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ORIGINAL ARTICLES

Angiographic Pattern of Arterial Stenosis Among Different Subtypes of Cerebral Infarct

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Abstract:

Background: *Ischemic stroke can be caused by atherosclerotic occlusion, cardio-embolism, occlusion of small vessels or hypoperfusion. These may lead to different types of infarcts like territorial, sub-cortical, lacunar or water-shed infarct. There are little data regarding the degree of stenosis of cerebral arteries and different subtypes of cerebral infarct.* ***Objective:*** *The objective of this study was to find out the angiographic pattern of arterial stenosis among different subtypes of ischemic stroke patients.* ***Materials and Methods:*** *We evaluated 93 ischemic stroke patients from indoor, outdoor, stroke and neuro intervention clinic, BSMMU. CT scan and/ or MRI of brain were done to each patient to confirm the diagnosis. After vascular imaging, the degree of stenosis was measured by the NASCET formula.* ***Results:*** *Total 93 ischemic stroke patients with significant symptomatic stenosis were studied. Analysis of age distribution showed that mean age was 57.4±1.01 years with range 35-79 years with male female ratio of 1.51:1. Among them 45(48.4%) had extra-cranial stenosis, 42(45.2%) had intra-cranial and 6(6.4%) had both extra-cranial and intra-cranial stenosis. Territorial infarct was seen in 40(43.0%) patients, subcortical infarct in 21(22.6%) patients, lacunar infarct in 26(28.0%) patients and water-shed infarct in 6(6.4%) patients. There was significant association of subtype of infarct with location of stenosis (p-value=0.50). We also observed significant association of subtype of infarct with degree of stenosis (p-value<0.001). Lacunar [n=17(43.6%)] and subcortical [n=13(33.3%)] infarcts were mostly seen in moderate stenosis [n=39]; whereas total arterial occlusion [n=22] presented as territorial [n=16(72.7%)] or water-shed [n=04(18.2%)] infarct.* ***Conclusion:*** *Extracranial vessel involvement was more than intracranial. Territorial infarction was more commonly associated with severe stenosis and lacunar stroke was more commonly associated with moderate stenosis.*

Key Words: *Ischemic Stroke, Angiogram, Infarct pattern, Stenosis.*

Introduction:

According to World Health Organization fact sheet, worldwide more than 5 million deaths occurred due to stroke alone among 56.9 million deaths in 2016 and the number is increasing day by day.[1] Stroke deaths in Bangladesh reached 128,190 or 16.27% of total deaths.[2] The age adjusted death rate is 125.64 per 100,000 of population, which ranks Bangladesh 34 in the world.[2]

Ischemic strokes are caused by one of three main processes like; atherosclerosis with superimposed thrombosis affecting large cerebral or extra-cerebral blood vessels, cerebral embolism, and occlusion of small cerebral vessels within the parenchyma of the

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brain.[3] Embolism from proximal artery may cause acute obstruction of distal cerebral arteries producing territorial infarction or lacunar infarction, whereas hemodynamically significant stenosis or obstruction of intracranial arteries may cause ischemia in the distal regions of hemisphere causing the so-called border zone infarction.[4]

Any narrowing of cerebral blood vessels can be due to atherosclerotic and non-atherosclerotic narrowing. Non-atherosclerotic vasculopathy includes Cervicocephalic arterial dissections, Vasculitis, Moyamoya disease, Fibromuscular dysplasia, Migrainous infarction and radiation induced vasculopathy.[5] These uncommon conditions represent 5% of all ischemic strokes and are relatively common in children and young adult.[6]

There are important differences in the distribution of cerebral atherosclerosis among different ethnic origins.[7] Extracranial stenosis is common in white patients, while intracranial atherosclerotic disease is highly prevalent in black, Hispanic and Asian (China, Japan, South Korea and India) population.[8]

There are little data about the distribution of arterial stenosis in different types of ischemic stroke like; territorial infarct, sub-cortical infarct, lacunar infarct, border-zone infarct. With the knowledge of subtypes of cerebral infarct and the differential frequency of extra-cranial and intra-cranial arterial stenosis; it will be easier to predict the site of arterial stenosis and intervene with the pathological process earlier. So, in this study we intended to observe the angiographic pattern of extra-cranial and intra-cranial stenosis in different sub-types of cerebral infarct.

