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The Yield of Cardiac Investigations in Patients Presenting with an Acute Ischemic Stroke

A single tertiary centre experience

Azhaar Alshukri,[1] *Sunil K. Nadar,[2] Arunodaya R. Gujjar,[2] Hatim Al Lawati,[2] Mohammed Al-Rawahi,[2] Isra Al-Kindi,[3] Maathar AlFarsi[3]

[1]Department of Medicine, Oman Medical Specialty Board, Muscat, Oman; [2]Department of Medicine, Sultan Qaboos University Hospital, Muscat, Oman; [3]Department of Medicine, College of Medicine, Sultan Qaboos University, Muscat, Oman.

**Corresponding Author's e-mail: sunilnadar@gmail.com*

Abstract

Objectives: Strokes are a major source of morbidity and mortality. The Aim of this study was to evaluate the effectiveness of routine cardiac investigations in identifying a cardioembolic aetiology for ischemic strokes. ***Methods:*** This was a retrospective study of patients who had presented with a stroke to our institution between January and December 2019. ***Results:*** A total 183 patients (mean age 66.2±13.5 years, 109 or 59.6% male) were included in the final analysis. The common risk factors were hypertension (74.9%) diabetes (61.7%), and hyperlipidaemia (54.6%). The Middle cerebral artery (MCA) was the commonest artery affected (44 or 24%). On admission, 14(7.6%) patients were in atrial fibrillation with the rest being in sinus rhythm. On 24-hour ECG holter monitoring, no abnormalities were noted in 135 patients. Atrial fibrillation was seen in 15(8.1%) patients (inclusive of the 14 who had AF on resting ECG). 32 (17.4%) patients had evidence of non-sustained atrial arrhythmia and 9(4.9%) had non sustained ventricular tachycardia. Thirty patients(16.3%) were also noted to have frequent supraventricular ectopics (>30/hour) while 5(2.7%) patients had a high ventricular ectopic burden (>10% burden). No significant

abnormalities were noted in the echocardiograms of the patients, but 10 out of 132 (7.5%) patients had a positive bubble echo. Twenty-four (13.1%) patients had enlarged left atria. ***Conclusion:*** The overall diagnostic yield of abnormalities from routine cardiac testing for patients with stroke appears to be low. Targeted screening of patients with crytogenic stroke as suggested by newer guidelines is recommended.

Keywords: Cerebrovascular Accidents; Echocardiography; Atrial Fibrillation; Oman.

Advances in knowledge

- Routine cardiac testing in patients with stroke has a low yield rate in terms of identifying cardiac source of embolism
- However, these tests help identify patients at high risk for future atrial fibrillation

Application to patient care

- Although 24 hour monitoring does not identify all patients with atrial fibrillation, it helps identify those at risk of atrial fibrillation
- Careful evaluation of these patients must be made to assess suitability for anticoagulation.

Introduction

Strokes are a leading cause of morbidity and mortality worldwide. According to figures from 2019, the reported prevalence was 101 million cases worldwide with around 12.2 million incident cases of stroke.[1] They are the second leading cause of death and the third leading cause of death and disability combined.[1] This is associated with increased costs and loss of productivity and in the United States alone, it is projected that the medical costs related to stroke will increase from around 75 billion dollars annually in 2010 to around 180 billion dollars by 2030, in addition to indirect costs due to loss of productivity from around 30 billion dollars annually in 2010 to around 55 billion dollars annually during the same period.[2] According to the latest data published by the WHO, stroke related deaths accounted for 11.1% of the total deaths, with the age adjusted death rate at 94.98 per 100,000 population in Oman. It is the third leading cause of mortality in Oman after coronary heart disease and diabetes mellitus.[3] Additionally, the prevalence of risk factors for stroke is high among the Omani population, adding to the potential economic burden of the disease.[4]

