Association of Aortic Knob Calcification with Intracranial Stenosis in Ischemic Stroke Patients in Tertiary Care Centre

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Abstract

Background: In the arterial bed, Deposition of calcium may indicate the extent of atherosclerotic lesions and aortic knob calcification (AC) is associated with increased risks of cardiovascular and cerebrovascular events. In this study, we evaluated the aortic knob calcification and its clinical importance in ischemic stroke patients with intracranial stenosis and without intracranial stenosis by using simple, non-invasive routine chest radiography.

Aim: To find the prevalence of Aortic Knob Calcification in Ischemic stroke patients with Intracranial Stenosis in Government Royapettah Hospital/Government Kilpauk Medical College. To find the Association of Aortic knob calcification in patients with and without Intracranial stenosis. To evaluate the clinical importance of Aortic knob calcification (AC) in ischemic stroke patients with intracranial (IC) stenosis using simple, non-invasive and routine chest radiography.

Materials and Methods: Patient admitted in medicine department of Government Royapettah Hospital / Kilapuk Medical College. All the cases undergo chest radiography in the posteroanterior (PA) view. The presence of calcification in the aortic knob is recorded. All the cases will undergo MRI Angiography of brain. Based on the findings of the cerebral angiogram, any segment of either intracerebral arteries or extra cranial arteries will be classified as normal, stenosis or occlusion. The classifications will be based on a Radiologist report and the existence of any degree of stenotic lesion will be interpreted as stenosis. Samples will be collected from venous blood after a 12-hour overnight fast, and lipid profiles and standard blood tests will be performed on admission. Here I will compare the proportion of Aortic knob calcification in those with Intracranial stenosis and those without Intracranial Stenosis.

Results: Among the study patients of 102 Aortic knob calcification was present in 32 subjects accounting for 31.4% . In Aortic Knob Calcification vs ICS, Aortic knob calcification was present in 22 subjects of Intracranial stenosis subjects accounting to 32.4%. Aortic Knob Calcification –ICS category was analysed using chi-square test, Fisher's Exact Test and pearson chi square, Among the study patients, there was no statistically significant difference.

Conclusion: There was significant association between increased age, Diabetes, Hypertension, Smoking, Alcohol, Aortic Knob calcification and subjects with intracranial stenosis. There was no significant association between Lipid profile Total cholesterol, TGL, HDL, LDL and subjects with Intracranial stenosis.

Keywords: Aortic Knob Calcification, Ischemic stroke, Intracranial Stenosis.
Introduction

In the arterial bed, Deposition of calcium may indicate the extent of atherosclerotic lesions and aortic knob calcification (AC) is associated with increased risks of cardiovascular and cerebrovascular events.\textsuperscript{11-15} As we know Aortic Knob Calcification associated with coronary artery calcification or carotid atherosclerosis, and might have predictive and prognostic value for coronary artery disease.\textsuperscript{11,16,17} Several reports, in addition have shown that aortic knob calcification or aortic atherosclerotic disease is related to ischemic stroke.\textsuperscript{14,18,19} Though its clinical significance for CVA ischemic stroke patients with intracranial (IC) stenosis, one of the major mechanisms of ischemic stroke, remains unclear. Even though digital subtraction angiograms or thoracic computed tomography (CT) are reliable in detecting aortic calcification,\textsuperscript{11,20} these imaging modalities are not routinely used. In this study, we evaluated the aortic knob calcification and its clinical importance in ischemic stroke patients with intracranial stenosis and without intracranial stenosis by using simple, non-invasive routine chest radiography.

Aim

1. To find the prevalence of Aortic Knob Calcification in Ischemic stroke patients with Intracranial Stenosis in Government Royapettah Hospital / Government Kilpauk Medical College.
2. To find the Association of Aortic knob calcification in patients with and without Intracranial stenosis.
3. To evaluate the clinical importance of Aortic knob calcification (AC) in ischemic stroke patients with intracranial (IC) stenosis using simple, non-invasive and routine chest radiography

Materials and Methods

Study setting: Patient admitted in medicine department of Government Royapettah Hospital/Kilpauk Medical College

Ethical Approval: Institutional ethical committee approval was obtained to conduct the study

Study Group: Acute ischemic stroke patients within 7 days of onset, who will be admitted in Medicine department and whom will undergo magnetic resonance angiography at Government Royapettah hospital/ Kilpauk Medical college

Study Design: Cross sectional study.

