Carotid Artery Intimal Medial Thickness in Acute Ischemic Stroke Subtypes and Intracerebral Hemorrhage

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ABSTRACT:

BACKGROUND:

Stroke is the second cause of adult death globally. The Intimal Medial Thickness of the Carotid Artery is regarded as a measure of atherosclerosis. Since the pathogenesis and treatment differ among stroke subtypes; therefore, evaluating the intimal medial thickness may help in distinguishing intracerebral hemorrhage from other ischemic stroke subtypes.

OBJECTIVE:

To assess the carotid artery intimal medial thickness in ischemic stroke Subdivisions and intracerebral hemorrhage.

METHOD:

A cross-sectional case-control study of 200 subjects, 100 patients with different Stroke subtypes and 100 control that are age and gender matched. All subjects were examined by B-mode ultra-sonography to measure the intimal medial thickness of both common carotid and internal carotid arteries on either side. Time of study is from January 2018 to January 2019.

RESULTS:

200 patients, 110 male, 90 female, with mean age of 61.59 ±9.1. The mean IMT for LA, SA, ICH, CE and control groups were 0.91±0.12, 0.77±0.04, 0.74±0.04, 0.70±0.09 and 0.62±0.07 mm respectively (p value <0.001). There was significant increase in Mean IMT with increasing age (p value <0.001).

CONCLUSION:

There is possible diagnostic ability of using IMT to differentiate Stroke subtypes from each other's.

KEYWORDS: Stroke subtypes, Intimal medial thickness, intracerebral hemorrhage.

INTRODUCTION:

Stroke is the second cause of adult death globally, the fifth in the United states of America.[1] According to American Heart Association/American Stroke Association 2013 , Definition of stroke is a neurological deficit due to an acute focal damage of the central nervous system by a vascular cause.[2]

According to pathology stroke is classified into two chief types: ischemic and hemorrhagic.[3] these two chief types are further classified into subtypes. Ischemic stroke classification is based on etiology and pathophysiology causing the blood vessel occlusion, this classification was produced by the Trial of Org in Acute Stroke Treatment (TOAST).[4] ischemic stroke was categorized into five subclasses :large artery atherosclerotic, small artery (lacunar) stroke, cardio-embolic ,stroke of other determined etiology and Stroke of undetermined etiology (cryptogenic).

Intracerebral Hemorrhage is less common than ischemic stroke but has a significant higher acute morbidity and mortality, [5] and is more likely to cause subsequent disability.[6] According to American Heart Association/American Stroke Association, Intracerebral hemorrhage is defined as rapid neurological deficit due to a non-traumatic focal collection of blood within the brain parenchyma or ventricular system.[2] The etiology of spontaneous ICH depends on the age group. ICH in younger patients is more likely due to chronic hypertension, and the hematoma is more likely to be in the basal ganglia or brainstem. ICH in older populations is more likely to be lobar and cerebral amyloid angiopathy is a possible cause. Other existing risk factors for ICH include age, and low serum cholesterol level. [7][8]

The increase in the intimal medial thickness of carotid artery is a practical measure of early atherosclerotic changes.[9] Intimal medial thickness is a measure of the thickness of both tunica intima and tunica media; the interior two layers of an artery wall. It involves endothelial cells, connective tissue, and smooth muscle and it is the site of lipid deposition in plaque development. IMT is used to detect the presence of atherosclerosis, and also to follow

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the regression, arrest or progression of atherosclerotic changes.[10] Intimal medial thickness has been seen as a strong predictor of future vascular events such as myocardial infarction and stroke,[11] and considered as predictor of future stroke even in the absence of carotid plaques.[12] Also, it has been seen that carotid artery IMT regresses after pharmacological treatment for different cardiovascular risk factors.[13]

High-resolution B mode carotid ultrasonography provides a reliable safe non-invasive method for measuring the intimal medial thickness of the carotid arteries. Also it is widely available and inexpensive compared to other methods for measuring IMT like MRI.

Normal common carotid artery mean IMT is approximately (0.4 to 0.5 mm) in the second decade of life, while from the fifth decade onward this progresses to (0.7 to 0.8 mm) or more, and significantly higher IMT values are found in men than in women.[14]

So our Aim of the study is evaluating the role of intimal medial thickness in distinguishing different subtypes of stroke.