The aetiology of ischemic strokes can be divided into five categories based on the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) criteria, large artery atherosclerosis, cardioembolism, small vessel occlusion, stroke of other determined aetiology, and stroke of undetermined ("cryptogenic") aetiology.[5] Cardioembolic stroke accounts for about 20–25% of all ischemic strokes and is associated with a worse prognosis with respect to disability, mortality and both early and long -term recurrences compared to other aetiologies.[6;7]

Sources for cardioembolism are further classified into major- or minor-risk sources according to their (thrombo-) embolic potential.[8] The most common major-risk source of cardioembolism is atrial fibrillation (AF).[9] Less frequent major-risk sources are cardiomyopathies with left ventricular (LV) dysfunction, intracardiac thrombi, cardiac tumours, prosthetic valves, and endocarditis. Minor-risk sources include patent foramen ovale (PFO), atrial septum aneurysm (ASA), and calcification of aortic and mitral valves.[8]

The overall purpose of such classification of strokes using TOAST system (or any other similar ones) is that it has major implications for preventive management.[6] Strokes have a high incidence of recurrence with a five-year recurrence rates of around 30%.[10] Identifying the aetiology of the stroke is therefore important in preventing future strokes. While the large majority of larger or small artery strokes are treated with antiplatelet agents and statin, their long term relative risk reduction in the recurrence of stroke is about 20-25%,[11] in contrast, using anticoagulants for prevention of definitively recognized cardio-embolic stroke results in a long term relative risk reduction of 60-65%.[11] Further, cardio-embolic strokes are associated with a much higher morbidity and mortality as compared to other forms of stroke by virtue of their tendency to cause large infarcts with poor cardiovascular support for re-establishment of cerebral circulation. Thus diagnosis and prevention of cardioembolic strokes is relatively more effective (with anticoagulation- as compared to non-cardioembolic strokes) as well as more cost-effective (in that it prevents higher morbidity and mortality).

In the above context, the American Heart Association/American Stroke Association (AHA/ASA) and the European Stroke Organisation (ESO) had recommended routine cardiac testing such as a minimum of 24 hours of cardiac ECG monitoring and a transthoracic echocardiogram for all

patients who have suffered a stroke.[11;12] The diagnostic yield from these sets of investigations is variable with many studies recommending longer durations of cardiac monitoring to improve the diagnosis and identification of atrial fibrillation.[9;13] Similarly, there are studies suggesting the routine use of transoesophageal echo over transthoracic echo to improve the identification of cardiac abnormalities that can predispose to strokes.[14] While the older guidelines recommended cardiac investigations in all patients presenting with a stroke, newer guidelines however recommend these investigations in patients with cryptogenic strokes.[15]

In our institution, it is standard practice to perform 24-hour ECG holter monitoring and a transthoracic echocardiogram (with a bubble study) for all patients presenting with an ischemic stroke. The aim of this study was to assess the rate of identification of abnormalities with these tests in our institution.

Methods

All patients aged 18 and above, who were admitted with a final diagnosis of stroke between January and December 2019 at The Sultan Qaboos University Hospital (SQUH) were identified. Their electronic case records were reviewed and only those who had full cardiac evaluation were included in the final analysis. We excluded those whose scans had demonstrated an intracranial bleed or who died before any cardiac investigations were performed or those on whom investigations were not done due to presumed very poor prognosis or for other clinical reasons. We also excluded those in whom the case records were incomplete. Patients were diagnosed to have a stroke based on clinical findings and from a CT scan of the brain. Carotid artery imaging and MRI scans of the brain were not routinely performed. Ethical approval was obtained from the Medical research ethical committee of the Sultan Qaboos university Hospital, Muscat, Oman (MREC number 1365).