Population to be studied: 102

Duration of Study: 6 Months (April 2017 – September 2017)

Consent: All the patients were given written informed consent

Inclusion Criteria

- Acute ischemic stroke patients within 7 days of onset

Exclusion Criteria

- Patients chest X-rays if not properly centered
- Any deviation of the trachea or shift of the mediastinum
- Patients if they had any known disease in the aorta such as aortitis.
- Patients who had cerebrovascular events related to trauma, medical instrumentation, severe concomitant kidney (serum creatinine≥2.0 mg/dL) or liver disease
- Patients with autoimmune disease, moyamoya disease, cerebral vaculitis or embolism from implants, such as an artificial heart valves or atrial fibrillation.

Materials to be Used

- Chest Radiograph Postero- Anterior view
- MRI Angiography Brain
- Blood samples for Total Cholesterol, Triglycerides, HDL, LDL.

Method of Collection of Data

Sample Size: 102 cases will be studied

Protocol of the Study

- Acute ischemic stroke patients within 7 days of onset
- For every case selected, detailed clinical history associated comorbid illnesses like
Diabetes Mellitus, Systemic Hypertension, Hyperlipidemia, Bronchial Asthma, Chronic Kidney disease, Family History of Diabetes Mellitus, Hypertension, geographical area from which patient residing, and results of routine investigations like Complete Blood count, Electrocardiography, X ray chest, Renal function test, Liver Function Test, Urine Routine examination, Blood sugar will be prospectively recorded in the semi-structured proforma. Also In all cases, blood for Fasting Lipid profile will be taken by performing venipuncture and estimation will be done in Clinical Biochemical Laboratory, Biochemical Department at Govt. Royapettah hospital/ Kilapuk Medical College Chennai.

- All the cases undergo chest radiography in the posteroanterior (PA) view. The presence of calcification in the aortic knob is recorded
- All the cases will undergo MRI Angiography of brain
- Based on the findings of the cerebral angiogram, any segment of either intracerebral arteries or extra cranial arteries will be classified as normal, stenosis or occlusion.
- The classifications will be based on a Radiologist report and the existence of any degree of stenotic lesion will be interpreted as stenosis
- Samples will be collected from venous blood after a 12-hour overnight fast, and lipid profiles and standard blood tests will be performed on admission.
- Here I will compare the proportion of Aortic knob calcification in those with Intracranial stenosis and those without Intracranial Stenosis.

The following investigations were done to all patients included in the study
1. Fasting Lipid Profile
   - Total cholesterol/Triglycerides/HDL/LDL
2. Renal Function test
   - Sugar
3. Liver function test
4. Complete blood count including Total count, differential count, ESR
5. Xray chest Posteroanterior view and Electrocardiography.
6. MRI Angiography of brain

Statistics
The collected data were analysed using IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics, percentage analysis, frequency analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in The Independent groups the Unpaired sample t-test was used. To find the significance in categorical data Chi-Square test was used similarly if the expected cell frequency is less than 5 in 2×2 tables then the Fisher's Exact was used. In all the above mentioned statistical tools the probability value .05 is considered as significant level.

Results
We conducted the study for the total number of 102 patients out of which 3 subjects were aged less than 50 years (2.9%), 52 subjects were 51-60 years age group (51%), 20 subject were 61-70 years age group(19.6%), 27 subjects belongs to above 70 years(26.5%). Predominant number of patients belong to 51-60 years comes to around 51% of the study.
Next major subgroup belongs to more than 70 years of age. Increased age is associated with Intracranial stenosis of mean age of 63 and without intracranial stenosis subjects of 59.
Table 2 showing relation of age group vs Intracranial stenosis in which more number of subjects and presence of Intracranial stenosis is maximum in age group within 51-60 years of age with 41 subjects (60.3%), followed by more than 70 year age group with 16 subjects 23.5%, 61-70 years with 11 subjects 16.2%. And Without intracranial stenosis of 8.8% in subjects upto 50 years of age, 32.4% in subjects 51-60 years, 26.5% in subjects 61-70 years of age and 32.4% in subjects of above 70 years
Age – ICS category was analysed using chi-square test and pearson chisquare value is 11.363 and degree of freedom is 3 and p value comes around p-0.010 (p< 0.05) which is statistically significant.

