



Association of Extracranial Carotid Artery Stenosis in Ischemic Stroke in a Sri Lankan Cohort of Patients - An Analytical Cross-Sectional Study

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Abstract

Background and Objectives: The burden of stroke in Sri Lanka is on the increase with the current demographic transition toward an ageing population. However, the association of symptomatic extracranial carotid artery stenosis (CAS) in ischemic stroke has not been prospectively evaluated in a Sri Lankan cohort of ischemic stroke patients. Globally population-based studies have estimated about 15% of ischemic strokes are caused by large vessel occlusions. It is commonly believed that the prevalence of significant extracranial CAS is low in Sri Lanka compared to western populations. The purpose our study is to systematically analyses and assess this long held notion and to search for other associated causative factors. **Methods:** The study population comprised of 164 acute ischemic stroke patients admitted consecutively to the National hospital of Sri Lanka over a period of 3 months. Carotid artery duplex scans were done by a single well-trained operator within 2 weeks of presentation and degree of CAS was classified as low (<50%), moderate (50-69%), severe (>70%) and complete occlusion according to NASCET criteria. Factors associated with CAS were identified by stepwise multiple logistic regression analysis. **Results:** Out of 164 ischemic stroke patients 104 (63.4%) were male and 60 (36.6%) were female. The mean age of stroke patients was 62.2+- 14.21 years. 139 (84.8%) had low grade stenosis, 10 (6.1%) had moderate stenosis, 7 (4.2%) had severe stenosis and 8 (4.9 %) had complete stenosis of carotid artery. Older age and presence of previous TIAs were significantly associated with CAS. Gender, hypertension, diabetes mellitus, hypercholesterolemia, IHD, previous stroke, previous TIA, previous use of antiplatelets, family history of stroke, previous use of statins and presence of carotid bruit were not significantly associated. **Conclusion:** Extracranial carotid artery occlusion previously considered a rare cause of ischemic stroke in Sri Lanka was found to be having prevalence similar to western populations in this study with over 15% having significant stenosis. Hence, we emphasize that early carotid doppler studies must be performed in all ischemic strokes at least within two weeks and necessary interventions carried out where it is deemed necessary.

Keywords: Extracranial Carotid artery stenosis, Sri Lanka, NASCET criteria, Ischemic stroke, Endarterectomy, Risk factors

Introduction

Stroke is one of the principal causes of disability and death worldwide. About 15 million suffer from stroke each year according to World Health Organization and 5 million out of them dies and another 5 million are permanently disabled [1]. The prevalence of stroke is 10.4 per 1000 population in urban Sri Lanka, but only limited data is available on true prevalence in whole population including rural population [2]. All thrombotic strokes can be due to small or large vessel disease. Large vessel thrombosis includes both intracranial and extracranial stenosis which causes approximately 15% ischemic stroke according large

population-based studies [4,5,6]. It is one of the commonest causes of early recurrent strokes [3]. Atherothrombosis is thought to be commonest cause for carotid artery occlusive disease.

The prevalence of extracranial CAS in Sri Lanka is not systematically evaluated to date in a prospective fashion. Timely diagnosis and correct intervention will help to prevent further episodes of ischemic events which can lead to permanent disability or even death. An early diagnosis of CAS is of paramount importance following TIA and ischemic stroke. The delay is usually due to unavailability of imaging facilities such as carotid duplex and CT angiogram (CTA) in some suburban and rural centers, huge patient loads leading to overcrowding and dearth of

dedicated trained neuro-radiologists. Even with an early diagnosis managing CAS with carotid endarterectomy (CAE) or carotid artery stenting is a challenging task in a resource poor setting. Currently in Sri Lanka evidence for a strong association between extracranial CAS and stroke is lacking. The findings in this study would be beneficial in taking management decisions such as CEA in the future.

Methods

The study population comprised of patients with acute ischemic stroke fulfilling inclusion criteria for the study and admitted to National hospital of Sri Lanka over a period of 3 months. They were randomly assigned to the study and patients with hemorrhagic strokes, head injury, underlying congenital or acquired thrombophilia causing ischemic strokes were excluded. Carotid artery duplex scan of all eligible patients was performed by a single well trained senior registrar in neuroradiology within 2 weeks of the diagnosis of ischemic stroke. The scan findings were documented for individual patients. Degree of CAS was classified as low (<50%), moderate (50-69%), severe (>70%) and complete occlusion according to NASCET criteria. Important data for evaluation was collected by a trained medical officer in neurology at the same time via an interviewer administered questionnaire combined with a section on patient details obtained through medical records of the patient. The questionnaire consisted of

demographic data, modifiable and non-modifiable risk factors such as diabetes mellitus, hypertension, hypercholesterolemia, ischemic heart disease, smoking, and alcohol, a positive family history, previous history of TIA and stroke, drug history including previous statin and antiplatelet use and details related to current admission and disability assessment. Data was entered with appropriate data checks and cleaning. They were analyzed using the SPSS. Findings were described as frequency percentages and factors associated with CAS were identified by stepwise multiple logistic regression analysis.

