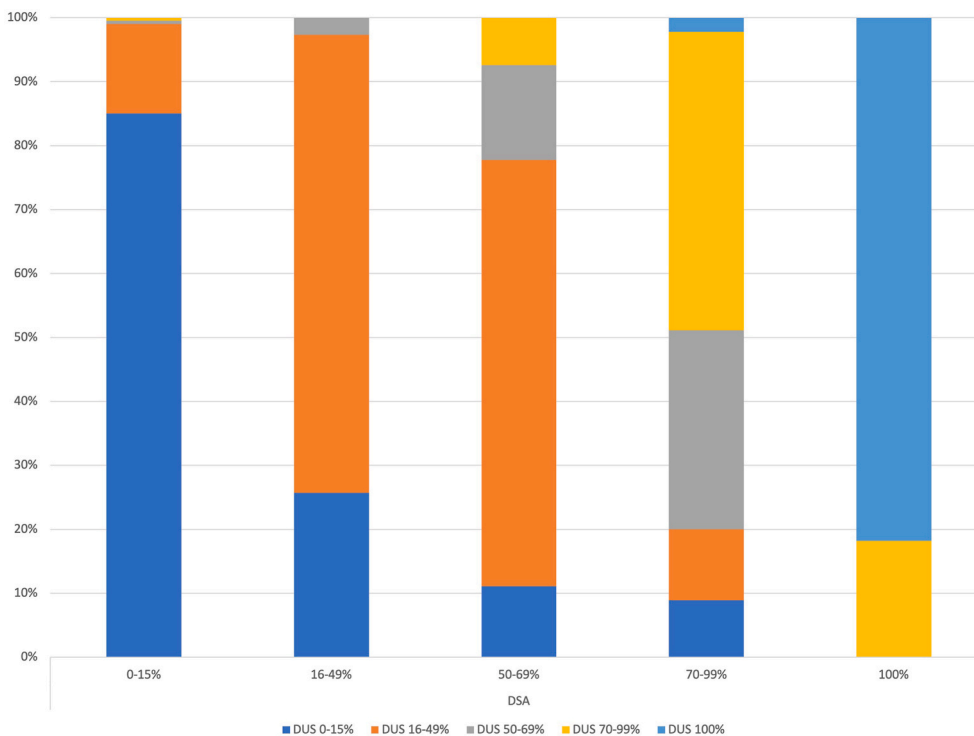


Fig. 1. Descriptive chart of percentage of stenosis reported by DUS within each DSA group.

diagnosed 93 patients with less than 50% stenosis, of which 91 were also diagnosed by DUS, and 15 with more than 50% stenosis, that 12 of them were also confirmed by DUS (Table 2).

Altogether, the agreement between DUS and DSA in classifying VA stenosis into two groups was fair (Kappa = 0.248, CI95 = -0.013 - 0.509, P < 0.01).

4. Discussion

This study found that DUS is a valuable diagnostic tool in detection of cerebral vascular stenotic events compared to DSA.

In this study, the agreement between DUS and DSA in classified ICA stenosis was moderate (Weighted Kappa = 0.565, CI 95% = 0.498–0.632). In addition, classifying ICA stenosis into two groups of above and below 50% showed a moderate agreement (Kappa = 0.583,

Table 2
Cross tabulation of DUS and DSA results of vertebral arteries.

		Digital Subtraction Angiography		Total
		0–49%	50–100%	
Doppler Ultrasound Sonography	0–49%	91	12	103
	50–100%	2	3	5
Total		93	15	108

CI95 = 0.497–0.692) and the agreement for stenosis below 50% was more than that of over 50%. Accordingly, previous studies have reported moderate and excellent agreements between the results of duplex scan studies and cerebral arteriography [17,18].

Birmpili et al., reported that computed tomography angiography (semiautomatic) had sensitivity and specificity of 75% and 91%, respectively for the detection of carotid artery stenosis for ≥50% whereas its agreement with DUS was moderate and agreement between USA and manual CTA was fair [19].