Table 1 Age category of the studied population

| Age Category | Frequency | Percent | Valid Percent | Cumulative Percent |
|--------------|-----------|---------|---------------|--------------------|
| Upto 50 yrs  | 3         | 2.9     | 2.9           | 2.9                |
| 51 - 60 yrs  | 52        | 51.0    | 51.0          | 53.9               |
| 61 - 70 yrs  | 20        | 19.6    | 19.6          | 73.5               |
| Above 70 yrs | 27        | 26.5    | 26.5          | 100.0              |
| Total        | 102       | 100.0   | 100.0         | 100.0              |

Table 2: Age Range
Age range

| Age Category | Frequency | Percent | Valid Percent | Cumulative Percent |
|--------------|-----------|---------|---------------|--------------------|
| Upto 50 yrs  | 3         | 2.9     | 2.9           | 2.9                |
| 51 - 60 yrs  | 52        | 51.0    | 51.0          | 53.9               |
| 61 - 70 yrs  | 20        | 19.6    | 19.6          | 73.5               |
| Above 70 yrs | 27        | 26.5    | 26.5          | 100.0              |
| Total        | 102       | 100.0   | 100.0         | 100.0              |

This above frequency table reveals that peak incidence of patients with intracranial stenosis is between 51-60 yrs and without intacranial stenosis is above 70 yrs & 51-60 yrs in my study.
The above Bar diagram shows the incidence of intracranial stenosis in CVA with respect to age group with maximum incidence being between 51-60 yrs.

**Sex Distribution**

Among these 102 patients studied, male patients were 58 in number (56.9%) of the study and female subjects were 46(43.1% of the study). Among the study patients, there was no statistically significant difference in relation to gender status majority are males 56.9%.

**Table 3: Sex distribution**

| Frequency | Percent | Valid Percent | Cumulative Percent |
|-----------|---------|---------------|-------------------|
| Valid Female | 44 | 43.1 | 43.1 |
| Male | 58 | 56.9 | 56.9 |
| Total | 102 | 100.0 | 100.0 |

**Hypertension**

Among the study patients, hypertension was present in about 49 Subjects of CVA of 48% and in subjects with ICS, 61.8% of subjects had hypertension. Hypertension –ICS category was analysed using chi-square test and pearson chisquare value is 15.396 and degree of freedom is 1 and p value comes around p< 0.05 which is statistically significant.

**Table 4: Frequency of hypertension**

| Frequency | Percent | Valid Percent | Cumulative Percent |
|-----------|---------|---------------|-------------------|
| Valid ABSENT | 53 | 52.0 | 52.0 |
| PRESENT | 49 | 48.0 | 48.0 |
| Total | 102 | 100.0 | 100.0 |

**Figure 4: Bar diagram With Hypertension**

**Diabetes Mellitus**

Among the study patients of 102, Diabetes was present in 30 subjects in which 28 diabetic patients had intracranial stenosis accounting for 41.2%. Diabetes –ICS category was analysed using chi-square test, Fisher's Exact Test and pearson chisquare value is 13.600 and degree of freedom is 1 and p value comes around p< 0.05 (p< 0.05) which is statistically significant.