All eligible patients had undergone 24-hour holter ECG monitoring and a standard transthoracic echocardiogram with an agitated saline contrast study. The Holter data were analysed by SEER 1000 (GE Medical systems technologies Ltd., Boston MA, USA). The abnormalities were classified as in other major studies. Atrial fibrillation was considered if the episode lasted more than 30 seconds. Anything less was classified as atrial tachyarrhythmia. [16;17] The frequency of

premature ventricular contractions (PVC) was reported as high if the burden was greater than 10% of the total QRS complexes in a 24-hour period. [18] We classified those from 1-10% as medium and anything less was considered low. The frequency of premature atrial contractions (PAC) was considered to be high if it exceeded 30 PACs/hour (720 PACs in 24 hours), medium if it was between 10-30 PACs per hour (240-720 PACs per 24 hours) and low if less than 10 PACs per hour.[19]

Echocardiograms were performed using a GE Vivid 7 machine as per standard protocol.[(20)] The abnormalities that were examined for included valvular abnormalities such as mitral stenosis, intracardiac masses such as vegetations, tumors or thrombi and evidence of intracardiac shunts. An agitated saline study was also performed according to standard protocol with normal respiration and post-Valsalva manoeuvre where possible.[(20)] The study was positive if agitated saline was noted at the left sided cardiac chambers in less than 4 cardiac cycles. This could then identify patients with a patent foramen ovale (PFO) or other causes of an intracardiac shunt. The left atrium was considered to be enlarged if it measured more than 4cm in men and 3.9cm in women. Pulmonary hypertension was defined as mild if the mean pressure was calculated to be 25-35mmHg, moderate if between 35-45 mmHg and severe greater than 45 mmHg. [16]

The RoPE (Risk of Paradoxical Embolism) score has been developed and validated as an assessment tool to determine the probability that a PFO is responsible for a cryptogenic stroke.[21] It can be used when assessing patients with a PFO preceding closure. A high score correlates with increased likelihood that a PFO is responsible for the index stroke. The PFO-attributable fraction of stroke for a score of 7, 8, and 9 is 72%, 84%, and 88%, respectively, and defines a subset of patients who may benefit from PFO closure. We calculated the RoPE score for our patients as described before. [21]

The collected data were analysed using statistical software SPSS Statistics (SPSS Inc., Chicago, US) version 22. A descriptive analysis of the categorized variables was presented as proportions, and continuous variables were presented as the mean and standard deviation. Chi-square test was used to check for differences among groups for categorical variables.

Results

A total of 215 patients were identified who were admitted with a diagnosis of stroke during the specified time period. Of these 32 patients did not fulfil our inclusion criteria and 183 patients (mean age 66.2±13.5 years, 109 (59.6%) male and 74 (40.4%) female) were included in the final analysis of the study. The risk factors of the patients are summarized in Table 1. Hypertension was the commonest risk factor (74.9%) followed by diabetes (61.7%), and hyperlipidiemia (54.6%). 79 (43.2%) of patients had three cardiovascular risk factors followed by 36 (19.7%) who had two risk factors. Forty patients (21.9%) had one risk factor, while 28(15.3%) did not have any cardiovascular risk factor. Data on smoking habits was incomplete. 26.2% of patients had a previous myocardial infarction and in 52 patients (28.4%), this was a recurrent stroke. One patient had a prosthetic cardiac valve, and one was already known to have atrial fibrillation and both patients were on anticoagulation. At the time of admission with a stroke both these patients had INR values that were in the therapeutic range. All the patients with previous myocardial infarction were on a single antiplatelet agent. There were no differences between the demographics of the patients who presented with a first stroke or a recurrent stroke.

As per the TOAST classification types, small vessel disease was the commonest mechanism of stroke in this cohort accounting for 112 (61.2%) patients. Large artery stroke was the mechanism in 56 (30.6%) patients, while in 15 (8.2%) it was of undetermined aetiology. Cardioembolism, on its own, was not identified as a mechanism of stroke in any of these patients. The patients with atrial fibrillation had multiple atherosclerotic risk factors and therefore classified as stroke of undetermined aetiology. The Middle cerebral artery (MCA) was the commonest artery to be affected (44 or 24%), followed by the posterior cerebral artery in 13 (7.1%) patients. Almost a third of the patients (67 of 183 or 36.6%) had involvement of the left sided limbs, while 45 of 183 (24.6%) had involvement of right sided limbs and in another 71 patients (38.8%), the side of hemiplegia was not documented or there was no focal hemiplegia as it was either symptoms of posterior circulation (such as dizziness, cerebellar signs etc.) or a lacunar infarct or the patient was comatose.

