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Assessment Of Echocardiographic Parameters, Left Atrial Volume And Left Atrial Volume Index As Markers Of Cardiovascular Involvement In Patients With CKD.

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Abstract

Background: Cardiovascular morbidity secondary to Chronic Kidney Disease (CKD) is a well-established entity. However, estimation of the extent of the former has no formal criteria. The present study was taken up with the aim to study left atrial volume and left atrial volume index as markers of cardiovascular involvement in CKD. **Methods:** This cross sectional study included sixty patients (n=60) from the randomly selected cases admitted in emergency and indoor medical wards of Guru Nanak Dev Hospital, Amritsar. The sample was divided into three groups of twenty each on the basis of GFR. Group 1 consisted of CKD stage 3 patients, Group 2 consisted of CKD Stage 4 patients and Group 3 consisted of CKD Stage 5 patients. Echocardiography were done in every patient. Values of Left Atrial Diameter (LAD), Left Atrial Volume (LAV) and Left Atrial volume index (LAVi) were assessed in each of the three groups. Diastolic Dysfunction and values of Ejection Fraction were also assessed in each of the three groups and correlated with Left Atrial Volume Index (LAVi). **Results:** Increased value of LAVi (>34 mL/m^2) was 15% in Group 1, 40% in Group 2, and 65% in Group 3. Increased left atrial volume was significantly related to decreased ejection fraction in CKD stage 4 and 5 ($p<0.05$). **Conclusion:** Left atrial volume and left atrial volume index provide quantitative estimation of cardiovascular morbidity in patients with CKD.

Keywords: CKD, Echocardiography, Left Atrial Volume, Left Atrial Volume Index

INTRODUCTION

Chronic kidney disease (CKD) is a fairly prevalent chronic disease and imposes significant burden on the current health infrastructure. The primary etiologies of CKD are immunologic reactions (initiated by immune complexes or immune cells), tissue hypoxia and ischemia, exogenous agents like drugs, endogenous substances like glucose or paraproteins, and genetic defects.[1] The global estimated prevalence of CKD is 13.4%.[2]

The presence of CKD accentuates the adverse outcomes associated with other non-communicable diseases. Cardiovascular diseases among patients with CKD and end stage renal disease (ESRD) is one such subset. This is supported by the evidence that in patients with eGFR <60 mL/min per 1.73m^2, there is doubling of the rate of occurrence of atrial fibrillation, congestive heart failure and coronary artery disease.[3,4,5,6,7]

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Among the spectrum of cardiovascular diseases in CKD, abnormalities in left ventricular structure and function are common. These often precede the onset of clinical cardiovascular disease in patients with CKD and ESRD. The incidence of left ventricular hypertrophy (LVH) increases with progressive decline in renal function.[8] The left atrium is prone to volume induced changes and hence, gets profoundly affected in patients with CKD.

Trans Thoracic 2D Echocardiography is an established, economical and non-invasive method for estimating the risk for cardiovascular complications and for guiding treatment of chronic kidney disease patients. Recent guidelines from the American Society of Echocardiography (ASE) have recommended quantification of left atrial size using left atrial volume (LAV) measured by biplane two dimensional (2D) echocardiography. LA volume responds to changes in extracellular fluid volume. The LA volume has hence been applied as a non-invasive measure for detecting and monitoring volume overload in clinical studies in CKD patients on dialysis.[9]
Left atrium provides a window to the burden and chronicity of underlying cardiovascular disease in CKD patients. Among the different echocardiographic parameters available for assessing left atrium including diameter, area and volume, the LA volume has been identified as the most accurate and robust predictor of cardiovascular outcomes. Appropriate indexing according to body surface area will provide a standardization of parameters in CKD patients. Hence, Left atrial volume index can emerge as an important marker of cardiovascular involvement in various stages of CKD.

Aim of work:

To estimate left atrial volume and left atrial volume index, and assess them as parameters of cardiovascular involvement in stages 3, 4 and 5 CKD.