PATIENTS AND METHODS:

This is a cross-sectional case-control study performed at the neurology department in Neuroscience Hospital in Baghdad from February 2018 to February 2019. The study included 200 subjects, 100 adult patients with acute first ever stroke of different subtypes who were admitted to the neurology department, and age and gender matched non stroke control (n. = 100) who were relatives of stroke patients, or patients consulted for disorders other than stroke or ICH.

Inclusion criteria: patient with acute ischemic stroke or intracerebral hemorrhage diagnosed by clinical and radiological features, age more than 45 years and first-ever in life stroke.

Exclusion criteria: recurrent strokes, stroke in patients younger than 45 years, stroke due to hypercoagulable state, vasculopathy, or hematologic disorders (stroke of other determined etiology). Stroke of undetermined etiology (cryptogenic stroke), venous infarction (CVT).

past medical History or family History of hyperlipidemia, subarachnoid hemorrhage, intracerebral hemorrhage caused by AVM, Aneurysmal rupture, intracranial neoplasm, Coagulopathy, Anticoagulant induced intracerebral hemorrhage, Hemorrhagic transformation of an ischemic infarct, cerebral venous thrombosis, Sympathomimetic drug abuse and traumatic brain injury, drug history of taking lipid lowering agents.

Patients with stroke and ICH had brain CT scan and ECG on admission, with the brain MRI and cardiac ECHO study if indicated thereafter. Patients with ischemic strokes were categorized into the following groups: large artery atherosclerotic stroke, cardioembolic stroke and small artery (lacunar) stroke after exclusion of patients with stroke of other determined etiology, stroke of undetermined etiology (cryptogenic strokes) and venous infarction (CVT). All patients and control had done Doppler ultrasonography; intimal medial thickness of four arteries (common carotid and internal carotid arteries on both sides) were measured by using high resolution real time with B-mode sonography equipped with 3-12 MHz frequency range linear transducer (PHILIPS HD11XE, USA). Measurements were done by a consultant neuroradiologist in the radiology department in neuroscience hospital.

Statistical analysis was done using IBM SPSS Statistics version 23.0.0.0 64-bit edition.

Comparison of the mean IMT was done between male and female, also IMT among different age groups was studied. Comparison of the IMT among different stroke subtypes vs. ICH vs. control was studied also. Independent-sample T test, paired-sample T test and one-way analysis of variance (ANOVA) were used for analysis.

RESULTS:

200 subjects were included in this study, (110 male and 90 females). Table 1 shows the number and the mean age of each stroke category, which showed higher mean age in large artery and lacunar groups than that of cardio embolic and ICH groups. Table 2 shows gender distribution of the study population

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Table 1:Number and mean age of study population.

Stroke subtype	Number	percentage	Mean age (years)	Standard Deviation	Minimum	Maximum
large artery stroke	20	10%	66.50	7.924	50	79
lacunar stroke	22	11%	64.05	7.300	50	75
intracerebral hemorrhage	30	15%	60.10	9.901	45	84
cardioembolic stroke	28	14%	60.39	7.524	46	77
control group	100	50%	60.84	9.599	45	85
Total	200	100%	61.59	9.128	45	85

Table 2: Gender distribution of study population.

Gender	stroke patients	control group	Total
Male	56	54	110
Female	44	46	90
Total	100	100	200

The comparison of the mean IMT for each stroke subtype (large artery, lacunar, ICH and cardioembolic stroke subtypes) was compared with the control group. It shows significant difference between means, with p value <0.001 (table 3). The mean IMT was higher in all stroke subtypes more than that of control group, highest correlation in large artery and lacunar groups than that of cardioembolic and ICH groups (figure 1).
Regarding Gender correlation, Table 4 shows that there is slightly higher IMT in male than female but it is not statistically significant. This is demonstrated clearly in figure 2.

For Age Relationship, the study subjects both stroke subtypes and control group were subdivided into 4 age categories (45-54, 55-64, 65-74, 75 and above) (table 5).
Mean IMTs were further analyzed according to age category for all stroke subtypes; table 6 shows the comparison of mean IMT among different stroke subtypes according to age group which is statically significant.
The relationship between age and mean IMT was tested using Pearson Correlation test, which show direct correlation (Pearson correlation = 0.853) with statistical significance p value <0.001 (figure 3).

Table 3:Comparison of IMT among each stroke category with the control group.

