Comparison of risk factors, severity and outcome between lacunar and non-lacunar stroke in a tertiary care center in Sri Lanka: A descriptive study

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(Index words: lacunar, non-lacunar, stroke, risk factors, Ischaemic stroke, stroke subtypes)

Abstract

This study compares demography, risk factors and outcome of lacunar (LAC) and non-lacunar (non-LAC) strokes from the prospective hospital based stroke registry at Colombo South Teaching Hospital from 1st March 2012 to 30th June 2013. Data on admission, discharge and at 28 days after discharge were analysed. There were 229 ischaemic stroke (IS) patients. Average age was 65.7 years (SD 12.2, range 34-94) and 116 (50.7%) were males. LAC (n=130, 56.8%) were common than non-LAC (n=99, 43.2%). There were 75 (64.7%) males and 55 (48.7%) females in the LAC group (adjusted OR 2.1, 95% CI 1.08-4.29). Atrial fibrillation was less frequent among LAC stroke (OR 0.3, 95% CI 0.09-0.99). Hypertension, diabetes, smoking, dyslipidaemia did not differ in the two groups. Lower NIHSS (5.34 Vs 6.6, p= 0.053), higher GCS (14.7 Vs 13.3, p=0.001) were seen in LAC. Disability (MRS, Barthel index) on discharge, at 28 days and mortality during hospital stay and within 28 days was lower in the LAC group (p <0.001).

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Introduction

Prevalence of stroke is rising worldwide and is particularly common in South East Asia [1]. It is the fourth commonest cause for in-hospital mortality in Sri Lanka [2]. Available studies on prevalence of stroke in Sri Lanka show a community prevalence of 1.6% [3].

Different classification systems have emerged and the division into lacunar (LAC) and non-lacunar (non-LAC) subtypes were proposed with the intent of identifying different pathogenic and risk factor profiles. First such information was provided by Fisher fifty years ago, based on autopsy findings [4]. He proposed that lacunar strokes, asymptomatic small infarcts in striatocapsule are due to small vessel disease in the penetrating arteries and was the result of lipohyalinosis or atherosclerosis. Thus emerged the 'lacunar hypothesis' and these findings have led to studies on the two subtypes of stroke further enumerating that hypertension, diabetes and hyperlipidaemia are common in lacunar stroke with cardio embolism and large artery disease deemed less important [1,5]. But recent studies show that the risk factor profile is not different in stroke subtypes questioning the validity of lacunar hypothesis [6-8]. Further data suggest that genetic predisposition might influence the type of stroke in patients with similar vascular risk factors [9].

LAC are commoner in Asians and Japan reports a 50-60% incidence among ischaemic strokes compared to 16-38% in European and North American populations [1,13]. Reasons for this difference is not clear and the pattern in Sri Lanka is not known. There is only one study on stroke subtypes from Sri Lanka [10]. This study showed a LAC occurrence of 41% among ischaemic stroke. Studies show that the early death rate as well as the risk of recurrence and disability are higher in non-lacunar strokes than lacunar strokes [5,8,11].

Aim of our study was to compare the risk factors, demographic factors and the outcome in lacunar and non-lacunar stroke patients admitted to Colombo South Teaching Hospital.

Methods

We recruited all ischaemic stroke patients from the stroke registry at Colombo South Teaching Hospital from the 01st March 2012 to 30th June 2013. This registry established in 2012 includes all stroke admissions to medical wards in the hospital. All patients had neuro imaging (CT brain). Stroke subtype was determined according to the TOAST classification [12]. These patients were further subdivided to lacunar and non-lacunar stroke by the treating physician depending on the imaging findings and clinical presentation. LAC was assigned if the following criteria were met: a) estimated

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Table 2. Vascular risk factors in and non-LAC stroke (univariate and multivariate logistic regression)

Risk factor	*LAC*	*Non-LAC*	*Univariate analysis*		*Multivariate analysis*	
	n (%)	*n (%)*	*OR (95% CI)*	*p value*	*OR (95% CI)*	*p value*
Average age	66.1+/-11.96	65.1+/-12.65	1.005 (0.98-1.03)	0.644		
Male sex	75 (57.7)	41 (41.4)	1.93 (1.14-3.28)	0.015	1.90 (1.09-3.31)[a]	0.023
DM	60 (46.2)	37 (37.4)	1.44 (0.84-2.45)	0.183		
HT	80 (61.5)	55 (55.5)	1.28 (0.75-2.18)	0.362		
Dyslipidaemia	60 (46.2)	32 (32.3)	1.79 (1.04-3.09)	0.034	1.58 (0.87-2.90)[b]	0.125
Smoking	43 (33.1)	25 (25.3)	1.46 (0.82-2.62)	0.199		
IHD	27 (20.8)	21 (21.2)	0.97 (0.51-1.85)	0.935		
Past history of TIA/ stroke	40 (30.7)	34 (34.3)	0.85 (0.48-1.48)	0.567		
Atrial fibrillation	04 (3.08)	11 (10.1)	0.26 (0.08-0.85)	0.026	0.30 (0.09-0.99)[c]	0.049

[a] Adjusted for DM, HT, Dyslipidaemia and presence of atrial fibrillation

[b] Adjusted for DM, HT, male sex and presence of atrial fibrillation

[c] Adjusted for male sex, dyslipidaemia

fibrillation was significantly less among patients with LAC than non-LAC infarcts.