MATERIALS AND METHODS

This cross sectional study included sixty patients (n=60) from the randomly selected cases admitted in emergency and indoor medical wards of Guru Nanak Dev Hospital, Amritsar. This study was undertaken after approval of the Institutional Ethics Committee. Written informed consent of cases was obtained for their inclusion in the study. The sample was divided into three groups of twenty each on the basis of GFR. Group 1 consisted of CKD stage 3 patients (GFR between 30-60 mL/min per 1.73m^2), Group 2 consisted of CKD Stage 4 patients (GFR between 15-29 mL/min per 1.73m^2) and Group 3 consisted of CKD Stage 5 patients (GFR <15 mL/min per 1.73m^2). GFR was calculated using "Cockcroft Gault Equation".

Inclusion and Exclusion Criteria:

Those patients who fulfilled the criteria for CKD Stage 3, Stage 4 and Stage 5, and having age more than 18 years were included in our study. Patients who aged less than 18 years, had acute kidney injury, malignancies, evidence of major valvular heart disease especially mitral valve disease, previous history of atrial fibrillation were excluded from our study. All patients underwent complete clinical examination including measurement of blood pressure, pulse rate and systemic examination. Chronic kidney disease (CKD) patients were screened for the following biochemical parameters: Serum Creatinine

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(Jaffe's method), Blood Urea (Berthelot method), Total Serum Protein, Serum Albumin, RBS, Glycated Hemoglobin, Serum Electrolytes(serum sodium and serum potassium), Complete Urine Examination (spot), CBC, Ultrasound Abdomen, 12 Lead Surface and Resting Electrocardiogram and X-ray Chest PA View (In full inspiration for heart size) and Two dimensional Transthoracic Echocardiography.

Echocardiography procedure and interpretations:

Echocardiography was done in all the cases. Two dimensional and two dimensionally guided M-Mode images were recorded from the standardized views. The measurements were done on Philips i E33 Echocardiography machine. Parameters were recorded in accordance with the guidelines by American Society of Echocardiography.

Recommended Normal LA diameter is 28-40 mm (2.8-4.0 cm). Recommended normal LA volume is 22-58 ml. Recommended upper normal indexed LA volume is 34 mL/m2.

The echocardiographic measurements included left atrial size, which was assessed by M-Mode measurement of anteroposterior dimension and left atrial volume, which was calculated by using Two dimensional planimetry with Biplanar Simpson's rule on the frame just before the mitral valve opening or planimetry. Left atrial volume index (LAVi) was calculated by the LA Volume to Body surface area ratio. Body surface area was calculated according to DuBois and DuBois's simplified formula ($0.20247*weight^{0.425}*height^{0.725}$).[10]

Values of Left atrial volume and Left atrial volume index were compared among three groups of twenty patients each. Values greater than upper limit of normal were taken as high or increased for Left Atrial Diameter (LAD), Left Atrial Volume (LAV) and Left Atrial volume index (LAVi). Diastolic Dysfunction and values of Ejection Fraction were also assessed in each of the three groups and correlated with Left Atrial Volume Index(LAVi).[11,12]

Statistical analysis:

The data from present study was collected systematically and analyzed statistically according to the appropriate standard statistical methods including Chi-Square Test, One-Way ANOVA, Student 't' test (unpaired) and Pearson Correlation coefficient test. Analysis was done using SPSS 19.0 software. 'p' value of less than 0.05 was considered statistically significant.

RESULTS

A total of sixty patients (n=60) with CKD were included in our study after matching our inclusion and exclusion criteria. Gender distribution showed that 25 cases (41.6%) were males and 35 (58.3%) were females. Their age ranged between 30-83 years with mean age 57.71±12.59 years.

Left atrial diameter (LAD)

Mean Left Atrial Diameter (LAD) values in different study groups as observed were 4.08±0.77 in Group 1, 4.34±0.70 in Group 2 and 4.34±0.79 in Group 3.There was no significant difference in mean LAD among these groups (p>0.05)(Table 1).

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Table 1: Mean value of left atrial diameter in various groups

	No. of Patients	LAD (cm)		p value	
		Mean	SD		
Group 1	**20**	**4.08**	**0.77**	**Group1 vs Group 2**	**0.005**
Group 2	**20**	**4.34**	**0.7**	**Group2 vs Group 3**	**1**
Group 3	**20**	**4.34**	**0.79**	**Group 3 v Group 1**	**0**

LEFT ATRIAL VOLUME (LAV)

Mean Left Atrial Volume (LAV) values in different study groups as observed were 48.45±8.46 in Group 1, 56.90±7.53 in Group 2 and 59.20±8.05 in Group 3. There was significant difference in mean LAD on comparing group 1 with group 2, and also on comparing group 1 with group 3. (p>0.05) (Table 2).