All the patients had undergone a resting 12-lead-ECG on arrival. This identified 14 patients to be in atrial fibrillation on presentation with the rest being in sinus rhythm. All patients underwent a

24- hour holter ECG monitoring. The findings are summarized in table 2. The 24- hour recording did not show any abnormality in 135 patients. Atrial fibrillation was seen in 15 patients (one newly diagnosed in addition to the 14 who had AF on their resting ECG). 32 patients had evidence of non-sustained atrial arrhythmia and 9 had non sustained ventricular tachycardia. Thirty patients were also noted to have frequent supraventricular ectopics (defined as more than 30/hour) while 5 patients had a high ventricular ectopic burden (more than 10% burden). There were no differences between the findings in patients with a first or recurrent stroke.

A total of 165 patients had an echocardiogram performed during their stay in the hospital [Table 3]. There is no documented reason why the remaining 18 did not have an echocardiogram. None of the patients had any mass or vegetation or thrombus noted in the scan. Severe aortic stenosis was identified in 3 patients, severe Mitral stenosis in one patient and severe mitral regurgitation in three patients. Two were found to have severe pulmonary hypertension. 132 patients had an agitated saline contrast scan done of which 10 were reported as positive for a left to right shunt (positivity rate of 7.7%). The RoPE score of these patients were a median of 5 with a range from 2 to 8. Three patients had a score of 6 and one of 8. Twenty-four patients had a left atrial size that was above the upper limits of normal (4cm in males and 3.9 cm in females). There were no differences between patients presenting with a first or recurrent stroke.

The relationship between left atrial size and atrial arrhythmias is shown in table 4. There was a higher proportion of patients having AF and atrial tachyarrhythmias in the group with enlarged left atria. Although numerically different, there was no statistical difference between the PAC burden in the two groups.

Discussion

The primary aim of cardiac investigations after a stroke is to identify any potential source of cardioembolism with the intention to treat and prevent recurrence of strokes. These could be obvious thrombi or masses within the cardiac chambers, cardiac valve abnormalities or arrhythmias such as atrial fibrillation. Though the old stroke guidelines recommended routine testing in all patients with strokes, the current guidelines recommend routine imaging in the form of transthoracic echocardiography and monitoring for rhythm disturbances especially atrial

fibrillation for patients with cryptogenic strokes. Similarly, whilst earlier guidelines recommended a minimum of 24 hours of ECG monitoring, subsequent studies have demonstrated that longer monitoring increases the detection rate of atrial fibrillation[17;22;23] The latest guidelines have embraced this and recommend prolonged ECG monitoring of at least 48 to 72 hours or longer if possible.[24] None of the patients in our study had undergone prolonged monitoring. Besides the 14 patients who had AF on their resting ECG, 24-hour monitoring identified only one further patient.

Besides episodes of atrial fibrillation, there has been interest in atrial ectopics or premature atrial contractions (PAC) as a precursor to AF. Studies have demonstrated conclusively that patients with a high burden of PACs have a higher risk of developing AF.[19;25] Binici et al have shown that patients with a PAC rate of more than 30 per hour had a 2.7-fold increase in the risk of developing AF and also had a greater than 60% increased risk of death or stroke.[(19)] They found that for each increase of 10 PAC per hour, the risk of the primary end point of death or stroke increased by 27% and the risk of atrial fibrillation by 50%. While the American guidelines on stroke prevention do not specifically mention these patients, it has been previously recommended that patients with a high PAC burden would benefit from anticoagulation especially if their $CHADS_2VASC$ score is greater than 2. However, there are no studies to back this recommendation. In our study, 36 patients had some form of atrial arrhythmia with a similar number having a high burden of PACs. Given the propensity of these patients to develop AF in the future and in the absence of facilities to perform long term ECG monitoring, careful consideration should be given regarding anticoagulation of these patients.

