

## ORIGINAL RESEARCH

### Significance of LADi (Indexed Left Atrial Diameter) as a predictive marker for acute ischemic stroke

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#### ABSTRACT

**Aims:** The present study was designed to assess LAD and LADi as a predictive marker for Acute Ischemic Stroke and to analyse their association in patients with AF in Acute Ischemic Stroke patients.

**Materials & methods:** This study was conducted on 50 patients with acute ischemic stroke and 50 patients without stroke who attended outdoor department or who were admitted in Medicine Department of Guru Nanak Dev Hospital, attached to Government Medical College, Amritsar. The patients were divided into two groups (Group A and B) as follows: Group A includes 50 Patients with acute ischemic stroke, and Group B includes Age and sex matched 50 patients without stroke. Left atrial diameter (LAD) was measured using Two-dimensional echocardiography from the posterior aortic wall to the posterior left atrial wall according to a leading edge to leading edge convention in the parasternal long-axis view at the end-ventricular systole (i.e., just before the mitral valve opening). Indexed left atrial diameter (LADi) was calculated by dividing Left atrial diameter with body surface area (BSA). The data was collected systematically and analysed using Microsoft excel sheet and statistical package for social science version 21.0 (SPSS, Chicago, IL, USA).

**Results:** In group A, the mean left atrial diameter was 4.02 cm and in group B, the mean left atrial diameter was 3.44 cm. The mean LADi was 2.30 cm/m<sup>2</sup> and 1.98 cm/m<sup>2</sup> in Group A and Group B respectively. The mean LADi was higher in group A as compared to Group B and the difference was significant statistically (p<0.0001). In addition, among 23 ischemic stroke patients who were having AF, 21.7% had normal LAD and 78.3% had increased LAD. Among 27 control patients who did not have AF, 63% had normal LAD and 37% had increased LAD. The difference was statistically significant (p=0.03). In group A patients in whom AF was absent, 48.1% had normal LADi and 51.9% had increased LADi. In group B patients in whom AF was absent, 84.6% had normal LADi and 15.4% had increased LADi. The difference was again statistically significant (p=0.002)

**Conclusion:** LAD and LADi are higher in patients with Acute Ischemic Stroke and this difference is statistically significant. Thus, LAD and LADi can be used as predictive

**marker for Acute Ischemic Stroke. Furthermore, LAD and LADi are found to be higher in patients with AF.**

**Key words: Stroke, Left atrial diameter, Indexed left atrial diameter, Atrial fibrillation**

## INTRODUCTION

Cerebrovascular disease or stroke is a major health hazard in the world irrespective of socioeconomic status and is one of the leading causes of mortality and morbidity. Stroke is becoming a significant cause of premature death and disability in developing countries like India, mainly because of rapidly increasing prevalence of modifiable risk factors such as Hypertension, Diabetes Mellitus and Obesity.<sup>1-3</sup>

Well-known risk factors for stroke can be categorized into non-modifiable and modifiable. Non-modifiable risk factors include age, race, gender, family history as well as genetic makeup of individuals. Modifiable risk factors include Hypertension, Diabetes Mellitus, Dyslipidemia, Ischemic heart disease, Atrial fibrillation (AF), valvular heart disease, carotid artery stenosis, cigarette smoking, and obesity.<sup>4</sup> Hypertension is the most readily recognized factor in the genesis of cerebrovascular accident.<sup>5</sup>

Stroke is broadly classified into two types: Ischemic stroke and Haemorrhagic stroke. Ischemic stroke is defined as an infarction of central nervous system tissue (brain, spinal cord or retinal cell) attributable to ischemia based on neuroimaging and/or clinical evidence of permanent injury.<sup>6</sup> Ischemic stroke is the most common type of stroke that accounts for almost 80–85% of all stroke cases.<sup>7,8</sup>

The left atrium (LA) is a crucial component of cardiac physiology. It is structurally and functionally linked to left ventricular (LV) function. Functionally, the LA has been described as a reservoir during LV systole, a conduit during early diastole, but actively contracts during late diastole to aid ventricular filling. Hence, LA is estimated to contribute about 15-30% of LV filling volume during the active phase.<sup>9</sup>