Table 2: Mean value of left atrial volume in various groups

	No. of Patients	LAV (mL)		p value	
		Mean	SD		
Group 1	**20**	**48.45**	**8.46**	**Group1 vs Group 2**	**0.005**
Group 2	**20**	**56.9**	**7.53**	**Group2 vs Group 3**	**1**
Group 3	20	59.2	8.05	Group 3 v Group 1	0

Left Atrial Volume Index

Mean Left Atrial Volume index (LAV) values in different study groups as observed were 27.94±5.86 in Group 1, 34.57±5.24 in Group 2 and 37.00±5.71 in Group 3. There was significant difference in mean LAVi on intergroup comparison (p<0.05) (Table 3).

Table 3: Mean value of left atrial volume index in various groups

	No. of Patients	LAVi (mL/m2)		p value	
		Mean	SD		
Group 1	**20**	**27.94**	**5.86**	**Group1 vs Group 2**	**0.001**
Group 2	**20**	**34.57**	**5.24**	**Group2 vs Group 3**	**0.001**
Group 3	**20**	**37**	**5.71**	**Group 3 v Group 1**	**0**

LAVi was high in 3, 8 and 13 patients in group 1, 2 and 3 respectively. A significant difference was observed between group 3 and 1 (p<0.05). (Table 4)

Table 4 : Group wise distribution of patients based on left atrial volume index

LAVi (mL/m2)	Group-1		Group-2		Group-3	
	No. of cases	%	No. of cases	%	No. of cases	%
Normal (<34)	**17**	**85**	**12**	**60**	**7**	**35**
High (>34)	**3**	**15**	**8**	**40**	**13**	**65**
	20	**100**	**20**	**100**	**20**	**100**
p value						
Group1 vs Group 2				**0.076**		

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Group2 vs Group 3	**0.113**
Group 3 v Group 1	**0.001**

Correlation Analysis

On correlating LAD and diastolic dysfunction, we observed that within group 1, Diastolic Dysfunction was present in 3 patients with LAD>4 and 4 patients with had LAD≤4. Similarly in group2, Diastolic Dysfunction was present in 12 patients with LAD >4 and 3 patients with LAD≤4. In Group 3, 10 patients with LAD>4 and 3 patients with LAD ≤4 showed diastolic dysfunction. The relationship was statistically significant only within group 3 ($p<0.05$).

For LAVi, Diastolic Dysfunction was present in 2 patients with LAVi>34 and 5 patients with LAVi≤34 within group 1, in 7 patients with LAVi>34 and 8 patients with LAVi ≤34 within group 2 and in 12 patients with LAVi>34 and 1 patient with LAVi≤34 within group 3. The results were statistically significant in relation to only group 3. ($p<0.05$).

Group Wise Analysis:

On correlating LAVi in group 1, we observed that LAVi was positively correlated with LAD and the correlation was significant ($p<0.05$). It was inversely correlated with both GFR and EF but only the decrease in GFR was significantly related to LAVi ($p<0.05$).

In group 2, LAVi positively correlated with LAD and the correlation was significant ($p<0.05$). With EF, the correlation was not significant ($p>0.05$). LAVi was found to be inversely correlated with GFR and the correlation was not significant ($p>0.05$).

In group 3, LAVi positively correlated with LAD and the correlation was significant ($p<0.05$). LAVi was inversely correlated with GFR and EF but the correlation was only significant with EF ($p<0.05$).