The other abnormality that is commonly identified on holter monitoring is frequent ventricular ectopics. These can predispose to impaired LV systolic function and formation of LV thrombus which can embolise.[(26)] In our study, almost a fifth of the patients had at least moderate to high burden of VEs. Although this can represent a high adrenergic stage in the immediate post stroke state, these patients should be monitored for development of tachycardia related cardiomyopathy or other abnormalities.[(26)] Conduction abnormalities are a commonly reported findings on holter monitoring, but in our study, we did not detect any patients with significant conduction abnormalities.

Echocardiography can detect many potential cardiac sources of embolism such as left atrial thrombus, patent foramen ovale, atrial septum aneurysm, valvular or myocardial disease, vegetations or cardiac tumors amongst others.[27] Furthermore, it can reveal other cardiac pathologies of potential therapeutic consequences such as wall motion abnormalities or a reduced left ventricular function. The mode of echocardiography could be either transthoracic (TTE), which is widely available, non-invasive, less personnel-intensive and cheap or transoesophageal echocardiography (TOE) which is otherwise superior for evaluation of the aortic arch, left atrium and its appendage, and atrial septum.[14]

Agitated saline contrast study is often considered to be part of the protocol for echocardiography in patients who have a stroke with the aim of identifying any left to right shunts notably PFOs. The role of closing a PFO post stroke is still not clear with conflicting data. Earlier randomized controlled trials failed to show a statistically significant benefit for a PFO closure;[28;29] thus, many investigators believed that a PFO, being a not uncommon occurrence, was an incidental bystander in patients with stroke. However, meta-analyses and more recent specific trials have eliminated several confounding factors and possible biases and have demonstrated a benefit of the use of a shunt closure over medical therapy in patients with cryptogenic stroke, particularly among those below the age of 60 years with no obvious risk factors explaining the incident stroke.[30-32]

In our study 10 out of the 132 patients who had undergone an agitated saline contrast study were positive for a PFO. This is lower than the reported incidence of PFOs in the general population (20-30%) and the stroke population (around 50%).[33;34] We are unable to explain this discrepancy. Except for one patient, all had a RoPE score of less than 7. The reason for the patient with a high RoPE score not being referred for further TEE assessment was not documented. It could be argued therefore that to be cost effective, the agitated saline study should be performed only in those with a high RoPE score.

The TTE may also identify other surrogate markers of potential AF such as increased left atrial volume and left atrial strain. Besides this, other anatomical variations that can favour the promotion of thrombi can also be diagnosed. These include aneurysm of the interatrial septum (defined as a septal protrusion of greater than 11 to 15 mm and which is often associated with

PFOs),[35] the persistence of eustachian valve (which directs fetal blood flow towards the PFO) [36] and a prominent chiari network (persistence of a remnant of the fetal atrial development).[37] In our study, the echo reports did not comment on the presence of any of these abnormalities in any of the patients. The other abnormalities that were diagnosed on TTE in our study were minor valve abnormalities. However, it is unlikely that this contributed to the stroke.

The overall yield of positive tests from routine cardiac investigations for all patients presenting with a stroke appears low from our study. 14 patients had newly diagnosed AF on their presenting ECG with only one extra patient identified on 24-hour holter monitoring. Echocardiography identified 4 cases with significant valve disease and a doubtful link to the presenting stroke This is similar to other reported studies, where the diagnostic yield of routine testing was low and where the cost effectiveness of such routine tests was questioned.[38] However, if we include all the cases with surrogate markers of potential atrial fibrillation such as high PAC burden and dilated left atria on echocardiography, the diagnostic yield for all directly and indirectly linked pathologies is higher. Additional studies are needed to systematically ascertain whether anticoagulation in such patients carries any long-term benefits, especially as it relates to stroke prevention. Furthermore, we observed that the results of the cardiac investigations (apart from those with AF) did not appreciably alter the final management, thereby questioning the usefulness of these investigations in all patients with a stroke. Indeed, the newer guidelines, recommend these tests only in patients with cryptogenic strokes in contrast to the older guidelines where these tests were recommended in all patients with a stroke and would suggest that we change the policy in our hospital.