Results

A cohort of 164 patients with first or recurrent ischemic strokes were evaluated. Demographic characteristics, modifiable and non-modifiable risk factors of the study population are presented in Table 1. Mean age of the population was 62.2+ 14.2 years. 14.6% were less than 45 years of age, 15.9% was above 76 years of age and majority of the study population belonged to 66-75 age category. Majority of the patients studied 63.4% (104/164) were males. Tobacco and alcohol usage amongst them was 39.6% and 43.9% respectively. Hypertension being the commonest non modifiable risk factor was present in 50.6% of those evaluated. Hypercholesterolemia, diabetes mellitus and ischemic heart disease was seen in 45.1%, 39.6% and 22% respectively.

Table 1: Frequency of demographic, risk factors and previous drug (antiplatelet and statin) exposure

		Number of patients	Percentage (%)
Demographics			
Age	<45	24	14.6
	46-55	24	14.6
	55-65	37	22.6
	66-75	53	32.3
	>76	26	15.9
Gender	Male	104	63.4
	Female	60	36.6
BMI (Body Mass Index)	<18	13	7.9
	19-23	65	39.6
	24-30	65	39.6
	>31	21	12.8
Risk Factors			
Tobacco used	No	99	60.4
	Yes	65	39.6
Alcohol used	No	92	56.1
	Yes	72	43.9
Hypertension	No	81	49.4
	Yes	83	50.6
Hypercholesterolemia	No	90	54.9
	Yes	74	45.1
Diabetes mellitus	No	99	60.4
	Yes	65	39.6
Atrial fibrillation	No	150	91.5
	Yes	14	8.5
Ischemic heart disease	No	128	78
	Yes	36	22
Previous TIA (Transient Ischemic attack)	No	137	83.5
	Yes	27	16.5
Previous Stroke	No	128	78
	Yes	36	22
Family history of stroke	No	133	81.1
	Yes	31	18.9

Previous antiplatelet used	No	128	78
	Yes	36	22
Previous statin used	No	99	60.4
	Yes	65	39.6

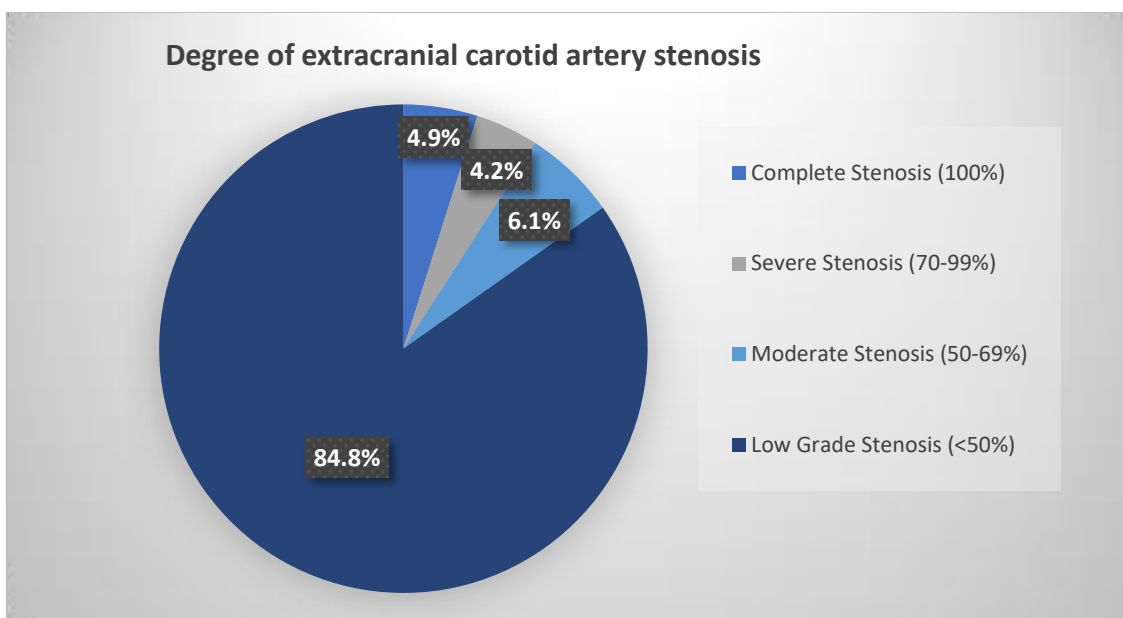
25 (15.2%) of ischemic strokes were attributed to extracranial CAS stenosis, out of which 8 (4.9%) patients had complete stenosis where no intervention was indicated. 7(4.2%) and 10(6.1%) had 70-99% and 50-69% ipsilateral extracranial CAS respectively. Carotid endarterectomy is indicated for these patients if the stroke is non - disabling, in selected cases within 2 weeks. All patients should undergo imaging either with CTA or MRA prior to surgery. All patients (17) who were eligible for carotid endarterectomy underwent either CTA or MRA. Amongst 17 patients who were