**Table 5: Hypertension Vs ICS**

| ICS | Absent | Present | Total |
|-----|--------|---------|-------|
| HYPERTENSION ABSENT | Count % within ICS | 27 | 79.4% | 26 | 38.2% | 53 | 52.0% |
| PRESENT | Count % within ICS | 7 | 20.6% | 42 | 61.8% | 49 | 48.0% |
| Total | Count % within ICS | 34 | 100.0% | 68 | 100.0% | 102 | 100.0% |

**Table 6: Frequency of Diabetes Mellitus**

| Frequency | Percent | Valid Percent | Cumulative Percent |
|-----------|---------|---------------|-------------------|
| Valid ABSENT | 72 | 70.6 | 70.6 |
| PRESENT | 30 | 29.4 | 29.4 |
| Total | 102 | 100.0 | 100.0 |

**Table 7: Diabetes Mellitus VS ICS**

| ICS | Absent | Present | Total |
|-----|--------|---------|-------|
| DIABETES MELLITUS | Count % within ICS | 32 | 94.1% | 40 | 58.8% | 72 | 70.6% |
| PRESENT | Count % within ICS | 2 | 5.9% | 28 | 41.2% | 30 | 29.4% |
| Total | Count % within ICS | 34 | 100.0% | 68 | 100.0% | 102 | 100.0% |

**Alcohol**

Among the study patients of 102, Alcohol was being consumed by 31 subjects in which 14 alcohol consumption subjects had intracranial stenosis accounting for 20.6%.
Alcohol–ICS category was analysed using chi-square test, and Pearson chi-square value is 9.269 and degree of freedom is 1 and p value comes around p<0.002 (p<0.05) which is statistically significant.

Table 8: Frequency of subjects with Alcoholism

|       | Frequency | Percent | Valid Percent | Cumulative Percent |
|-------|-----------|---------|---------------|--------------------|
| Valid | NO        | 71      | 69.6          | 69.6               |
|       | YES       | 31      | 30.4          | 100.0              |
| Total |           | 102     | 100.0         | 100.0              |

Table 9: Alcohol Vs ICS

|       | ICS Absent | ICS Present | Total |
|-------|------------|-------------|-------|
| ALCOHOL NO | 17 (50.0%) | 54 (79.4%) | 71 (69.6%) |
| YES | 17 (50.0%) | 14 (20.6%) | 31 (30.4%) |
| Total | 34 (100.0%) | 68 (100.0%) | 102 (100.0%) |

Smoking

Among the study patients of 102, Smokers were 34 subjects in which 16 smokers subjects had intracranial stenosis accounting for 23.5%. Smoking–ICS category was analysed using chi-square test, and Pearson chi-square value is 8.824 and degree of freedom is 1 and p value comes around p<0.003 (p<0.05) which is statistically significant.

Table 10: Frequency of Smokers

|       | Frequency | Percent | Valid Percent | Cumulative Percent |
|-------|-----------|---------|---------------|--------------------|
| Valid NO | 68        | 66.7    | 66.7          | 66.7               |
| YES | 34        | 33.3    | 33.3          | 100.0              |
| Total | 102       | 100.0   | 100.0         | 100.0              |

Table 11: Smoking Vs ICS

|       | ICS | Count | Absent | Present | Total |
|-------|-----|-------|--------|---------|-------|
| SMOKING NO | % within ICS | 16 | 47.1% | 76.5% | 66.7% |
| YES | % within ICS | 18 | 52.9% | 23.5% | 33.3% |
| Total | % within ICS | 34 | 100.0% | 100.0% | 100.0% |

Aortic Knob Calcification

Among the study patients of 102 Aortic knob calcification was present in 32 subjects accounting for 31.4%. In Aortic Knob Calcification vs ICS, Aortic knob calcification was present in 22 subjects of Intracranial stenosis subjects accounting to 32.4%

Aortic Knob Calcification –ICS category was analysed using chi-square test, Fisher's Exact Test and Pearson chi square. Among the study patients, there was no statistically significant difference. Table 13 Shows association and comparison of Aortic knob calcification subjects which was 32 with Intracranial stenosis, in which out of 32 Aortic knob calcification subjects, 22 patient had Intracranial stenosis. Accounting for 69% association of Aortic Knob calcification with Intracranial stenosis and 31% without intracranial stenosis. Hence Subject with Aortic knob Calcification had 69% significant association of Intracranial stenosis.

