

# Digital Subtraction Angiogram (DSA) is Superior to Duplex Ultrasound (USD) in Diagnosis of Extracranial Carotid Stenosis — A Comparative Study

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## Abstract:

*This retrospective cross-sectional observational study was conducted in the department of Neurology, DMCH, Dhaka from December 2008 to December 2009. This study included a total of 40 patients, out of all, 35 suffered from non-disabling ischaemic stroke, other 5 had TIAs. Patients with  $\geq 50\%$  extracranial carotid stenosis on Duplex Ultrasound were then selected for DSA. DSA was done on these vessels and stenosis was measured using NASCET criteria. Results of USD and DSA were compared to determine the sensitivity, specificity and accuracy of Duplex Ultrasound (USD). ROC graph of RICA and LICA showed that most left and upper point of the curve lies at the level of 70% stenosis. At  $\geq 70\%$  stenosis of RICA and LICA the Sensitivity, Specificity and Accuracy were 91.2%, 50%, 85% and 86.83%, 50%, 85% respectively. This level of diagnostic efficiency of USD is less than that of DSA of carotid arteries. Study revealed that USD underestimates or overestimates degree of carotid stenosis, and DSA is safe and effective in determining stenosis. So before taking any decision to intervene in the form of Carotid endarterectomy or carotid artery stenting, it would be wise to do Digital Subtraction Angiogram of carotid vessels.*

**Key word:** Digital Subtraction Angiogram, Duplex Ultrasound, carotid vessels.

## Introduction:

Stroke is the leading cause of disability worldwide and ranks third among the leading causes of death in the developed world.<sup>1</sup> Even in a developing country like Bangladesh stroke is a cause of significant mortality and morbidity. The incidence of an ischemic cause of stroke increases with age and is up to 85% after age of 50 years.<sup>1,2</sup> About 85% of stroke is caused by primary cerebral ischemia resulting in infarction (ischemic stroke) and 15% are caused by cerebral haemorrhage (haemorrhagic stroke).<sup>1,2</sup> Ability to accurately assess the degree of stenosis has become important with studies like ACAS (Asymptomatic Carotid Atherosclerosis Study), NASCET (North American Symptomatic Carotid Endarterectomy) and ECST (European Carotid Surgery Trial).<sup>3,4,5</sup> In 659 patients with 70% to 99% stenosis randomized by NASCET, the cumulative risk of any ipsilateral stroke at 2 years was 26 % in medically treated patients and 9% in surgically treated patients.<sup>3,4,5</sup> For moderate carotid stenosis 50% to 69 %, the 5 years risk of any ipsilateral stroke is

15.7% with surgical treatment and 22.2% with medical treatment. On the basis of these results, patients with either symptomatic stenosis 50% or asymptomatic stenosis 60% are presently considered for carotid recanalization. Carotid recanalization can be done by endarterectomy or stenting.<sup>6,7</sup> Before doing any of the above procedures, diagnosis of site, size & severity of extracranial carotid stenosis should be confirmed.

Duplex Ultrasound (USD), combining high-resolution imaging and Doppler spectrum analysis has proved to be popular, non invasive accurate and cost effective means of detecting and assessing carotid disease.<sup>8</sup> Whereas Digital Subtraction Angiogram (DSA) is gold standard for carotid artery disease in demonstrating lesion, but it is invasive, costly and uses radio contrast dye.<sup>9</sup> Keeping all these in mind, the purpose of this study was to assess, determine and compare the sensitivity of two diagnostic procedures in detecting extracranial carotid stenosis. The result of the study can help in selecting patients for carotid intervention.