There were a few limitations in our study. This was a retrospective study that involved examining past electronic case records of the enrolled patients. The comprehensiveness of the case records therefore was a limiting factor as some patients had incomplete data and these were not included in the final diagnosis. We did not follow up the prognosis of these patients to see whether they had a recurrent stroke. Another limitation was the fact that the left atrium size was measured in two-dimension, but newer guidelines suggest that the LA area is to be calculated and adjusted to body surface area. This could have given us a more accurate account of the state of the LA.

Conclusion

The overall yield from cardiac investigations in patients presenting with a stroke is relatively low. They are, however, useful in identifying surrogate markers that increase the future risk of atrial fibrillation, though studies are required to investigate the effectiveness of long-term anticoagulation in these patients. Further studies are also required to ascertain the cost effectiveness of routine cardiovascular testing in all patients with a stroke and whether they influence management and outcome beyond identifying patients with AF.

Author Contribution

AA, IA and MA collected the data. SKN, ARG, HA and MAR analysed the data and drafted the manuscript. All authors approved the final version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

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Table 1: Demographics of the patients

	Overall group (percentage)	First stroke (n=131)	Recurrent stroke (n=52)	P value
Age	66.2+ 13.5	65.6+13.7	67.9+12.8	0.2
Gender				
Male	109(59.6%)	79 (60.3%)	30 (57.6%)	0.7
Female	74(40.4%)	52 (39.7%)	22 (42.4%)	
Diabetes	113 (61.7%)	82 (62.5%)	31 (59.6%)	0.7
Hypertension	137 (74.9%)	95(72.5%)	42 (80.7%)	0.2
Dyslipidemia	100(54.6%)	66 (50.3%)	34 (65.3%)	0.06
Previous MI	48 (26.2%)	29 (22.1%)	19 (36.5%)	0.04
Artery involved				
MCA	44(24%)	25 (19.1%)	19 (36.5%)	
PCA	13(7.1%)	10 (7.6%)	3 (5.7%)	
Basilolateral	5(2.7%)	5 (3.8%)	0	
ACA	5(2.7%)	3 (2.3%)	2 (3.8%)	
PICA	2 (1.1%)	1 (0.7%)	1 (1.9%)	
ICA	2(1.1%)	2 (1.4%)	0	
No clear artery identified	112(61.2%)	85 (64.8%)	27(51.9%)	0.14
Site of hemiplegia				
Right	45(24.6%)	35 (26.7%)	10 (19.1%)	

Left	67(36.6%)	45 (34.3%)	22 (42.3%)	
*Indeterminate**	71(38.8%)	51 (38.9%)	20 (38.4%)	0.59

MI- Myocardial infarction, MCA- Middle cerebral artery, PCA- Posterior cerebral artery, ACA- Anterior cerebral artery, PICA- Posterior inferior cerebellar artery, ICA- Internal carotid artery

**"Indeterminate" includes patients without hemiplegia such as lacunar infarcts, posterior circulation strokes, or where patient was comatose and it was difficult to ascertain the site of infarct or where site of hemiplegia was not documented.*