Table 12: Frequency of Aortic Knob Calcification

|       | Frequency | Percent | Valid Percent | Cumulative Percent |
|-------|-----------|---------|---------------|--------------------|
| Valid ABSENT | 70 | 68.6 | 68.6 | 68.6 |
| PRESENT | 32 | 31.4 | 31.4 | 100.0 |
| Total | 102 | 100.0 | 100.0 | 100.0 |
Conclusion
1. In my study patients with intracranial stenosis and without intracranial stenosis were compared and studied.
2. There was significant association between increased age and subjects with intracranial stenosis.
3. There was significant association between diabetes and subjects with Intracranial stenosis.
4. There was significant association between Hypertension and subjects with Intracranial stenosis.
5. There was significant association between Smoking and subjects with Intracranial stenosis.
6. There was significant association between Alcohol and subjects with Intracranial stenosis.

Table 13: Aortic Knob Calcification vs ICS

|                | ICS |       |       |       |
|----------------|-----|-------|-------|-------|
|                | Absent | Present | Total |
| AORTIC KNOB ABSENT CALCIFFICATION | 24 | 46 | 70 |
|                | 70.6% | 67.6% | 68.6% |
| PRESENT | 10 | 22 | 32 |
|                | 29.4% | 32.4% | 31.4% |
| Total | 34 | 68 | 102 |
|                | 100.0% | 100.0% | 100.0% |

7. There was no significant association between Lipid profile Total cholesterol, TGL, HDL, LDL and subjects with Intracranial stenosis.
8. There was significant association between Aortic knob stenosis and Intracranial stenosis when compared to patients without intracranial stenosis of 69%, signifying the importance of simple Chest Radiography in prediction of CVA.

In conclusion, my results suggest that Aortic knob calcification is a reliable predictor for Intracranial stenosis in ischemic stroke patients. An increase in the use of chest radiography as a screening or risk factor assessment tool may be justified, as AC has a strong specificity for infarcts that may enable a clinician to start medical management on asymptomatic atherosclerosis so as to prevent Cerebrovascular events and also improve the subject outcome; still larger studies are needed in this area as it is first study in our population, to become it generalize.

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Conflict of interest
All authors contributed equally in developing the manuscript.

References
1. Gorelick PB, Wong KS, Bae HJ, Pandey DK. Large artery intracranial occlusive disease: a large worldwide burden but a relatively neglected frontier. Stroke. 2008;39:2396–99.
2. Sacco RL, Kargman DE, Gu Q, Zamanillo MC. Race-ethnicity and determinants of intracranial atherosclerotic cerebral infarction. The Northern Manhattan Stroke Study. Stroke 1995;26:14–20.
3. Qureshi AI, Safdar K, Patel M, Janssen RS, Frankel MR. Stroke in young black patients. Risk factors, subtypes, and prognosis. Stroke. 1995;26:1995–98.
4. Weisberg LA. Clinical characteristics of transient ischemic attacks in black patients. Neurology. 1991;41:1410–14.
5. Wityk RJ, Lehman D, Klag M, Coresh J, Ahn H, Litt B. Race and sex differences in the distribution of cerebral atherosclerosis. Stroke. 1996;27:1974–80.
6. Wong LK. Global burden of intracranial atherosclerosis. Int J Stroke. 2006;1:158–59.
7. Kumar G, Kalita J, Kumar B, Bansal V, Jain SK, Misra U. Magnetic resonance angiography findings in patients with ischemic stroke from north India. J Stroke Cerebrovasc Dis. 2010;19:146–52.
8. Moustafa RR, Moneim AA, Salem HH, Shalash AS, Azmy HA. Intracranial steno-occlusive arterial disease and its associations in Egyptian ischemic stroke patients. Stroke. 2013;44:538–41.
9. Feldmann E, Daneault N, Kwan E, et al. Chinese-white differences in the distribution of occlusive cerebrovascular disease. Neurology. 1990;40:1541–45. [PubMed]
10. Gorelick PB, Caplan LR, Langenberg P, et al. Clinical and angiographic comparison of asymptomatic occlusive cerebrovascular disease. Neurology. 1988;38:852–58.