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### Materials and Methods

This was a retrospective cross-sectional observational study. This study was carried out from December 2008 to December 2009 for a period of one year in Neurology Department of Dhaka Medical College Hospital (DMCH). Patients of TIAs and ischaemic stroke admitted or attending Neurology outdoor, were included in this study. Estimated sample size was 40. Patients of non-disabling ischaemic stroke and or TIAs were included. Patient of haemorrhagic stroke, unconscious patients, echocardiographic evidence of a cardiac source of embolism (e.g valvular heart disease, septal defect) were excluded from this study. Right and left carotid arteries were evaluated for carotid stenosis by USD and DSA. So that a total of 80 vessels were studied. Data were collected by a semi-structured questionnaire. Both common carotid arteries, bulb, cervical segment of ICA were examined in transverse and longitudinal way in Gray- scale, Color doppler and Power doppler mode with digital high resolution liner transducer. Findings were recorded in data sheet of the patient. 40 patients of significant carotid stenosis (symptomatic  $\geq 50\%$  or asymptomatic  $\geq 60\%$  stenosis on USD were then selected for Intra-arterial DSA. Angiography was performed as intra-arterial (IA) DSA via a femoral arterial approach by two interventional neurologist blinded of USD findings. Intra-arterial DSA was done within 2 weeks of USD. Each patient was advised to attend Neurology OPD for subsequent follow-up. During both the procedures (USD and DSA), the investigator was present and maintained equal standard for all the patients. Analysis of data was done by SPSS program.

### Result

Among forty patients two patients belonged to age group 41-50, 12 patients in 51-60, 16 in 61-70, 10 in > 70 year group. Maximum 40% (n-16) patients were in age group 51-60. Minimum age was 45, and maximum 80 years, with a mean of  $62 \pm 10.32$ . There were 36 male patients and 4 female patients. among all the forty patients 52.5% (n-21) patients had history of TIA, and rest 47.5% (n-19) patients did not give any history suggestive of TIA. out of 40 patients, carotid bruit was found to be present in 17.5% (n-7), and in 82.5% (n-33) there was no carotid bruit. 4 patients had bruit over right side and rest on the left side.

Direct comparison between Duplex Ultrasound (USD), Digital Subtraction Angiography (DSA) findings of degree of stenosis of Right Internal Carotid Artery (RICA) with Cut-off point  $\geq 50\%$  stenosis found that in case of RICA, out of 30 < 50% angiographic extra-cranial carotid stenosis, USD could identify only 19 cases. 11 cases were false negative. So at 50% cut-off point sensitivity, specificity and accuracy

were low. Here Sensitivity = 63.3%, Specificity = 50%, Accuracy = 60%, PPV (Positive predictive value) = 79.17%, NPV (negative predictive value) = 31.2%.

**Table-I**

*Direct comparison between Duplex Ultrasound (USD), Digital Subtraction Angiography (DSA) findings of degree of stenosis of Right Internal Carotid Artery (RICA). Cut-off point  $\geq 70\%$  stenosis. USD-RICA-70, DSA-RICA-70 Cross tabulation*

	DSA-RICA-70		Total
	<70%	>70%	
USD-RICA-70 <70%	31 (91.2%)	3 (50.0%)	34 (85.0%)
USD-RICA-70 >70%	3 (8.8%)	3 (50.0%)	6 (15.0%)
Total	34 (100.0%)	6 (100.0%)	40 (100.0%)

Note: Results are expressed as percentage. PPV, Positive predictive value, NPV, negative predictive value. RICA; Right Internal Carotid Artery.

In Table-I it is found that in case of RICA out of 34 < 70% angiographic extra-cranial carotid stenosis, USD could identify 31 cases. 3 cases were false negative. So at 70% cut-off point sensitivity and accuracy of USD were higher than that of 50% stenosis. Here Sensitivity = 91.2% Specificity = 50%, Accuracy = 85%, PPV = 91%, NPV = 50%.

**Table-II**

*Direct comparison between Duplex Ultrasound (USD), Digital Subtraction Angiography (DSA) findings of degree of stenosis of Right Internal Carotid Artery (RICA). Cut-off point  $\geq 90\%$  stenosis. USD-RICA-90, DSA-RICA-90 Cross tabulation*

	DSA-RICA-90		Total
	<90%	>90%	
USD-RICA-90 <90%	35 (100.0%)	4 (75.0%)	39 (97.5%)
USD-RICA-90 >90%	0 (0%)	1 (20.0%)	1 (2.5%)
Total	35 (100.0%)	5 (100.0%)	40 (100.0%)

Table-II shows that at 90% cut-off point sensitivity and accuracy of USD is higher than that of lesser degrees of stenosis. Here specificity = 100% Specificity = 20%, Accuracy = 90%, PPV = 89%, NPV = 100%.