Several mechanisms can explain a pathophysiologic link between ischemic stroke and left atrial enlargement (LAE). First, LAE promotes blood stasis, which in turn predisposes to thrombus formation and the potential for embolization.<sup>10</sup> Second, left atrial diameter (LAD) can be related to atrial fibrillation (AF) duration, or arrhythmia burden. Alternatively, LAE may be a surrogate marker representing an adaptive response to endothelial dysfunction that affects the systemic vascular bed.<sup>11,12</sup>

LAE has been suggested as an independent risk factor for stroke and is associated with a 20% chance of thromboembolism per year in the presence of indexed left atrial diameter (LADi) > 2.5 cm/m<sup>2</sup> with moderate to severe LV contractility changes. The present study was designed to assess LAD and LADi as a predictive marker for Acute Ischemic Stroke and also to analyse association of LAD and LADi with AF in Acute Ischemic Stroke patients.

## MATERIALS & METHODS

This study was conducted on 50 patients with acute ischemic stroke and 50 patients without stroke who attended outdoor department or who were admitted in Medicine Department of Guru Nanak Dev Hospital, attached to Government Medical College, Amritsar. The patients were divided into two groups as follows: Group A: 50 Patients with acute ischemic stroke, and Group B: Age and sex matched 50 patients without stroke. Detailed history, physical examination and necessary investigations were undertaken. Demographic, clinical, echocardiographic data and medication were collected at baseline for all patients. As per the recommendations of the American society of Echocardiography, Transthoracic Echocardiography was performed in the left lateral decubitus position using standard imaging planes. Left atrial diameter (LAD) was measured using Two-dimensional echocardiography from the posterior aortic wall to the posterior left atrial wall according to a leading edge to

leading edge convention in the parasternal long-axis view at the end-ventricular systole (i.e. just before the mitral valve opening). Left atrial diameter (LAD) was indexed to BSA (body surface area) using Mosteller formula:

$$BSA (cm/m^2) = \frac{\sqrt{\text{Height (IN CMS)} \times \text{WEIGHT (IN KG)}}}{3600}$$

The American Society of Echocardiography (ASE) recommendations for Left atrium quantification in adults are as following:

Parameter	Male	Female
Left Atrial Diameter (LAD) in cm	3.0-4.0	2.7-3.8
Left Atrial Diameter indexed by BSA (LADi) in cm/m <sup>2</sup>	1.5-2.3	1.5-2.3

## STATISTICAL ANALYSIS

The data was collected systematically and analysed using Microsoft excel sheet and statistical package for social science version 21.0 (SPSS, Chicago, IL, USA). Continuous variables were expressed as mean  $\pm$  standard deviation (SD) and categorical variables as count and percentage. Comparisons between groups were performed using Student's t test for continuous variables and the chi-square test and ANOVA for categorical variables.

## RESULTS

The mean age of the patients in Group A was 59.08 years and In Group B was 59.18 years. The difference in age distribution was not significant. ( $p=0.95$ )

In group A, 60% of the patients were males and 40% were females. In group B, 56% of the patients were males and 44% were females. In group A, the mean body surface area was 1.75 m<sup>2</sup> and in group B, the mean body surface area was 1.73 m<sup>2</sup>. In group A, 46% of the patients had atrial fibrillation and in group B, 22% of the patients had atrial fibrillation. Group A had a greater number of patients with atrial fibrillation as compared to Group B and the difference was significant ( $p=0.01$ ). In group A, the mean left atrial diameter was 4.02 cm and in group B the mean left atrial diameter was 3.44 cm. The mean left atrial diameter was higher in group A as compared to Group B and the difference was significant statistically ( $p=0.0002$ ).

In group A, 38% of the patients had normal LADi and 62% of the patients had increased LADi. In group B, 72% of the patients had normal LADi and 28% of the patients had increased LADi. In group A, the mean LADi was 2.30 cm/m<sup>2</sup> and in group B, the mean LADi was 1.98 cm/m<sup>2</sup>. The mean LADi was higher in group A as compared to Group B and the difference is significant statistically ( $p<0.0001$ ).