Methods

Patient selection

This cross-sectional observational study was carried out with an aim to find out the angiographic pattern of arterial stenosis among different subtypes of ischemic stroke patients. Patients were purposively selected from Indoor, Outdoor and Stroke and Neuro-Intervention clinic of the Department of Neurology, BSMMU. Only the patients with first ever ischemic stroke having significant symptomatic stenosis (e"50% stenosis) on angiography, presenting within 14 days of symptom onset were included in this study. Patients with previous stroke, concomitant arterial embolism of limbs or other parts of body, or presumed cardio-embolic sources (rheumatic heart disease, atrial fibrillation, prosthetic heart valves, recent myocardial infarction, cardiomyopathy, left atrial or ventricular thrombus, endocarditis) were excluded.

Total 155 patients with ischemic stroke were preliminarily selected, among them 12 had previous stroke, 17 had cardioembolic factors present and were excluded. 25 patients had normal angiographic findings and were excluded from the study. 8 patients had insufficient data and were excluded. So total 93 patients with ischemic stroke who had significant stenosis on angiography were selected as cases. After ethical clearance from Institutional Review Board (IRB), informed written consent was taken from each patient or his/her attendant. Proper history was taken, physical and neurological examination, keeping in mind of the demographic and clinical variables, were done. All relevant investigations were completed including CT Scan of brain or MRI of brain with DWI sequence. Cerebral angiogram was then performed in the form of MRA or DSA. But significant stenosis (>50%) was confirmed by cerebral DSA. In angiogram, the degree of stenosis was measured according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET).[9]

Percentage of Stenosis = [(Dn -Ds)/Dn]× 100, where Dn is normal diameter and Ds is stenosed diameter.

Then, we classified the patients into 3 groups according to the following grading scale: moderate (50%–69%), severe (70–99%), or total occlusion (no flow detected).[10]

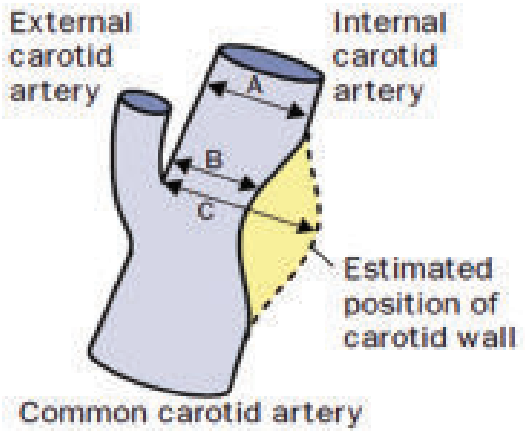

Fig.-1: *NASCET criteria for measuring degree of stenosis.*[9]

Topography of infarct

Topography of infarct was determined by commonly accepted arterial territories and watershed areas.[11] Each infarct was subdivided into one of four subtypes: territorial, subcortical, lacunar or watershed zone infarct. Territorial infarction was considered when a large ischemic lesion involving the cerebral cortex and subcortical structures in 1 or more major cerebral artery territories was encountered.[4] It was subdivided into ACA, MCA or PCA territory infarct according to accepted cortical supply. [11] Subcortical infarction was considered when (a) the infarcts are restricted to the basal ganglia and/or white matter and the overlying cerebral cortex appears normal; and (b) the maximum diameter of the lesion was more than 20mm.[12] Small infarcts, occurring in the white matter, deep grey matter nuclei, and brainstem; and of less than 15mm in diameter was considered as lacunar infarct. [13] Watershed infarctions were