Direct comparison between USD and DSA findings of degree of stenosis of Left Internal Carotid Artery (LICA). Cut-off point  $\geq 50\%$  stenosis were done. It was found that in case of LICA out of 38 < 70% angiographic extra-cranial carotid stenosis, USD could identify 33 cases. 5 cases were false negative. So at 70% cut-off point sensitivity and accuracy

of USD were higher than that of 50% stenosis. Here Sensitivity = 86.83%, Specificity = 50, Accuracy = 85%, PPV = 97.06%, NPV = 28%.

**Table-III**

*Direct comparison between Duplex Ultrasound (USD), Digital Subtraction Angiography (DSA) findings of degree of stenosis of Left Internal Carotid Artery (LICA). Cut-off point  $\geq$  70% stenosis. USD-LICA-70, DSA-LICA-70 Crosstabulation.*

USD-LICA-70	DSA-LICA-70		Total
	<70%	>70%	
<70%	33 (86.8%)	1 (50.0%)	34 (85.0%)
>70%	5 (13.2%)	1 (50.0%)	6 (15.0%)
Total	38 (100.0%)	2 (100.0%)	40 (100.0%)

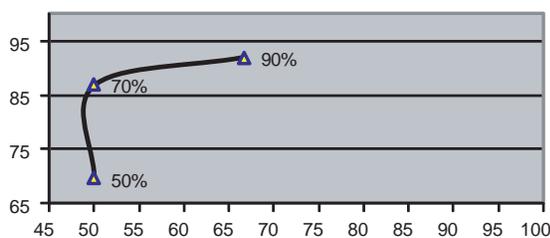
In Table III it is found that in case of LICA out of 38 < 70% angiographic extra-cranial carotid stenosis, USD could identify 33 cases. 5 cases were false negative. So at 70% cut-off point sensitivity and accuracy of USD were higher than that of 50% stenosis. Here Sensitivity = 86.83%, Specificity = 50, Accuracy = 85%, PPV = 97.06%, NPV = 28%.

**Table-IV**

*Direct comparison between Duplex Ultrasound (USD), Digital Subtraction Angiography (DSA) findings of degree of stenosis of Left Internal Carotid Artery (LICA). Cut-off point  $\geq$  90% stenosis. USD- LICA 90%, DSA-LICA-90 Crosstabulation*

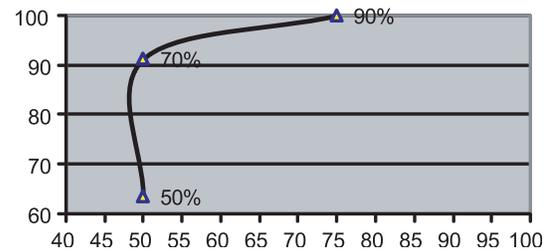
USD-LICA-90	DSA-LICA-90		Total
	<90%	>90%	
<90%	34 (91.89%)	2 (66.6%)	36 (90.0%)
>90%	3 (8.4%)	1 (50.0%)	4 (10.0%)
Total	37 (100.0%)	3 (100.0%)	40 (100.0%)

In table IV results shows that at 90% cut-off point sensitivity and accuracy of USD is higher than that of lesser degrees of stenosis. Here USD findings of both RICA and LICA were similar. Here Sensitivity = 91.89 %, Specificity = 33.33 %, Accuracy = 87.50 %, PPV = 90%, NPV = 10%.



**Fig.-1:** ROC Graph of LICA: The most left & upper point of the curve lies at the level of 70% stenosis. ( Here Y axis: Sensitivity, X axis: 100-Specificity ).

The figure 1 showing ROC graph of LICA, comparing sensitivity & specificity of USD with DSA findings of LICA. The sensitivity at the level of 50% was 69.44 % and specificity was 50%. The sensitivity at the level of 70% was 86.83% and specificity was 50%. The sensitivity at the level of 90% was 91.89 % and specificity was 33.33%.