**Table 1: Differences In Baseline Parameters In Both Groups**

Parameter	Group A	Group B	P Value
	Mean $\pm$ SD	Mean $\pm$ SD	
Mean age	59.08 $\pm$ 10.743	59.18 $\pm$ 8.67	0.95
Body surface area (m <sup>2</sup> )	1.75 $\pm$ 0.10	1.73 $\pm$ 0.09	0.34
Total cholesterol (mg/dL)	194.38 $\pm$ 55.15	186.54 $\pm$ 57.12	0.48
LDL (mg/dL)	117.94 $\pm$ 39.28	114.16 $\pm$ 39.58	0.63
HDL (mg/dL)	39.92 $\pm$ 6.70	39.52 $\pm$ 7.05	0.77
FBS (mg/dL)	112.32 $\pm$ 27.07	113.38 $\pm$ 25.80	0.84
PPBS (mg/dL)	177.26 $\pm$ 57.54	192.06 $\pm$ 40.88	0.14
Blood Urea (mg/dL)	38.86 $\pm$ 19.76	37.53 $\pm$ 3.41	0.69
Serum creatinine (mg/dL)	1.08 $\pm$ 0.36	0.96 $\pm$ 0.31	0.078
Serum sodium (mEq/L)	139.10 $\pm$ 5.64	137.78 $\pm$ 6.22	0.26
Serum Potassium (mEq/L)	4.05 $\pm$ 0.42	3.94 $\pm$ 0.46	0.23
Serum Bilirubin (mg/dL)	0.86 $\pm$ 0.37	0.79 $\pm$ 0.30	0.30
SGOT (U/L)	36.53 $\pm$ 15.17	40.40 $\pm$ 20.15	0.28

SGPT(U/L)	36.36±16.80	43.26±21.19	0.075
Left atrial diameter(cm)	4.02±0.62	3.44±0.62	0.0002
LADi(cm/m <sup>2</sup> )	2.30±0.36	1.98±0.40	<0.0001

**Table 2: Comparison Of Prevalence Of Atrial Fibrillation In Group A And Group B**

Atrial Fibrillation	Group A		Group B		P Value
	Number of patients	Percentage	Number of patients	Percentage	
Yes	23	46%	11	22%	<b>0.010</b>
No	27	54%	39	78%	
Total	50	100%	50	100%	

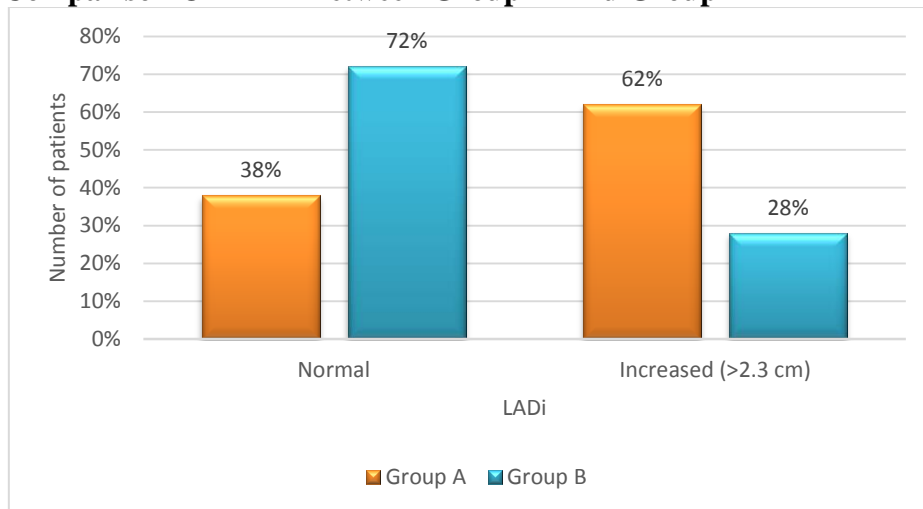
**Table 3: Comparison Of Left Atrial Diameter (LAD) Between Group A And Group B**

Left atrial diameter (LAD)	Group A		Group B	
	Number of patients	Percentage	Number of patients	Percentage
Normal	22	44%	40	80%
Increased (> 4 cm for males and >3.8 cm for females)	28	56%	10	20%
Mean ±SD	4.02±0.62		3.44±0.62	
p value	0.0002			