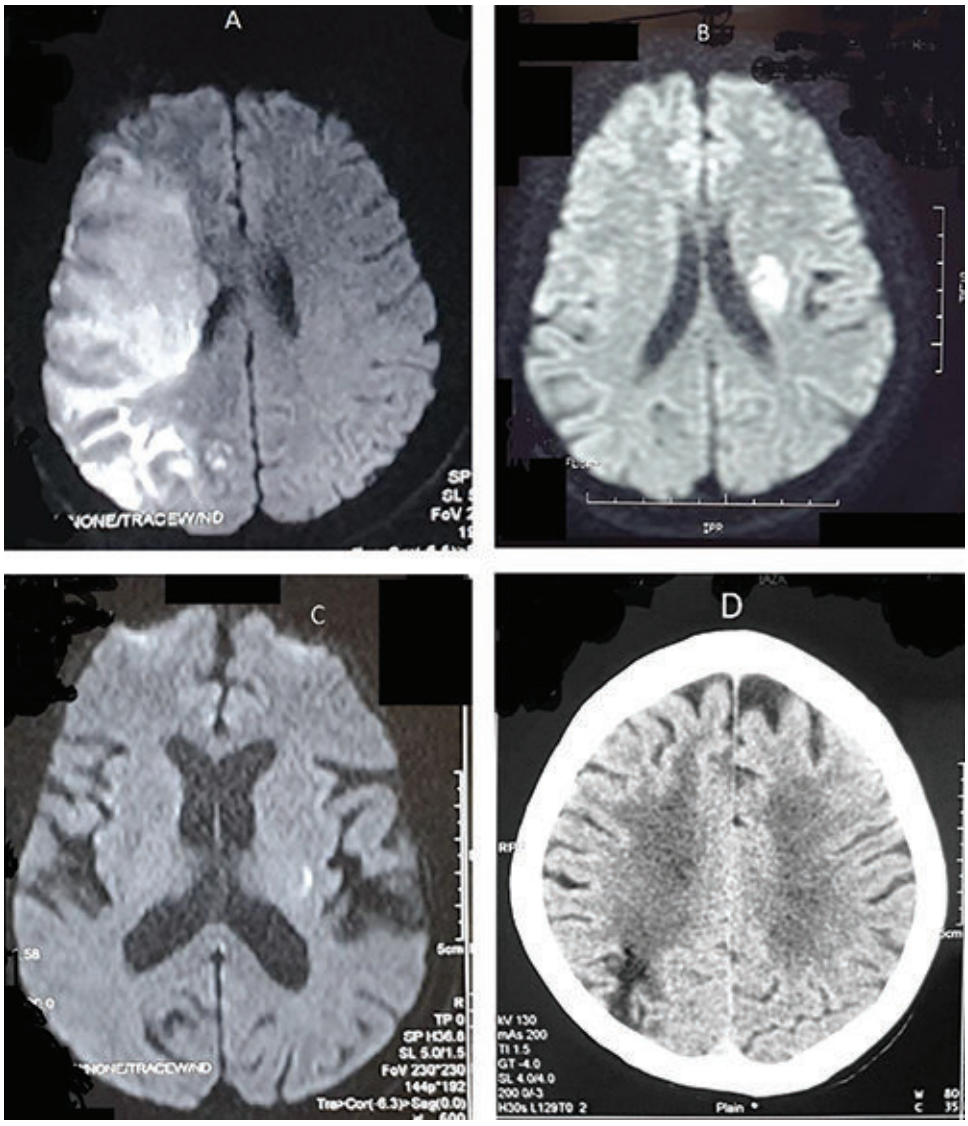

Fig.-2: *Definition of infarct pattern. A: MRI-DWI sequence showing territorial infarct involving right MCA territory. B: MRI-DWI sequence showing subcortical infarct involving left side. C: MRI-DWI sequence showing lacunar infarct involving left internal capsule. D: CT scan showing watershed infarct between right MCA and PCA territory.*

lesions in one of the hemodynamic risk zones between major cerebrovascular territories: the superficial border zones wedged between the ACA and MCA or between the MCA and PCA, and the deep border zone located in the vascular territory between deep and superficial arterial systems.[4]

Segments of cervico-cephalic arteries

The common carotid arteries usually bifurcate into ICA and ECA at the hyoid bone level, between the body of C4 and C6 vertebra. The ICA can be divided into the cervical, petrous, cavernous, and supraclinoid segments.[14] The vertebral artery (VA) originates bilaterally from the subclavian artery. The anatomy of the vertebral artery is sometimes described in four parts. The first segment, V1, extends from the subclavian artery to the foramen transversarium of the C6 vertebral body. The second segment, V2, ascends vertically within the foramina transversaria from C6 to the atlas. V3 segment leaves the transverse foramen of the atlas and extends posteriorly and horizontally on the superior surface of the posterior arch of the atlas. The V4 segment pierces the dura and enters the intracranial cavity via the foramen magnum. It joins the contralateral artery at the bulbopontine junction to form the basilar artery (BA).[15]

Results:

Total 93 ischemic stroke patients with significant symptomatic stenosis were studied. Analysis of age distribution showed that mean age was 57.4±1.01 years with range 35-79 years. The age group 60-69 year was most commonly encountered (38.7%) [Figure:4]. Male patients were 56 in number and female were 37, with male female ratio of 1.51:1. Among them 45(48.4%) had extra-cranial stenosis, 42(45.2%) had intra-cranial and 6(6.4%) had both extra-cranial and intra-cranial stenosis. The internal carotid artery (cervical segment) was most

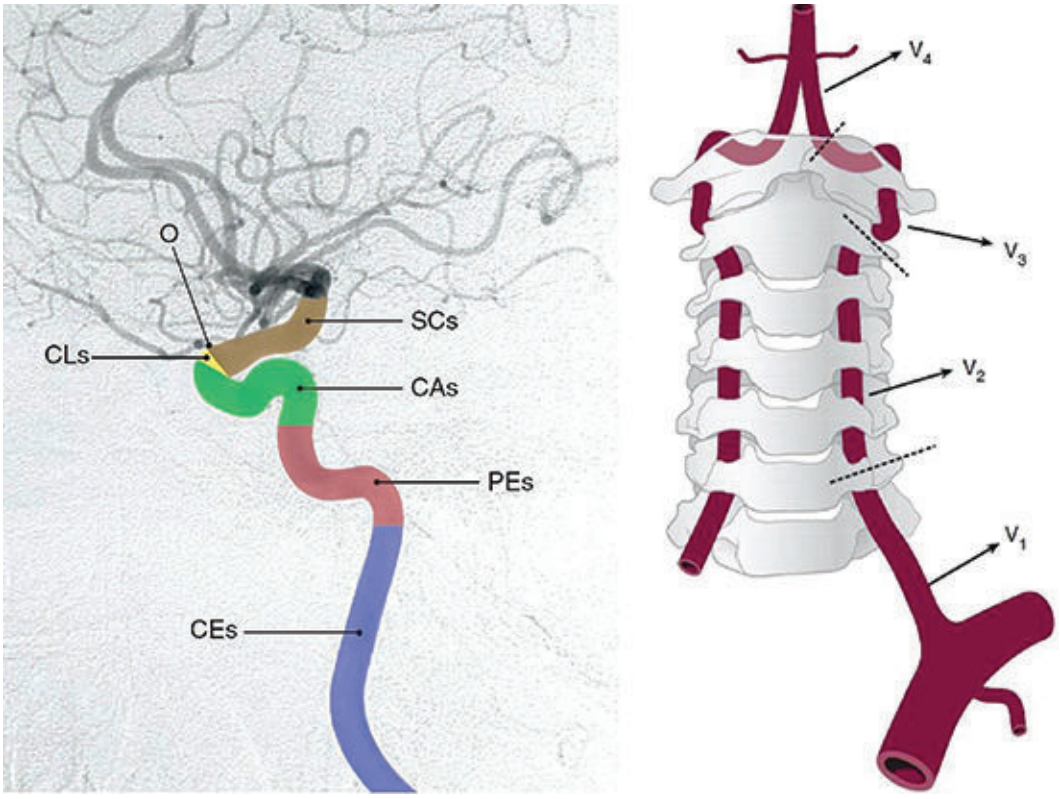

Fig.-3: *Drawing showing portions of the ICA in the left with their segments[16] and vertebral artery (VA) and their segments[15]. CEs: Cervical segment, PEs: Petrous segment, CAs: Cavernous segment, CLs: Clinoid segment, O: ophthalmic segment, SCs: Supraclinoid segment, V_1-V_4: vertebral artery segments.*

commonly involved [n= 45 (88.2%)] in extra-cranial segment whereas in the intra-cranial segment; middle cerebral artery was most commonly involved [n= 28 (58.3%)], followed by intracranial portion of ICA [n= 07 (14.6%)].

Our study revealed moderate stenosis was the most common type of severity [n=39(41.9%)]. Severe stenosis was observed in 32(34.4%) and total occlusion was observed in 22(23.7%) patients. Territorial infarct was seen in 40(43.0%) patients, subcortical infarct in 21(22.6%) patients, lacunar infarct in 26(28.0%) patients and water-shed infarct in 6(6.4%) patients [Figure:5].