Netuka et al. compared histological findings with non-invasive imaging modalities and found that carotid DUS underestimated moderate stenosis and overestimate severe stenosis [20].

Our results showed that DUS is not a good modality to estimate the degree of stenosis in patients with 50%–69% stenosis as it has a very low sensitivity in this range.

It can be inferred that Doppler ultrasound conducted by an expert sonographer may be an acceptable primary screening tool, yet it is suggested that DUS findings of 50–69% degree ICA stenosis should be double checked with other modalities as well before making a final treatment decision.

In this study, we found that DUS had fairly adequate results for detecting vertebral artery stenosis compared to DSA, which is less satisfying compared to that of ICA stenosis. Some earlier studies have corroborated the same results [21,22]. The possible explanation is that

in cases of vertebral artery duplex there are some technical difficulties, of which posterior and deep origin are the most significant along with calcified lesions, or a short neck stature can inevitably add to the complexity [21]. In terms of VA Doppler, we evaluated B-mode image along with Peak Systolic Velocity (PSV), end-diastolic velocity (EDV), and certain spectral waveform. Nevertheless, PSV is renowned as the most accurate measure of stenosis in the extra cranial vertebral artery [23]. Altogether, we deduce that the value of DUS in diagnosing extra cranial vertebral stenosis is limited [22].

The strength of our study is the relatively large sample size in comparison to other studies and quite short interval between DUS and DSA, which adds to the accuracy of the results. The current study has some limitations. First, the focus of our study was on the arterial stenosis instead of plaque morphology. Also, this study is not multi-centric, and modalities are assessed in one academic center. Consequently, the generalization must be made with caution.

DSA as an invasive, and expensive modality that includes contrast injection and radiation exposure. Thus it is not considered as the first-line modality for detection of carotid and vertebral stenosis, however it is still the gold standard to assess the degree of arterial stenosis [24]. DUS, on the other hand, can be recommended as the first line screening tool for detecting vascular stenotic events [24]. DUS when compared to other modalities, offers many advantages including its non-invasiveness, economically desired, and availability with no harmful radiations. Additionally, providing anatomical information of the vessels adds to the DUS's usefulness in determining the cause of stroke. This is more evident in particularly posterior circulation stroke or TIA, which might be a thromboembolic event rather than hemodynamic. However, as mentioned above, complete evaluation of plaque morphology is more difficult with ultrasound in the vertebral arteries due to the so-called poor window [3,21,24,25]. Its disadvantages are that DUS precision relies on the sonographer's expertise, and patients' anatomical variations in the neck area, which can create difficulties in detection of stenosis and flow measurements [24]. Furthermore, only 5 patients with vertebral stenosis were over 50%, which reduces the power of the study.

5. Conclusion

DUS can be used as the first-line screening tool for detecting extra cranial arteries stenosis. The usefulness of the DUS as a screening tool for extra cranial vertebral artery stenosis appears to be limited.

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No funding was secured for this study.

Ethical approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent

Not applicable.

Author contribution

Dr. Sara Esmaeili, Dr. Seyed Farzad Maroufi, Dr. Seyedeh Niloufar Rafiee Alavi, Dr. Sepideh Allahdadian and Dr. Aryan Shahidi: conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Dr. Mohammad Hossein Abbasi, Dr. Mohammad Reza Motamed, Dr. Ali Famouri, Dr. Sepehr Armaghan and Dr. Hosein Nazari: Designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised

the manuscript. Dr. Maryam Bahadori, Dr. Mahya naderkhani and Dr. Mohammad Taghi Joghataei: Coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

Registration of research studies

- 1.Name of the registry: N/A
- 2.Unique Identifying number or registration ID: N/A
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Guarantor

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Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

The authors deny any conflict of interest in any terms or by any means during the study.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2021.103202>.

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