**Fig.-2:** ROC Graph of RICA: The most left & upper point of the curve lies at the level of 70% stenosis. ( Here Y axis: Sensitivity X axis: 100-Specificity ).

The figure 2 showing ROC graph of RICA, comparing sensitivity & specificity of USD & DSA findings of RICA. The sensitivity at the level of 50% was 63.33% and specificity was 50%. The sensitivity at the level of 70% was 91.2% and specificity was 50%. The sensitivity at the level of 90% was 100 % and specificity was 25%.

**Discussion**

Carotid atherosclerosis is one of the main risk factors of ischemic cerebrovascular accidents (CVAs).<sup>6</sup> The area of the carotid artery most commonly affected by atherosclerosis is the proximal internal carotid artery i.e bifurcation of the common carotid artery. Carotid stenosis is responsible for about 30% of CVAs.<sup>10</sup> The prevalence of haemodynamically significant carotid stenosis varies with age, other risk factors, such as cigarette smoking and high fat diet. Estimates indicate that 5 per 1000 persons aged 45-60 years and approximately 10% of persons older than 80 years have carotid stenosis greater than 50%.<sup>11</sup> Patients may present with TIAs or stroke. Asymptomatic patients are most often identified when a cervical bruit is heard on physical examination but lack of carotid bruits in CVAs does not exclude a carotid stenosis.<sup>12,13</sup> Among investigations Color doppler ultrasonography is the screening method of choice, as it is cheap and noninvasive. Carotid angiography is the gold standard for diagnosis of carotid stenosis.<sup>9</sup>

In this study the mean age of ischaemic stroke and TIA was 62 ± 10.32. Minimum age was 45 and maximum 80 years. This study shows that male patients (n-36) outnumbers female (n-4), with a ratio of 9:1. Stroke is a male predominant disease as shown in different studies.<sup>14,15</sup> In this study there were 5 cases of TIAs and 35 cases of ishaemic stroke. Among 35

cases of ischaemic stroke 16 had history of one or more attacks of TIA. So, 52.5% of patients had TIAs. TIA is an established risk factor of ischaemic stroke. In a prospective study of 390 patients with TIAs caused by atherosclerotic vascular disease, the 5 year cumulative rate of fatal or nonfatal cerebral infarction was 23%.<sup>16,17,18</sup> In this study, carotid bruit was found in 17.5% (n=7) of patients. There was no clinically evident carotid bruit in rest 33 patients. DSA procedure resulted in TIA in 1 patient (2.5%) and arterial puncture site haematoma in 1 patient (2.5%) during the study. Both patients recovered completely with conservative treatment. Previous studies have reported a neurological complication rate of 0.5% to 4%, arterial puncture site haematoma rate 5%, contrast induced renal dysfunction in 1 to 5% of undergoing carotid angiogram.<sup>19,20</sup>

40 patients of ischaemic stroke and TIAs were included with having significant carotid stenosis  $\geq 50\%$  on Duplex ultrasound (USD). Digital subtraction angiogram (DSA) was done on right and left carotid arteries, thus studying 80 vessels in total. Degree of stenosis was measured in each internal carotid arteries using NASCET criteria. Findings of USD and DSA were directly compared. There were 3 standard angiographic cut-off points eg;  $\geq 50\%$ ,  $\geq 70\%$ , and  $\geq 90\%$ . Sensitivity, Specificity, Accuracy PPV and NPV of USD was calculated at these 3 cut-off points.

