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Thirty-day Readmission is Higher in Patients with Brainstem vs. non-Brainstem Lacunar Stroke

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ABSTRACT:

Background: *A quarter of all ischemic strokes are classified as lacunar. We explored whether certain lacunar stroke locations are associated with a certain set of risk factors or clinical characteristics.*
Methods: *This is a retrospective study of stroke patients admitted to a tertiary hospital over five years. Lacunar strokes were confirmed on CT or MRI. Locations included: internal capsule, thalamus, basal ganglia and brainstem. Clinical characteristics and outcomes were compared between different locations.*
Results: *Out of 548 stroke patients, 50 (38% female) had lacunar strokes. The median age was 60.5 years and hypertension was the most common risk factor (86%), followed by DM (78%). The commonest location for lacunar stroke was basal ganglia (48%), and the least common was the brainstem (16%). There was no correlation between the patients' characteristic with lacunar location. There was a significant correlation between readmission and brainstem lacunars ($p<0.001$, Spearman correlation coefficient 0.464) but not in other locations. Readmissions in brainstem lacunar infarctions were mostly due to recurrent stroke.*
Conclusion: *Brainstem lacunar strokes have higher risk of 30day re-admission, mainly due to recurrent stroke. Those patients require further investigations with vascular imaging to roll out basilar artery stenosis to mitigate their risk of recurrent stroke.*

Keywords *:* ischemia, brain, epidemiology, vascular, infarction

INTRODUCTION

One quarter of all ischemic strokes are classified as lacunar strokes. These are defined as small deep ischemic lesions ranging from 2–20 mm in diameter located in the deep cerebral white matter, internal capsule, thalamus, basal ganglia and brain stem based on imaging. [1,2] The pathology of lacunar strokes was described by Fisher's clinicopathological observations which stated that lacunar infarcts result from either occlusion of small perforating cerebral arteries as known as atherosclerosis, or by a destructive process he termed 'segmental arterial disorganization' or 'lipohyalinosis'. [3]

Diabetes mellitus, and hypertension, are frequent risk factors for lacunar infarcts. [2,3] According to a

prospective series study conducted in the University Hospital of Maastricht, Netherlands, 27.2% of patients with lacunar infarcts had diabetes mellitus. [4] These risk factors are prevalent in the Saudi population and thus the proportion of patients with lacunar infarctions are expected to be relatively higher than the other stroke subtypes. This study aims to describe the frequency of lacunar strokes and their clinical and radiological findings in relation to common risk factors among all strokes patients admitted to a tertiary center.

SUBJECTS AND METHODS

This was a retrospective cohort of all stroke patients admitted to King Abdulaziz University Hospital with ischemic or hemorrhagic stroke from January 2010 to December 2014. Patients with primary diagnosis of stroke were identified using International Classification of Diseases codes (ICD-9 or ICD-10).

Adults of 18 years or more with the diagnosis of ischemic stroke were included. Images of those patients were reviewed to document the diagnosis of lacunar stroke on CT or MRI scans. These were defined as small deep ischemic lesions ranging from 2–20 mm in diameter located in the deep cerebral white matter, internal capsule, thalamus, basal ganglia and brain stem. Subsequently, the medical records were reviewed to gather clinical data, all in-hospital complications and discharge time, medications and destinations. The frequency and indication of readmission within 30 days were also collected.

Demographics and vascular risk factors were described as proportions. Measured variables are reported in means (and standard deviation “SD”) or medians (and interquartile range “IQR”), as appropriate. The correlation between lacunar stroke locations and various clinical and outcome variables were investigated using Spearman's rank correlation coefficient. All testing was two-tailed and was measured at the 0.05 level of significance. Analyses were done using SPSS software package.

RESULTS

Out of 548 stroke patients, 50 patients (19/50 female) had lacunar stroke. Hypertension and diabetes mellitus were the commonest risk factors, described in 86% and 78% of patients, respectively. 28% had hyperlipidemia as a risk factor. Atrial fibrillation was present in 14% of patients and coronary artery disease was present in 8%. The length of hospital stay of lacunar infarction patients had a mean of 10.3 days. During the admission, the HbA1C percentage, in 15/50 patients fell into the category of non-diabetics (HbA1C level less than 6.5% or not measured). Nine patients had HbA1C level 5.7-6.4%while 26 patients (78%) were diabetics (HbA1C level equal to and above 6.5%). 20 diabetics measured HbA1C greater than 7.5% that reflected poor control of the blood sugar. The median HbA1C was 6.6%.

Lipid profile was LDL was measured for 33 patients with a median of 1.98 mmol/l (normal below 3.57). HDL was measured for 29 patients with a median of 0.75 mmol/l (normal above 0.9) and 40 patients measured cholesterol with a median of 3.86 mmol/l (normal below 5.20).

In regards to hypertension, we evaluated the discharge medications of 43 patients that had been diagnosed with hypertension. The Captopril was most commonly prescribed for these patients.The locations of the lacunar strokes are summarized in Table 1. The basal ganglia is by far is the most common area affected.

Table 1: area affected by the lacunar infarction and frequency of attacks

Area affected by lacunar infarction	*Frequency (n=50)*
Basal ganglia	24 (48%)
Internal capsule	12 (24%)
Corona radiata	9 (18%)
Thalamus	10 (20%)
Brain stem	8 (16%)

Ten patients (20%) with lacunar infarction required readmission within 30 days. There was no correlation found between age ($p>0.05$) and the lacunar location. However, a significant correlation was noticed with brainstem lacunar location ($p<0.001$, Spearman correlation coefficient 0.464). Readmissions in brainstem lacunars were due to recurrent stroke, pulmonary embolism, and electrolytes disturbance. There was no correlation found between HbA1C levels ($p>0.05$) and area affected.