	Number	Mean IMT in mm	SD	Minimum	Maximum	Correlation coefficient	P value
large artery ischemic stroke	20	0.91	0.118	0.75	1.22	0.736	<0.001
lacunar small artery ischemic stroke	22	0.77	0.046	0.70	0.90	0.395	<0.001
intracerebral hemorrhage	30	0.74	0.042	0.68	0.86	0.361	<0.001
cardioembolic stroke	28	0.70	0.093	0.52	0.90	0.254	<0.001
control group	100	0.62	0.074	0.50	0.83		

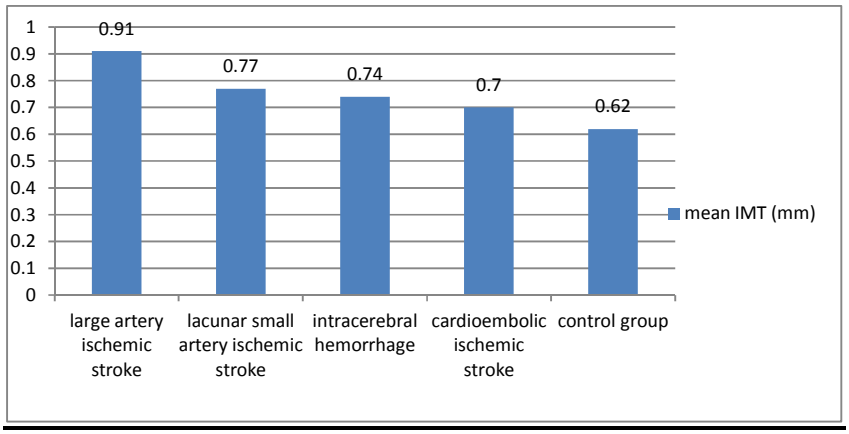

Figure 1: Mean IMT in each stroke subtype and the control group.

Regarding Gender correlation Table 4 shows that there is slightly higher IMT in male than female but it is not statistically significant. This is demonstrated clearly in figure 2.

Tables 4:Mean IMT in male and female according to age group.

	Male IMT (mm)	Female IMT (mm)	P value
from 45 to 54 years	0.56	0.54	0.299
from 55 to 64 years	0.63	0.61	0.273
from 65 to 74 years	0.67	0.63	0.025
from 75 and above	0.80	0.74	0.314

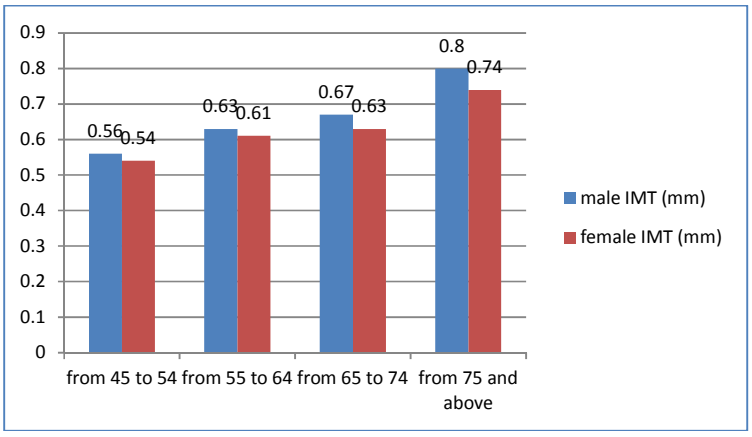

Figure 2: Mean IMT in male and female according to age group.

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Table 5: Show number distribution of subjects according to age groups.

	45 to 54 years	55 to 64 years	65 to 74 years	75 and above	Total
large artery stroke	2	4	10	4	20
lacunar stroke	4	4	13	1	22
intracerebral hemorrhage	8	12	8	2	30
cardioembolic stroke	4	16	6	2	28
control group	30	36	26	8	100
Total	48	72	63	17	200

Table 6: Comparison of mean IMT between stroke subtypes according to age group.

	large artery stroke	lacunar stroke	ICH	Cardioembolic stroke	control	P value
from 45 to 54	.83	.73	.72	.64	.55	<0.001
from 55 to 64	.85	.76	.73	.70	.62	<0.001
from 65 to 74	.90	.78	.74	.72	.65	<0.001
75 and above	1.04	.90	.85	.80	.76	.050