In this study sensitivity is the proportion of patients with carotid stenosis on DSA that could be diagnosed by USD. In RICA for  $\geq 50\%$ ,  $\geq 70\%$  and  $\geq 90\%$  stenosis sensitivity were 63.33%, 91.18%, 100% respectively. In LICA for  $\geq 50\%$ ,  $\geq 70\%$  and  $\geq 90\%$  stenosis sensitivity were 69.44%, 86.83%, 91.89% respectively. In RICA for  $\geq 50\%$ ,  $\geq 70\%$  and  $\geq 90\%$  stenosis specificity were 50%, 50% and 20% respectively. In LICA for  $\geq 50\%$ ,  $\geq 70\%$  and  $\geq 90\%$  stenosis specificity were 50%, 50%, 33.33% respectively. The combined power of the diagnostic efficiency of the test is the accuracy. In RICA for  $\geq 50\%$ ,  $\geq 70\%$  and  $\geq 90\%$  stenosis accuracy were 60%, 85% & 90% respectively. In LICA for  $\geq 50\%$ ,  $\geq 70\%$  and  $\geq 90\%$  stenosis accuracy were 67.5%, 85% & 87.50% respectively. In RICA for  $\geq 50\%$ ,  $\geq 70\%$  and  $\geq 90\%$  stenosis PPV were 79.17%, 91% & 94% respectively. In LICA for  $\geq 50\%$ ,  $\geq 70\%$  and  $\geq 90\%$  stenosis PPV were 92.59%, 97.06%, and 90% respectively. In RICA for  $\geq 50\%$ ,  $\geq 70\%$  and  $\geq 90\%$  stenosis NPV were 31.25%, 50%, and 100% respectively. In LICA for  $\geq 50\%$ ,  $\geq 70\%$  and  $\geq 90\%$  stenosis NPV were 15.38%, 16.66%, 10% respectively. Dinkel in their 1.5 year study on 116 patients yielded the following diagnostic performance of USD: sensitivity for a 50% stenosis 91.4%, specificity 93.2% and accuracy 92.4%; sensitivity for a 70% stenosis 89.2%, specificity 96.2% and accuracy 92.4%.<sup>21</sup> Modaresi in their

retrospective study tried to find out correlation between DSA and USD findings. For stenosis  $>70\%$  USD had sensitivity and specificity of 94% and 84%, in relation to DSA. For  $>90\%$  stenosis it was 96% and 99% respectively.<sup>22</sup> Shiami compared results of carotid angiography and carotid ultrasound of 53 patients. Poor sensitivity in the 50-69% and 70-79% grades was of concern. 80-99% had the best sensitivity.<sup>23</sup> Findings of these studies correlate well with the present study carried out in the Department of Neurology, DMCH.

Hayee et al. compared USD findings with DSA in 158 patients, and found positive predictive value of carotid ultrasound for identifying appropriate symptomatic candidates for intervention (angiographic stenosis  $\geq 50\%$ ) was 70%, with a false positive value of 30%.<sup>24</sup> Qureshi et al. also had similar findings with PPV of USD for symptomatic patients for intervention (angiographic stenosis  $\geq 50\%$ ) was 80%, with a false positive value of 20%. Positive predictive value of carotid ultrasound for identifying appropriate asymptomatic candidates for intervention (angiographic stenosis  $\geq 60\%$ ) was 59%, with a false positive value of 41%.<sup>25</sup> Here it is observed that sensitivity is high at  $\geq 90\%$  stenosis in both RICA (100%) and LICA (91.89%). It is also noted that accuracy is 90% for RICA and 87.5% for LICA. But at 50% and 70% angiographic stenosis sensitivity and accuracy is much lower in both RICA and LICA. 2 vessels with  $>90\%$  stenosis and 4 vessels with  $>70\%$  were missed by USD, that was reported to be positive by DSA. In other situation USD reported nonsignificant stenosis which later proved to have significant stenosis by DSA. So DSA seems to be more effective in demonstrating carotid stenosis than USD. Investigation module used here can be utilized in future for selecting patients with significant extra-cranial carotid stenosis for carotid intervention by doing USD and DSA. With modern day technology, DSA is associated with less mortality and morbidity. So before taking decision for carotid intervention, on the basis of USD findings, DSA should be done for confirmation of diagnosis.

### Conclusion

Duplex Ultrasound of carotid vessels is less sensitive, specific and accurate than Digital Subtraction Angiogram for evaluation of carotid stenosis. Main concern about DSA is it's invasiveness and cost. With modern day's technique and in expert hand complications have become minimum. Although DSA is costlier than USD, with government support the expenditure can be minimized. So USD is not an alternative to DSA rather supportive in cases where intervention is required for management of significant extra-cranial carotid stenosis (symptomatic carotid stenosis  $\geq 50\%$  and asymptomatic stenosis  $\geq 60\%$ ).

**Conflict of Interest:** None

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