Analysis by chi-square test or students t-test as appropriate

Table 2: ECG and Holter monitoring

Test	Overall group Number(percentage)	First stroke (n=131)	Recurrent stroke (n-52)	P value
Rhythm on resting ECG	169(92.3%)	122 (93.1%)	47 (90.3%)	
Normal sinus rhythm	14(7.7%)	9 (6.9%)	5 (9.7%)	0.5
Atrial fibrillation				
Holter findings				
Normal	135 (73%)	98 (74.8%)	37 (71.1%)	
Atrial fibrillation	15(8.2%)	9 (6.8%)	6(11.5%)	
Atrial tachycardia	32 (17.5%)	21 (16%)	11 (21.1%)	
SVT	4(2%)	4 (3%)	0	
VT	9(4.9%)	5 (3.8%)	0	
Conduction abnormalities	2(1.1%)	2 (1.5%)	4 (7.6%)	0.38
PVC burden				
<1%	148(80.9%)	109 (83.2%)	39(75%)	
1-10%	30(16.4%)	20 (15.2%)	10 (19.2%)	
>10%	5(2.7%)	2 (1.5%)	3(5.7%)	0.21
PAC burden				
<10/hr	143(78.1%)	102 (77.8%)	41(78.8%)	
10-30/hr	10(5.5%)	7 (5.3%)	2 (3.8%)	
>30/hr	30(16.4%)	21(16%)	9(17.3%)	0.9

SVT- supraventricular tachycardia, VT- Ventricular tachycardia, PVC- premature ventricular contraction, PAC- premature atrial contraction

Analysis by Chi-square test

Table 3: Echo findings

Findings	Overall group (N=165)	First stroke (n-120)	Recurrent stroke (n=45)	P value
Ejection fraction (%)	54.2 ±11.1	54.8+11.2	52.6+10.7	0.23
LA size (mm)	25.7 (23.8-33.7)	26.86(24-34)	25.0(22.8-29.9)	0.07
LVIDd (mm)	4.2±0.73	4.19+0.72	4.13+0.69	0.66
Aortic regurgition				
No/Mild	157 (85.7%)	114 (95%)	43 (95.5%)	
Moderate	8 (4.4%)	6(5%)	2(4.4%)	
Severe	0	0	0	0.64
Aortic stenosis				
No/mild	161 (97.6%)	117(97.5%)	44(97.7%)	
Moderate	1(0.6%)	1(0.8%)	0	
Severe	3(1.8%)	2 (1.7%)	1(2.3%)	0.68
Mitral stenosis				
No/Mild	164(99.4)	120 (100%)	44 (97.7%)	
Moderate	0	0	0	
Severe	1(0.6)	0	1(2.3%)	0.21
Mitral regurgitation				
No/mild	150(90.9%)	108(90%)	42(93.3%)	
Moderate	12(7.3%)	9(7.5%)	3(6.7%)	
Severe	3(1.8%)	3(2.5%)	0	0.26
Pulmonary hypertension				
No	144(87.3%)	101(84.1%)	43(95.5%)	
mild	12(7.3%)	10(8.3%)	2(4.4%)	
Moderate	7(4.2%)	7(5.8%)	0	
Severe	2(1.2%)	2(11.7%)	0	0.20
Agitated saline echo (n=132) positive	10 (7.6%)	6(5%)	4(8.9%)	0.38
Enlarged LA	24 (13.1%)	21(17.5%)	3(6.7%)	0.08

LA- Left atrium, LVIDd- Left ventricular internal diameter in diastole, Left atrium was considered to be enlarged if it measured more than 4cm in men and 3.9cm in women. Analysis by chi-square test, students t-test or Mann-Whitney U test as appropriate

Table 4: Left atrial size and atrial arrhythmias

	Normal LA size (n=139)	Enlarged LA (n=24)	P value
PAC burden			
Low	113 (81.2%)	15 (62.5%)	
Medium	7 (5.1%)	2 (8.3%)	
High	19 (13.7%)	7 (29.2%)	0.11
Atrial fibrillation	8 (5.7%)	5 (20.8%)	0.01
Atrial tachyarrhythmias	24 (17.2%)	5 (20.8%)	0.1
PAC count	6(0-58)	33 (80-2402)	0.06*

*Values are number (percentage) or Median(Interquartile range) Analysis by chi-square test, *Analysis by Mann-Whitney test; PAC- Premature atrial contraction*