Aspirin was prescribed for 68% of our patients and clopidogrel for 44%. Almost half of the patients (26%) received dual antiplatelet therapy of aspirin and clopidogrel. There was no significant correlation between 30days readmission and treatment with dual antiplatelet therapy ($p>0.05$).

DISCUSSION

In this retrospective cohort study of lacunar infarction, we described the clinical, radiological, and outcome characteristics of a cohort of patients with lacunar stroke in a single tertiary center in Western Saudi Arabia. We found that brainstem lacunar stroke patients had higher rates of the 30-day readmission. Most of these were due to recurrent stroke. In addition, we observed a high prevalence of hypertension and diabetes in this cohort.

There is limited data on the incidence and prevalence of lacunar strokes in Saudi Arabia. In the Saudi Stroke Data bank, the prevalence of lacunar stroke was estimated at about a third of the entire ischemic stroke cohort.[5] The same proportion was described in a prior study from our center.[6]

In another study from Hafouf region, 46% of all ischemic strokes were described to be lacunar.[7] However in these studies, the diagnosis of lacunar stroke was made either clinically or based on CT changes. Thus, the true prevalence may have not been accurately estimated. About 10% of patients from Hafouf study had a normal CT scan and were classified as lacunar stroke on clinical grounds. Evidence suggests that almost one in six patients with a classical clinical lacunar syndrome actually have an embolic stroke when Diffusion MRI is performed.[8]

In our study, 14% of patients underwent MR imaging to confirm the diagnosis while 86% had acute lacunar infarct seen on CT scan. This rigorous criterion we used for patients' inclusion may explain the relatively low

frequency of lacunar stroke among our stroke patients' population compared to other national studies. In consistent with previous studies, hypertension and diabetes mellitus were prominent risk factors in our cohort and previous studies.[9,10] We assessed hypertension control by accounting for blood pressure medications upon discharge. However, evidence suggests that lacunar stroke patients may require more aggressive blood pressure control than previously described. In a follow up paper, the SPS3 investigators [12] in treatment target trial, grouped patients into higher-target (average systolic blood pressure of 138 mm hg) and lower-target (average systolic blood pressure of 127 mm hg) groups in which lower-target groups received greater number of antihypertensive medications. Lowering of the systolic blood pressure reaching <130 mm hg in recent lacunar infarcted patients resulted in a non-significant stroke recurrence reduction rate irrespective of the stroke type. No specific antihypertensive agent was tested in this trail.

The SPS3 trial[11] was a double blind, randomized, multicenter trial involved 3020 patients with recent symptomatic lacunar infarcts identified by MR imaging. Patients were grouped into a group receiving aspirin daily and a group receiving aspirin combined with clopidogrel or placebo. Both were followed-up for 3.4 years. The aim was to observe the outcome of recurrent strokes and intracranial hemorrhage. Results showed patients with recent lacunar infarction did not benefit from adding clopidogrel to aspirin in order to lower the risk of recurrent strokes, while the risk of bleeding and death was significantly higher.

Another study[13] investigated the predictors of recurrent strokes after an index lacunar stroke in consistent with the most grounded and most predictable 4 independent indicators, patients with prior symptomatic lacunar stroke or TIA (HR=2.2) were the highest predictors of recurrence followed by diabetes , black race (HR=2.0),(HR=1.7) respectively and male sex was the least (HR=1.5) .

However, no significant correlation was found with risk factors according to blood pressure management targets neither antiplatelet therapy nor aspirin. But it's critical to note that aggressive control of blood pressure with antiplatelet treatment and high predominance of statin treatment that reasonable added to the moderately low ischemic stroke recurrence rate (2.2% per year). They influence that dual antiplatelet therapy has a relative risk in reduction of recurrence of stroke (19%) vs. aspirin alone (15%). Hence, based on the statistics aspirin use alone has a significant risk in developing ischemic stroke.

We observed a high readmission rate in patients with brainstem lacunar infarction compared to capsuloganglionic lacunes. Those subset of patients have not been well characterized in the literature. In a study by Huang et al[14], stated that brainstem lacunars have more prominent propensity to progress due to several potential explanations classified those patients at high risk for recurrent stroke suggested that vascular imaging was not done in all of these patients and thus a large artery disease, e.g. basilar stenosis, that would require different treatment modality may have been missed. In addition to the small size of the lesions were detected in brainstem lacunars, which make them difficult to be visualized on CT.

This study has limitations. First, patients with acute lacunar strokes usually have another stroke type at time of presentation. Second, imaging were obtained immediately following admission and during the hospital stay, few records of follow-up imaging were obtained later on. This limits our ability to precisely know the prognostic factors in these patients. Third, around half of the patients did not undergo vigorous laboratory investigations and vascular imaging studies to rule out other large artery disease and to determine whether they suffer from poor-controlled co-morbidities such as diabetes and dyslipidemia. Lastly, we studied the causes of no longer than 30 days readmission

rate. We may find reliable prognostic factors if we looked into longer than 30 days of readmission.

CONCLUSION

We found that brainstem lacunar stroke has a higher risk of 30day re-admission compared to other lacunar stroke subtypes, mainly due to recurrent stroke. Those patients may require further investigations with vascular imaging to roll out an associated large artery disease to mitigate their risk of recurrent stroke.

Conflict of interest statement: The authors declares that there is no conflict of interest regarding the publication of this paper.

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