evaluated for endarterectomy, 5(29.4%) patients had tandem lesions and these patients were not eligible for endarterectomy as they demonstrated both intracranial and extracranial CAS. Among 25 patients with ipsilateral CAS 12% (3) had lacunar strokes and all other had MCA/ACA stroke. Among 25 patients with large vessel mechanisms, none had a potential cardiac source of embolus or atrial fibrillation.

Degree of extracranial stenosis are presented in table 2 and graph 1.

Table 2: Degree of extracranial carotid artery stenosis

Degree of Stenosis	Number of Cases	Percentage (%)
Complete Stenosis (100%)	8	4.9
Severe Stenosis (70-99%)	7	4.2
Moderate Stenosis (50-69%)	10	6.1
Low Grade Stenosis (<50%)	139	84.8



Graph 1: Degree of extracranial carotid artery stenosis

Association of demographic characteristics, risk factors and previous drug exposure are elaborated in table 3. There is significant association of older age (p value = 0.272) and previous TIA (p value = 0.140) with extracranial CAS where as other factors are not significantly associated.

Table 3: Association of extracranial carotid artery stenosis (CAS) with demographics, risk factors and previous drug history

	Degree of extracranial CAS				P value
	Complete stenosis (100%) – 08	Severe stenosis (70-99%) – 07	Moderate stenosis (50-69%) – 10	Low grade stenosis (<50%) - 139	
Gender					<0.05
Male	6 (75%)	4 (57.1%)	3 (30%)	91 (65.5%)	
Female	2 (25%)	3 (42.9%)	7 (70%)	48 (34.5%)	
Age (years)					0.272
Less than 45	1 (12.5%)	1 (14.3%)	1 (10%)	21 (15.1%)	
46- 55	1 (12.5%)	3 (42.8%)	2 (20%)	18 (12.9%)	
56- 65	1 (12.5%)	2 (28.6%)	3 (30%)	31 (22.3%)	
66- 75	1 (12.5%)	1 (14.3%)	4 (40%)	47 (33.8%)	
More than 76	4 (50%)	0 (0)	0 (0)	22 (15.9%)	
Body Mass Index					<0.05
Less than 18	0 (0)	0 (0)	1 (10%)	12 (8.6%)	
19- 23	5 (62.5%)	5 (71.4%)	4 (40%)	51 (36.7%)	