Stroke severity was assessed using NIHSS and GCS. Table 3 compares the stroke severity, disability and mortality during hospital stay and within 28 days of discharge.

Disability assessed by MRS and Barthel index has improved following discharge in both stroke subtypes. However, disability was significantly less in the LAC group. Stroke recurrence and re-hospitalisation could not be correlated due to the low number of events and short follow up. Deaths during hospital stay and at 28 days were less in LAC infarcts compared to non-LAC.

Table 3. Stroke severity, death and disability of LAC versus non-LAC stroke determined by chi-square and t-tests

Outcome variable	*LAC n=130*	*Non-LAC n=99*	*p value*
*Stroke severity**			
NIHSS	5.34 (3.93)	6.6 (5.29)	0.053
GCS	14.66 (1.2)	13.34 (3.0)	<0.001
*Disability on discharge**			
MRS	3.27 (1.4)	4.26 (1.4)	<0.001
Barthel Index	11.98 (5.3)	8.05 (6.6)	<0.001
*Disability at 28 days**			
MRS	2.38 (1.7)	3.62 (1.9)	<0.001
Barthel index	16.06 (4.8)	13.8 (5.8)	0.007
Mortality			
Death during hospital stay	01 (0.77)	17 (17.1)	<0.001
Death within 28 days	07 (5.5)	22(25.0)	<0.001

** These variables are given as mean (SD) and analyzed by t-test. Other variable was analyzed using chi-square test*

Discussion

This is a study comparing risk factors and outcome of ischaemic stroke subtypes in Sri Lanka. LAC stroke comprised 56.8% of ischaemic stroke included in our hospital based stroke registry. This finding is comparable to data from other Asian countries such as Japan and China [1, 13]. Studies on stroke in European and North American countries show a higher non-LAC burden [1, 14]. Small vessel disease appears to be commoner in the Asian region than in the West.

Interestingly, males were twice more likely to develop LAC than non-LAC stroke while females had higher number of non-LAC but the difference was not significant. Previous studies do not report a gender difference in developing different stroke subtypes. However, one study reported that males had more non-LAC than LAC in their population based survey conducted in China [1]. Our study showed that males had more LAC stroke despite having a lower incidence of diabetes and hypertension than females. As a result, males had a lower disability (MRS, Barthel Index) and less severe stroke in our study. This finding suggests that vascular disease in Sri Lankan females was different. Vascular risk factors and atrial fibrillation were commoner in females than males in our study.

Risk factors were not different in the LAC and non-LAC groups. Contrary to studies demonstrating an increased incidence of hypertension, diabetes, dyslipidaemia, smoking in Caucasians and Asians with LAC, our study did not reveal a significant excess of these risk factors [1,5-7]. But a later systematic meta-analysis, reported that except for a marginal excess of hypertension in LAC, none of the other risk factors were predictive of either stroke subtype [11]. Most of the earlier studies have

infarct size ≤2cm, b) anatomic site typical of LAC (basal ganglia, brainstem, thalamus, internal capsule or cerebral white matter) and c) compatible clinical presentation [1].

All patients were interviewed and examined to assess the severity of stroke using National Institute of Health Stroke Scale (NIHSS). Glasgow coma scale (GCS) was adopted if NIHSS could not be used due to reduced level of consciousness. Demographic factors, smoking history, history or a new diagnosis of DM, HT, ischaemic heart disease, atrial fibrillation and dyslipidaemia were documented. Modified Rankin scale (MRS) and the Barthel index were assessed on discharge as a measure of residual disability. Death during hospital stay was noted. These patients were re-assessed at 28 days to document MRS, Barthel index, occurrence of re-infarction and hospitalisation during follow up. There were 22 dropouts at one month at a rate of 9.6%.

Data were entered and analysed using SPSS version 19.0. Descriptive data were described using frequencies, means and standard deviations. Logistic regression was used to find the association between vascular risk factors and stroke subtype. Multivariate analysis was used to eliminate the effect of confounding variables. Association between mean NIHSS, MRS, Barthel index and stroke subtype was assessed using t-test. Chi-square test was adopted to find the association between death, stroke recurrence and stroke subtype.

Informed consent was obtained from all participants. Ethical approval was obtained from the Ethics Review Committee of Faculty of Medical Sciences, University of Sri Jayewardenepura.