**TABLE 4: Comparison Of LADi {Indexed Left Atrial Diameter (Left Atrial Diameter/Body Surface Area)} Between Group A And Group B**

LADi	Group A		Group B	
	Number of patients	Percentage	Number of patients	Percentage
Normal	19	38%	36	72%
Increased (>2.3 cm)	31	62%	14	28%
Mean ±SD	2.30±0.36		1.98±0.40	
p value	<0.0001			

**Figure 1: Comparison Of LADi Between Group A And Group B**



## DISCUSSION

Stroke is a catastrophic condition with a great burden of disability and death. Furthermore, as the world population is aging, the global burden of stroke is expected to increase dramatically. Thus, identifying the risk factors of stroke and manage patients will have a pertinent individual and social impact.<sup>14</sup>

Ischemic stroke is the most common type of stroke that accounts for almost 80–85% of all stroke cases.<sup>7,8</sup> Ischemic stroke is caused by cutting off cerebral blood flow and thereby oxygen to the brain. Acute occlusion of an intracranial vessel causes reduction in blood flow to the brain region it supplies. The magnitude of flow reduction is a function of collateral blood flow and this depends on individual vascular anatomy, the site of occlusion and systemic blood pressure.<sup>2</sup>

LA of human heart act as a contractile pump that delivers 15-30 % of the LV filling and as a conduit for the passage of stored blood from the LA to LV during early LV diastole.<sup>15</sup> LAE had been found to be associated with increased cardiovascular events such as stroke, congestive heart failure, cardiovascular death and AF.<sup>16</sup> In the Framingham study, a 5 mm incremental increase in Antero-posterior LA diameter was associated with increased risk for subsequent development of AF.<sup>17</sup> LAD as determined by Transthoracic Echocardiography is a robust predictor of cardiovascular outcomes.

Various studies have found that left atrial size was associated with an increased risk of ischemic stroke and stroke related mortality.<sup>18,19,20</sup> Several theories have been proposed in an attempt to explain the mechanism underlying the relation between LA size and ischemic stroke. The most plausible hypothesis is that LA dilatation promotes stasis of blood, which in turn results in propensity for thrombus formation and increased risk of embolism. The thrombogenicity of a dilated LA has been supported by echocardiographic studies showing an association between an enlarged LA and spontaneous echo contrast.<sup>21,22</sup>

Alternatively, LA enlargement may be a surrogate marker representing an adaptive response to endothelial dysfunction that affects systemic vascular bed. Abnormal cytokines such as Angiotensin-2 and its receptor, endothelin, plasminogen inhibitor-1, thrombomodulin are well known enhancers of fibrosis and thrombogenicity, can hinder myocardial electrical coupling in the atrium, resulting in atrial dilatation and thromboembolism.<sup>23,24</sup> Another explanation for increased risk of stroke is that LA enlargement also promotes development of asymptomatic atrial fibrillation.

The present study was done to demonstrate the above proposition and show that increased LAD and LADi {indexed left atrial diameter (LA diameter/ BSA)} was associated with acute ischemic stroke. We found that patients with Acute ischemic stroke tend to have significantly higher LAD and LADi as compared to control group. Likewise, Similar observations were made by other investigators, where LAD and LADi were found to higher in patients with Stroke. The results of present study are comparable with study conducted by Gagne Brosseau M-S et al found positive correlation between LAD and ischemic stroke. Here mean LAD in stroke group was 4.9 cm and in control group was 3.7 cm. The difference was found to be statistically significant ( $p < 0.001$ ).<sup>25</sup> Similar study by Di Tullio et al demonstrated that LADi was higher in patients with ischemic stroke,  $2.31 \pm 0.40 \text{ cm/m}^2$ , as compared to control group,  $2.18 \pm 0.33 \text{ cm/m}^2$  in control subjects.<sup>26</sup>

The study has several limitations, such as the follow up of patients was not possible to examine the prognostic value of our findings and to examine correlation between the LAD/LADi and mortality rate.

## CONCLUSION

LAD and LADi are higher in patients with Acute Ischemic Stroke and this difference is statistically significant. Thus, LAD and LADi can be used as predictive marker for Acute

Ischemic Stroke. Furthermore, the data showed that LAD and LADi have been found to be higher in patients with AF.

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