There was significant association of subtype of infarct with location of stenosis (p-value=0.50) [Table: II]. We also observed significant association of subtype of infarct with degree of stenosis (p-value<0.001) [Figure:6]. Lacunar [n=17(43.6%)] and subcortical [n=13(33.3%)] infarcts were mostly seen in moderate stenosis [n=39]; whereas total arterial occlusion [n=22] presented as territorial [n=16(72.7%)] or water-shed [n=04(18.2%)] infarct. Figure 7 describes the stenotic vessels and their presenting subtype of infarct. In Table III, the diseased segments of individual artery, their degree of stenosis and presenting sub-type of individual infarct pattern is enlisted.

Table-I

Demographics of the cases

		All (n=93)
Age, years mean (SD)	57.4 (1.01)	
Sex category	Men, n (%)	56 (60.2%)
	Women, n (%)	37 (39.8%)
Education	Illiterate, n (%)	5(5.4%)
	Primary, n (%)	22(23.7%)
	Secondary, n (%)	30(32.3%)
	Higher Secondary, n (%)	21(22.6%)
	Graduate, n (%)	15(16.1%)
Religion	Muslim, n (%)	88(94.6%)
	Hindu, n (%)	4(4.3%)
	Christian, n (%)	1(1.1%)
Residence	Urban, n (%)	39(41.9%)
	Rural, n (%)	54(58.1%)
Occupation	Service Holder, n (%)	16(17.2%)
	Business, n (%)	37(39.8%)
	Housewife, n (%)	35(37.6%)
	Others, n (%)	5(5.4%)
Risk factors	Hypertension	72(77.4%)
	DM	50(53.8%)
	Dyslipidemia	90(96.8%)
	Smoking	40(43.0%)
	Ischemic Heart Disease	13(14.0%)
	Family history	10(10.8%)
	Oral contraceptive drugs	11(11.8%)

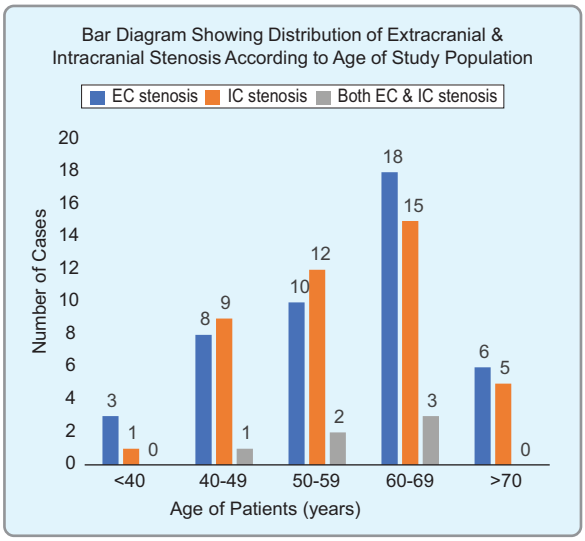

Fig.-4: *Bar diagram showing distribution of extracranial & intracranial stenosis according to age of study population.*

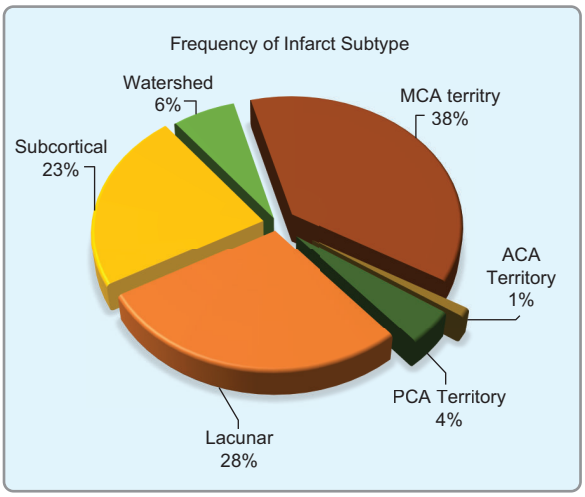

Fig.-5: *Pie-chart showing frequency of infarct subtype.*

Table-II

Distribution of infarct subtype according to location of stenosis (n=93)

Subtype of infarct	Location of Stenosis			Total	p-value
	Extra-cranial stenosis	Intra-cranial stenosis	Both Extra and Intra- cranial stenosis		
Territorial	21(46.7%)	15(35.7%)	4(66.7%)	40(43.0%)	0.050 *
Subcortical	7(15.6%)	12(28.6%)	2(33.3%)	21(22.6%)	
Lacunar	11(24.4%)	15(35.7%)	0(0.0%)	26(28.0%)	
Watershed	6(13.3%)	0(0.0%)	0(0.0%)	6(6.5%)	
Total	45(100.0%)	42(100.0%)	6(100.0%)	93(100.0%)	

* significant (P value d" 0.05), figures in the parentheses indicate corresponding percentage;
Chi-squared (÷2) Test was done to analyze the data.