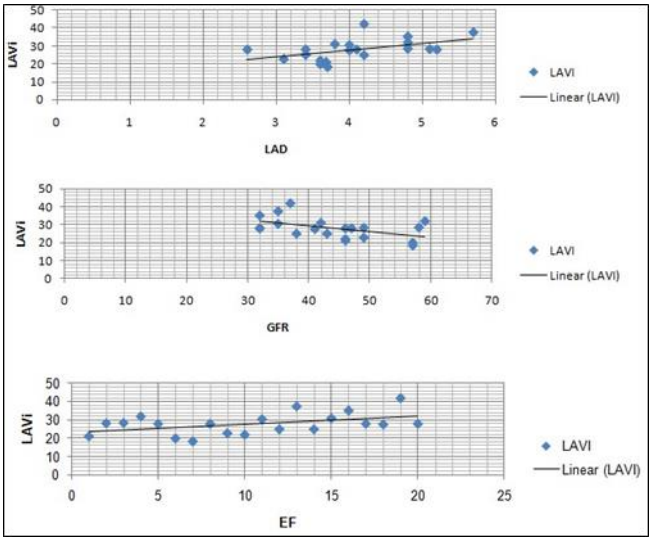

Fig 1. Correlation analysis for group 1

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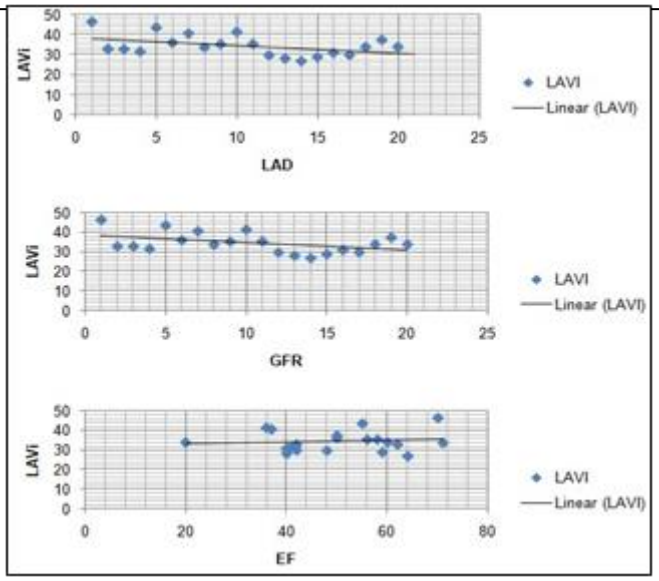

Fig 2.Correlation analysis for group 2

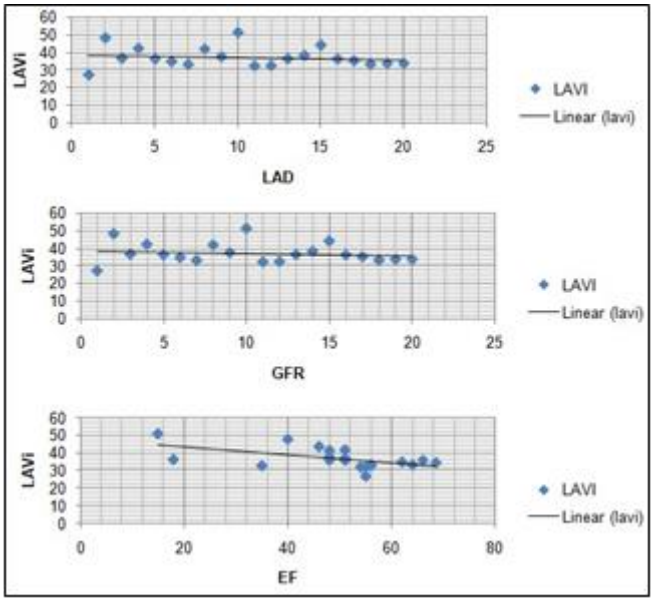

Fig 3. Correlation analysis for group 3

DISCUSSION

The present study suggests that an increase in LAVi values, independent of other echocardiographic parameters, correlates with the increase in the CKD stage. This increase in the value of LAVi has a significant relation with diastolic dysfunction and decreased ejection fraction as the disease progresses from stage 3 to stage 5 CKD.

In the present study, it was observed that the mean age of the patients was 57.71±12.59 years. It was comparable to a previous studies conducted by Cai et al, where mean age was 60±10 years in patients with CKD stages 3-5.[13] Also, it was comparable to the study with that

of Kadappu *et al* where mean age was 65.5±16 years.[14]
Female population predominated in our study accounted for 58.33%. On contrary, Cai *et al* and Chen *et al* reported male predominance in their studies, with males accounting for 56.1% and 63.9% respectively.[13,15]
Mean creatinine (mg/dl) observed in our study was 3.01±1.55. In a study by Cai et al,[13] they reported mean creatinine levels of2.52±1.39. This difference could be attributed to the difference inthe sample size included in both studies.Mean body surface area (m^2) in our study came out be 1.65±0.17. This was not comparable to previous reports by Kadappu et al.[14] and Hee et al.[16] These differences could be attributed to the difference in the genetic inbuilt of the population studied. Various parameters of two-dimensional (2D) echocardiography including Left atrial diameter, Left atrial volume, Diastolic dysfunction and Ejection fraction were recorded in accordance with American Society of Echocardiography.[14,17]