24- 30	3 (37.5%)	2 (28.6%)	5 (50%)	55 (39.6%)	
More than 31	0 (0)	0 (0)	0 (0)	21 (15.1%)	
Tobacco use					
No	6 (75%)	5 (71.4%)	3 (30%)	85 (61.2%)	<0.05
Yes	2 (25%)	2 (28.6%)	7 (70%)	54 (38.8%)	
Alcohol use					
No	6 (75%)	5 (71.4%)	4 (40%)	84 (60.4%)	<0.05
Yes	2 (25%)	2 (28.6%)	6 (60%)	55 (39.6%)	
Diabetes mellitus					
No	6 (75%)	4 (57.1%)	9 (90%)	80 (57.6%)	<0.05
Yes	2 (25%)	3 (42.9%)	1 (10%)	59 (42.4%)	
Hypertension					
No	3 (37.5%)	2 (28.6%)	8 (80%)	68 (48.9%)	<0.05
Yes	5 (62.5%)	5 (71.4%)	2 (20%)	71 (51.1%)	
Hypercholesterolemia					
No	3 (37.5%)	4 (57.1%)	8 (80%)	75 (53.9%)	<0.05
Yes	5 (62.5%)	3 (42.9%)	2 (20%)	64 (46.1%)	
Ischemic heart disease					
No	6 (75%)	5 (71.4%)	8 (80%)	109(78.4%)	<0.05
Yes	2 (25%)	2 (28.6%)	2 (20%)	30 (21.6%)	
Atrial fibrillation					
No	8 (100%)	7 (100%)	10 (100%)	125(89.9%)	<0.05
Yes	0 (0)	0 (0)	0 (0)	14 (10.1%)	
Previous TIA					
No	7 (87.5%)	6 (85.7%)	5 (50%)	119(85.6%)	0.140
Yes	1 (12.5%)	1 (14.3%)	5 (50%)	20 (14.4%)	
Previous Stroke					
No	2 (25%)	3 (42.9%)	5 (50%)	118(84.9%)	<0.05
Yes	6 (75%)	4 (57.1%)	5 (50%)	21 (15.1%)	
Family history of stroke					
No	6 (75%)	7 (100%)	8 (80%)	112(80.6%)	<0.05
Yes	2 (25%)	0 (0)	2 (80%)	27 (19.4%)	
Antiplatelet use					
No	6 (75%)	5 (71.4%)	6 (60%)	111(79.9%)	<0.05
Yes	2 (25%)	2 (28.6%)	4 (40%)	28 (20.1%)	
Statin use					
No	6 (75%)	5 (71.4%)	5 (50%)	83 (59.8%)	<0.05
Yes	2 (25%)	2 (28.6%)	5 (50%)	56 (40.2%)	
Presence of carotid bruit					
No	4 (50%)	5 (71.4%)	6 (60%)	135(97.1%)	<0.05
Yes	4 (50%)	2 (28.6%)	4 (40%)	4 (2.9%)	

Discussion

Large vessel atherosclerotic disease is an important etiologic factor for ischemic stroke and TIA. Its timely detection and treatment prevent strokes. Prevalence of extracranial CAS is considered low in Asian population compared to the west. This long held belief may lead to a delay in diagnosis. However extracranial CAS remains an important and treatable cause for ischemic stroke and TIA. Also, timely interventions will reduce recurrent strokes and related morbidity whilst helping to minimize the stroke burden in ant society. According to the AHA/ASA guidelines (2011) on the management of CAS duplex ultrasonography is recommended for asymptomatic as well as symptomatic patients.

Furthermore, MR angiography (MRA) or CT angiography (CTA) should be performed in cases where the duplex scan is inconclusive and where surgical intervention is planned. If the surgical risk is low in patients with over 50% stenosis causing non-disabling ischemic stroke or TIA, carotid revascularization should

be performed soon, preferably within 2 weeks. For patients who have low risk of post intervention complications carotid arterial stenting is recommended as an alternative to CEA. Patient's comorbidities and life expectancy should be taken into consideration if they are asymptomatic. Carotid revascularization is not recommended if the luminal narrowing is less than 50% or 100% (complete) and in those with severe disability.

Screening for extracranial CAS is cost effective as devastating recurrent strokes can be prevented. However, CAS screening is inadequate in Sri Lanka like in other Asian countries, especially since it was long assumed to be of a low prevalence compared to the west. It is interesting to note that in this study the prevalence of CAS in acute ischemic stroke in Sri Lanka is 15.2%, similar to western populations. Advanced age and previous TIAs are significantly associated with CAS. Therefore, it is imperative that all patients with acute ischemic stroke are screened.

The main limitation noted in our study is using only duplex ultrasonography to detect extracranial CAS. Other imaging

modalities were not included in the protocol. However, compared to 4 vessel digital subtraction angiography (DSA), duplex ultrasonography has an overall sensitivity of 91%- 95% and a specificity of 86% - 97% [7]. Few patients underwent imaging such as CTA and MRA. Our operator bias was minimal as all duplex scans were done by single trained operator and data was collected by a single trained neurology medical officer. This study was carried out in a prospective manner in the largest neurology care center in Sri Lanka on consecutive patients hence can be considered representative.

Conclusion

The prevalence of extracranial CAS is not rare in Sri Lanka, and is comparable to western figures. Early CAS screening within two weeks should be an integral part of stroke work up.

Ethics approval and consent to Participate

The ethical approval obtained from the Ethical Review Committee (ERC), National Hospital of Sri Lanka and a copy of approval letter is available for review. The informed written consent obtained from all eligible participants and copies of written consents are available for review.

Declaration of interest

None; the authors have no competing interests.

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Availability of data and materials

All data and study materials are available for review.

Author contribution

All authors were equally contributed, read and approved the final manuscript.

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