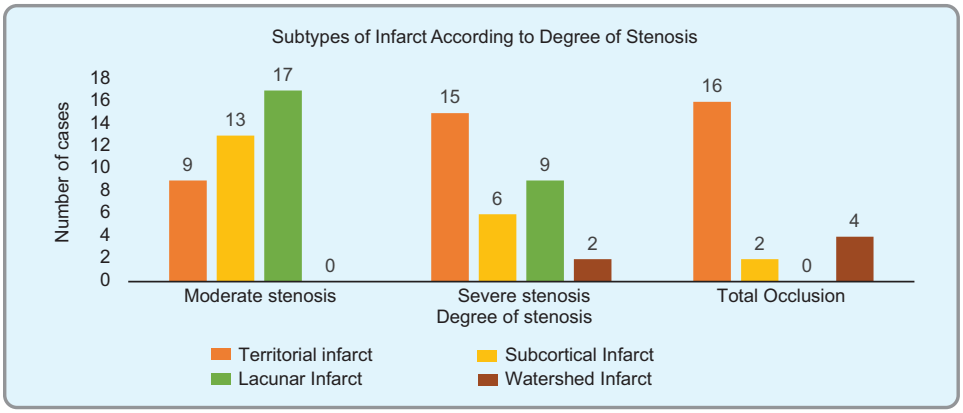

Fig.-6: *Bar diagram showing distribution of subtype of infarct according to degree of stenosis (n=93, p-value<0.001, significant). Chi-squared (÷2) Test was done to analyze the data.*

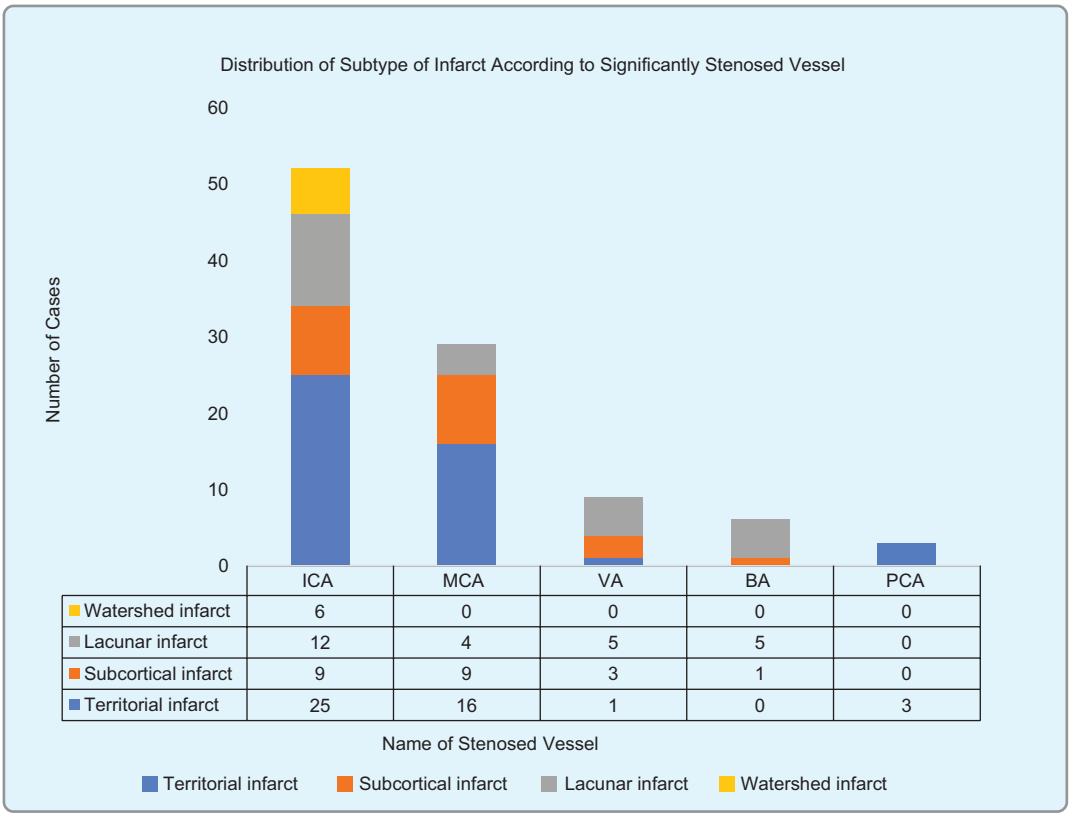

Fig.-7: *Bar diagram showing distribution of subtype of infarct according to significantly stenosed vessel*