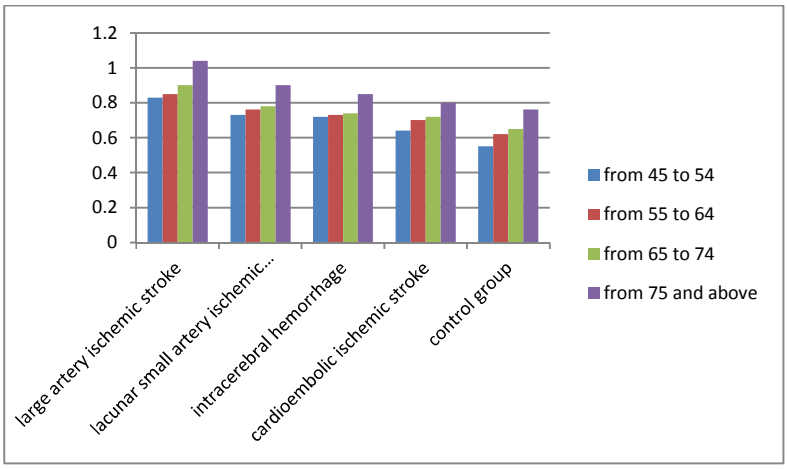

Figure 3: Mean IMT stroke subtypes according to age group.

Regarding comparison between ischemic stroke and ICH according to IMT, Table 7 shows no statistical difference in mean IMT between ischemic stroke and ICH.

Table 7: Comparison of mean IMT between ischemic stroke and ICH.

	N	Mean IMT in mm	SD	Minimum	Maximum	P value
ischemic stroke	70	0.785	0.122780	0.525	1.225	.053
ICH	30	0.740	0.041793	0.680	0.860	

DISCUSSION:

Several previous studies have evaluated the association of increased intimal medial thickness with ischemic stroke. Salim Harris from Indonesia at 2012[15] found association between IMT and stroke. Others like Polak. et al USA 2011,[16] Touboul. et al France 2000 [17], Prati. et al Italy 2008[18] and Kitamura. et al Japan 2004[19] found that increase intimal medial thickness is associated with increase in the incidence of stroke.There are few studies evaluated the association of Germany 2004 [21] and Moghtaderi. et al Iran 2014[22] found possible ability of IMT to differentiate between ischemic versus hemorrhagic strokes. Our study found that intimal medial thickness was significantly increased in all types of stroke including ICH when compared to control but the increase is varying according to stroke subtype. Highest intimal medial thickness was observed in the large artery ischemic stroke group followed by the lacunar stroke group, the ICH group, and the cardioembolic stroke group respectively. These findings were consistent even after adjustment of age and gender on comparison. This difference in mean IMT across stroke subtypes is mostly due to different pathophysiology in each type of stroke. This finding was consistent with Ohira. et al 2011 [20] and Touboul. et al 2000. [17]Our study showed higher mean IMT in male compared with female but it was not statistically significant. This may be due to that most of our female cases are at the age of menopause, at this age the female sex hormones that have protective effect against atherosclerosis will not be found and so the risk of atherosclerosis becomes equal to that of male patients.Our study shows increase in the mean intimal medial thickness with increasing age in both cases and control subjects, and this association is statistically significant. This may be due to increasing atherosclerosis with advancing age because of normal vascular aging. This is also found by Estibaliz. et al 2010[23] and Lim. et al 2008 [24]Our study also found no significant difference in the mean intimal medial thickness when comparing ischemic stroke of all subtypes as one block with the hemorrhagic stroke. As the results showed increase mean IMT among ICH patients in a similar manner to that of ischemic stroke patients, the cause of this may be because the ICH patients in our study are of hypertension induced arterial intracerebral hemorrhage as we exclude the other causes of hemorrhagic stroke as SAH or cerebral venous thrombosis or amyloid angiopathy. These findings disagree with the results of Moghtaderi. Et al,[22] and Vemmos. Et al studies[21] that founded no significant increase in the mean IMT of intracerebral hemorrhage when compared to control subjects.Limitations in our study were that we did not study all variables that associated with increased intimal medial thickness; secondly the sample size was relatively small and taken from only one center.

CONCLUSION:

Intimal medial thickness was found to increase in all stroke subtypes including the ICH group. We think there is a possible diagnostic ability of using IMT to differentiate stroke subtypes from each other's.

Recommendations: Further analysis is needed to confirm the association between IMT and stroke subtypes with large multicenter studies.

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