The mean value of Left atrial diameter (LAD) (cm) in our study was 4.25±0.75. It was found to be different from the study conducted by Yang et al [18], where mean LAD of 3.73±0.63 was present among patients of CKD stages 3-5. Mean LAD of 3.9±0.6 was found in a study by Chen et al,[15] where patients involving CKD stages 3-5 were included. The differences could be attributed to the variation in the sample size included in each study.

The mean value of Left Atrial Volume Index (LAVi) (mL/m^2) in our study was calculated to be 33.17±6.74. It was comparable to the mean LAVi of 32.6±12.3 present in CKD patients in a

study done by Hee et al.[16] Mean LAVi of 38.5±10.3 was present in a study by Kadappu et al,[14] where stage 3 CKD patients were compared with risk factor matched subjects and normal healthy population. Mean LAVi of 34±15 was present in a study by Barberato et al,[19] but these results were taken from a population on hemodialysis.

Kim et al,[20] in a study evaluated the impact of an enlarged left atrium on all cause and CV mortality in 216 patients with CAPD. They found that increased left atrial volume index (>32mL/m2) predicted all cause and CV mortality. This is in contrast to our study, where LAVi>34mL/m2 was taken to depict increased cardiovascular involvement in CKD.

In our study, LAVi was correlated with increased diastolic dysfunction, as the disease progresses. In a study done by Barberato et al,[19] it was demonstrated that LAVi was correlated with diastolic dysfunction severity in hemodialysis patients.

Our study used Body surface area (BSA) as an indexing method for left atrial volume. It was similar to the study done by Barberato et al,[19] where they indexed left atrial volume with body surface area as well. Left atrial volume was also indexed to BSA in a study by Kadappu et al.[14] Similarly, BSA was used asan indexing method in a study by Heeet al.[16] In contrast, Tripepiet al,[21] in a study estimated the CV risk in end stage renal disease (ESRD) using height as an indexing method for left atrial volume. It has been shown that adjustment to body size using height failed to nullify the gender influence on atrial size, unlike the adjustment to body surface area.
Many studies have proven the significance of LAVi assessment in end stage renal disease but LAV and LAVi as a marker of CV involvement

in CKD stage 3, 4 and 5 is not well illustrated.

Hence, in our study, we have assessed the values of left atrial volume index in stage 3, 4 and 5 CKD. It was interpreted from our study that as the CKD stage increases, there is increase in the value of left atrial volume index (LAVi). This increment in LAVi values with progression of CKD from stage 3 to stage 5 was associated with increase in diastolic dysfunction and decrease in ejection fraction.

CONCLUSION

Cardiovascular morbidity in a patient with CKD can be assessed objectively using Left Atrial Volume index. There is an associated increase in diastolic dysfunction and decrease in ejection fraction which parallels the increment in CKD stage. Hence, it provides a window for the physician to foresee the prognosis of the patient.