Table-III

Diseased arteries with their degrees of stenosis and presenting types of infarct (n=93)

Name of Diseased Vessel	Segment	Degree of Stenosis	Frequency of cases	Type of Infarct			
				Territorial	Subcortical	Lacunar	Water -shed
ICA	Cervical	Moderate	13	5	2	6	0
		Severe	17	9	5	1	2
		Total Occlusion	15	11	0	0	4
	Cavernous	Moderate	2	0	0	2	0
		Severe	2	0	2	0	0
	Supraclinoid	Severe	4	1	0	3	0
MCA		Moderate	14	4	6	4	0
		Severe	7	6	1	0	0
		Total Occlusion	8	6	2	0	0
VA	V1	Moderate	3	0	1	2	0
		Severe	2	1	0	1	0
	V4	Moderate	3	0	1	2	0
		Severe	1	0	1	0	0
BA		Moderate	5	0	0	5	0
		Severe	1	0	1	0	0
PCA		Severe	3	3	0	0	0

Discussion:

Total 93 ischemic stroke patients with significant symptomatic stenosis were studied. Analysis of age distribution showed that mean age was 57.4±1.01 years with range 35-79 years. 60-69 year group was seen most commonly encountered (38.7%). There was no significant association found between age of the study population and location of stenosis. An epidemiological survey of stroke in Bangladesh revealed that highest prevalence of stoke was among 65-79 years of age.[17] Another DSA based study from BSMMU revealed mean age was 61.55 ± 8.85 years with 60-69 year group being most commonly (42.9%) encountered.[18] These results are almost similar to our study.

In our study, among 93 patients, 56 were male and 37 were female with male female ratio 1.51:1. There was no association found between sex of patient and location of stenosis. A study in 2018 revealed that male female ratio was 1.53:1.[17] In another DSA based study found male female ratio to be 1.65:1.[19] The reason behind this discrepancy in male female ratio may be explained by increased incidence of stroke in male and also negligence of female ischemic stroke patients.

We encountered 51 patients with extracranial stenotic segments. Among them, internal carotid artery (cervical segment) was most commonly involved [n= 45 (88.2%)], followed by extracranial portion of vertebral artery [n= 06 (11.8%)]. In case of intracranial stenotic segments, we found 48 patients. Among them, middle cerebral artery was most commonly involved [n= 28 (58.3%)], followed by intracranial portion of ICA [n= 07 (14.6%)] and basilar artery [n= 06 (12.5%)]. An epidemiological study of intracranial and extracranial large artery stenosis in the middle-east revealed that in the extracranial segment carotid stenosis was more common than vertebral stenosis (89% vs 11%) and in the intracranial segment MCA was involved in 50% cases followed by VA (25%) and intracranial portion of ICA (12.5%).[20]

Our study with 93 patients revealed, 60-69 year is the most common age group having maximum number of patients 36(38.7%) with stenosis. Among them, 33.3% patients had moderate stenosis, 38.9% had severe stenosis and 27.8% had total occlusion. Also, among 93 patients, moderate stenosis was the most common type of severity [n=39(41.9%)]. Severe stenosis was observed in 32(34.4%) and total occlusion was observed in 22(23.7%) patients. In a recent study at BSMMU, moderate, severe and total occlusion were observed in 26.2%, 40.5% and 33.3% respectively among 42 patients.[18]

Among 93 of our patients, territorial infarction was the most common subtype of infarct [n=40(43.0%)], followed by lacunar [n=26(28.0%)], subcortical [n=21(22.6%)], and watershed zone infarct [n=06(6.4%)]. 84 patients had single stenosis, among them 40.5% had territorial infarct and 31.0% patients had lacunar infarct. 9 patients had multiple stenosis, among them 66.7% had territorial infarct. Thorough literature review revealed, the relative frequency of lacunar infarction occurred among 20-30% of ischemic stroke patients, subcortical infarction occurred among 25%, watershed zone infarction were 10% of ischemic stroke, and rest being territorial infarction.[21,22,23]