Results

Two hundred and twenty nine IS patients were studied. Average age was 65.7 years (SD 12.2, range 34-94). There were 116 (50.7%) males and 113 (49.3%) females (Table 1). Commonest stroke subtype was stroke due to small artery occlusion (n=127, 55.5%). Others were stroke due to large artery atherosclerosis (n=79, 34.5%), cardio embolism (n=15, 6.6%) and undetermined aetiology (n=8, 3.5%). LAC stroke (n=130, 56.8%) was more than non-LAC stroke (n=99, 43.2%).

The association of risk factors with LAC and non-LAC is shown in table 2. LAC stroke was significantly more in males. Dyslipidaemia was commoner in LAC than non-LAC stroke on univariate analysis but became non-significant when adjusted for confounding factors (Table 2). Presence of HT, DM, smoking or past TIA/ stroke did not differ in LAC and non-LAC groups. Atrial

Table 1. Patient characteristics, presence of vascular risk factors and stroke type in males and females

Patient characteristic	*Males Total=116 n (%)*	*Females Total=113 n (%)*	*Total Total=229 n (%)*	*p values*
Age mean (SD)	63.69 (12.07)	67.68 (12.15)	65.7 (12.2)	p=0.016
Time to hospital admission				
≤4.5 hrs	34 (29.3)	33 (29.2)	67 (29.2)	p=0.98
>4.5 hrs	82 (70.7)	80 (70.8)	162 (70.7)	
Systolic BP mean (SD)	149.9 (24.3)	152.4 (26.7)	151.2 (25.5)	p=0.451
Diastolic BP mean (SD)	86.36 (14.7)	84.45 (15.8)	85.4 (15.3)	p=0.346
Risk factors				
Diabetes	44 (37.9)	53 (46.9)	97 (42.4)	p=0.17
Hypertension	59 (50.9)	76 (67.3)	135 (58.9)	p=0.012
Dyslipidaemia	49 (42.2)	43 (38.1)	92 (40.2)	p=0.518
Atrial fibrillation	05 (4.3)	10 (8.8)	15 (6.5)	p=0.171
Past history of stroke or TIA	44 (37.9)	30 (26.5)	74 (32.3)	p=0.066
Smoking	66 (56.9)	02 (1.8)	68 (29.7)	p<0.001
Type of stroke				
Lacunar stroke	73 (62.9)	61 (54.9)	134 (58.5)	p=0.169
Non-lacunar stroke	43 (37.1)	52 (46.0)	95 (41.5)	
*Severity of stroke**				
NIHSS, mean (SD)	6.01 (4.87)	5.61(4.12)	5.82 (4.52)	p=0.53
GCS, mean (SD)	14.43 (1.8)	13.7 (2.6)	14.09 (2.3)	p=0.019
*Disability on discharge**				
Barthel Index	11.28 (6.2)	9.39 (6.1)	10.34 (6.2)	p=0.023
MRS Index	3.51 (1.5)	3.89 (1.43)	3.7 (1.5)	p=0.052

* These variables are given as mean (SD)

included aetiological risk factors in the definition of LAC or non-LAC leading to a selection bias [11]. The presence of chronic atrial fibrillation predisposes to non-LAC as seen in all previous studies as well as ours. The reasons for LAC being commoner among Asians are unknown. Several studies have evaluated the possibility of endothelial dysfunction, abnormal coagulation in LAC strokes but findings were not consistent (15). Identification of arterial pathology in LAC is important and could provide targets for preventive therapy in the future.

Our study evaluated the severity and the residual disability of each stroke subtype. We found that LAC group had less severe stroke and a significantly lesser disability than non-LAC on discharge. This difference persisted at 28 days and LAC group had a better overall outcome. Deaths were significantly less in the LAC group during the hospital stay and at 28 days after discharge. These findings are not surprising. Most previous studies reported similar results and this difference could be related to the size of the infarct. However, analysis of the long term outcome in these studies showed that mortality and stroke recurrence appear to be similar after the first 1-2 years. Follow up of our study cohort would help identify whether this is the same for Sri Lankans.

This was a hospital based study conducted in a tertiary care hospital in Colombo. But patients are admitted directly from the community in addition to referrals and transfers from smaller hospitals. Our sample included patients from different social backgrounds and ethnicities and an adequate sample to allow inferences. Therefore our findings can be generalized to other parts of Sri Lanka.

LAC stroke appears to be commoner than non-LAC in Sri Lanka. Males were more likely to develop LAC. Diabetes, hypertension, smoking, dyslipidaemia or advanced age did not differ among subtypes of stroke but atrial fibrillation predisposed to non-LAC. Stroke severity and disability were more and early survival was better in the LAC than non-LAC group.

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Conflicts of interests

There are no conflicts of interest.

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