We found significant difference between subtype of infarct and severity of stenosis (p-value <0.001). Overall 39 patients had moderate stenosis. Among them, most (43.6%) had lacunar infarct, followed by subcortical (33.3%) and territorial infarct (23.1%). 32 patients had severe stenosis among them most (46.9%) had territorial infarct, 28.1% had lacunar infarct, 18.8% had subcortical infarct. 22 patients had total occlusion among them 72.7% had territorial infarct, 18.2% had watershed infarct. An MRI based study about acute ischemic stroke pattern revealed, among 19 patients with moderate stenosis 36.8% had lacunar infarct and 26.3% had subcortical infarct.[4] Among 41 patients with severe stenosis, 51.2% had watershed infarct and 26.8% had territorial infarct and among 42 patients with total occlusion, 61.9% had territorial infarct and 21.4% had watershed zone infarct.[4] In another large study among 413 ischemic stroke patients with ICA disease, 33.4% had lacunar infarct and 26.2% had watershed zone infarct. They also showed that 63% of watershed infarct was encountered in ICA stenosis of 70% or more, whereas 42% of such patients presented with lacunar infarct.[24]

In our study, we found significant difference between subtype of infarct and severity of stenosis in both extracranial and intracranial segment. Among 51 patients with extracranial stenosis, 35 had stenosis of 70% or more, and territorial infarction (n=30) was the most common subtype of infarct. All patients with watershed zone infarct were observed in this sub-group of extracranial stenosis of 70% or more. Among 48 patients with intracranial stenosis, 24 patients had moderate stenosis. 50.0% had lacunar infarct, and 33.3% had subcortical infarct. 24 patients had stenosis of 70% or more among them 62.5% had territorial infarct, 25% had subcortical infarct.

The fact that severity of stenosis is associated with increased infarct size, hence severity of stroke; can be attributed to several mechanisms. With more severe stenosis, there is more hemodynamic compromise distal to stenosis and decreased vasomotor reserve of cerebral vessels.[7] The extent of collaterals also determines the severity of infarct.[25]

Among 93 patients, we found 40 patients with territorial infarction. 87.5% had infarction in MCA territory, 10.0% had infarction in PCA territory and 2.5% had infarction in ACA territory. 52.5% had extracranial stenosis, 37.5% had intracranial stenosis and 10% had both extra and intracranial stenosis. Among patients with MCA territory infarct, 42.9% had total occlusion, 32.3% had severe stenosis, and 22.9% had moderate stenosis. A large study in 2014 revealed that MCA was the most frequently involved territory (49.6%) and PCA was involved in (8.5%).[26] Another hospital based study of young patient with ischemic stroke revealed 14(21.86%) had large artery stenosis among the 77.7% had MCA territory infarct.[27] A DSA based study from India revealed, among 161 patients 81.5% had MCA territory infarction, 4.35% had PCA and 1.2% had ACA territory infarction.[28] Another study about the etiology of MCA territory infarct showed that, 40% ICA occlusion was found among MCA territory infarct.[29]

Conclusion:

Our study population had more extracranial vessel involvement than intracranial. Among involved vessels, cervical part of ICA was most commonly involved followed by MCA. Territorial infarction was most commonly encountered followed by lacunar infarction. Territorial infarction was more commonly associated with severe stenosis and lacunar stroke was more commonly associated with moderate stenosis. Watershed infarction was an indicator of severe stenosis.

Ethical issues:

All patients gave informed written consents and the study was approved by Institutional Review Board of Bangabandhu Sheikh Mujib Medical University.

Conflict of interests:

The authors declare that they have no conflict of interest.

Abbreviations

ACA: Anterior Cerebral Artery, BSMMU: Bangabandhu Sheikh Mujib Medical University, CTA: Computed Tomography Angiogram, DSA: Digital Subtraction Angiography, ICA: Internal Carotid Artery, MCA: Middle Cerebral Artery, MRA: Magnetic Resonance Imaging, NASCET: North American Symptomatic Carotid Endarterectomy Trial, PCA: Posterior Cerebral Artery, SD: Standard Deviation, TOF: Time of Flight MRI.

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