REFERENCES

1. Matovinović MS. Pathophysiology and Classification of Kidney Diseases. EJIFCC. 2009;20(1):2-11.
2. Lv JC, Zhang LX. Prevalence and Disease Burden of Chronic Kidney Disease. Adv Exp Med Biol. 2019;1165:3-15. doi: 10.1007/978-981-13-8871-2_1.
3. Kottgen A, Russell SD, Loehr LR, Crainiceanu CM, Rosamond WD, Chang PP, et al. Reduced kidney function as a risk factor for incident heart failure: the atherosclerosis risk in communities (ARIC) study. J Am Soc Nephrol. 2007;18(4):1307-15. doi: 10.1681/ASN.2006101159.
4. Abramson JL, Jurkovitz CT, Vaccarino V, Weintraub WS, McClellan W. Chronic kidney disease, anemia, and incident stroke in a middle-aged, community-based population: the ARIC Study. Kidney Int. 2003;64(2):610-5. doi: 10.1046/j.1523-1755.2003.00109.x.
5. Wattanakit K, Folsom AR, Selvin E, Coresh J, Hirsch AT, Weatherley BD. Kidney function and risk of peripheral arterial disease: results from the Atherosclerosis Risk in Communities (ARIC) Study. J Am Soc Nephrol. 2007;18(2):629-36. doi: 10.1681/ASN.2005111204.
6. Astor BC, Coresh J, Heiss G, Pettitt D, Sarnak MJ. Kidney function and anemia as risk factors for coronary heart disease and mortality: the Atherosclerosis Risk in Communities (ARIC) Study. Am Heart J. 2006;151(2):492-500. doi: 10.1016/j.ahj.2005.03.055.
7. Alonso A, Lopez FL, Matsushita K, Loehr LR, Agarwal SK, Chen LY, Soliman EZ, Astor BC, Coresh J. Chronic kidney disease is associated with the incidence of atrial fibrillation: the Atherosclerosis Risk in Communities (ARIC) study. Circulation. 2011;123(25):2946-53. doi: 10.1161/CIRCULATIONAHA.111.020982.
8. Levin A, Singer J, Thompson CR, Ross H, Lewis M. Prevalent left ventricular hypertrophy in the predialysis population: identifying opportunities for intervention. Am J Kidney Dis. 1996;27(3):347-54. doi: 10.1016/s0272-6386(96)90357-1.
9. Ozkahya M, Ok E, Cirit M, Aydin S, Akçiçek F, Başçi A, et al. Regression of left ventricular hypertrophy in haemodialysis patients by ultrafiltration and reduced salt intake without antihypertensive drugs. Nephrol Dial Transplant. 1998;13(6):1489-93. doi: 10.1093/ndt/13.6.1489.
10. Fraser SD, Blakeman T. Chronic kidney disease: identification and management in primary care. Pragmat Obs Res. 2016;7:21-32. doi: 10.2147/POR.S97310.
11. Jameel FA, Junejo AM, Khan QUA, et al. Echocardiographic Changes in Chronic Kidney Disease Patients on Maintenance Hemodialysis. Cureus. 2020;12(7):e8969. doi:10.7759/cureus.8969
12. Kosaraju A, Goyal A, Grigorova Y, Makaryus AN. Left Ventricular Ejection Fraction. 2021 May 3. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 29083812.
13. Cai QZ, Lu XZ, Lu Y, Wang AY. Longitudinal changes of cardiac structure and function in CKD (CASCADE study). J Am Soc Nephrol. 2014;25(7):1599-1608. doi:10.1681/ASN.2013080899
14. Kadappu KK, Abhayaratna K, Boyd A, French JK, Xuan W, Abhayaratna W, et al. Independent Echocardiographic Markers of Cardiovascular Involvement in Chronic Kidney Disease: The Value of Left Atrial Function and Volume. J Am Soc Echocardiogr. 2016;29(4):359-67. doi: 10.1016/j.echo.2015.11.019.

15. Chen SC, Su HM, Hung CC, Chang JM, Liu WC, Tsai JC, et al. Echocardiographic parameters are independently associated with rate of renal function decline and progression to dialysis in patients with chronic kidney disease. Clin J Am Soc Nephrol. 2011;6(12):2750-8. doi: 10.2215/CJN.04660511.
16. Hee L, Nguyen T, Whatmough M, Descallar J, Chen J, Kapila S, et al. Left atrial volume and adverse cardiovascular outcomes in unselected patients with and without CKD. Clin J Am Soc Nephrol. 2014;9(8):1369-76. doi: 10.2215/CJN.06700613.
17. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al; American Society of Echocardiography's Nomenclature and Standards Committee; Task Force on Chamber Quantification; American College of Cardiology Echocardiography Committee; American Heart Association; European Association of Echocardiography, European Society of Cardiology. Recommendations for chamber quantification. Eur J Echocardiogr. 2006;7(2):79-108. doi: 10.1016/j.euje.2005.12.014.
18. Chen SC, Chang JM, Tsai YC, et al. Left atrial diameter and albumin with renal outcomes in chronic kidney disease. Int J Med Sci. 2013;10(5):575-584. doi:10.7150/ijms.5845
19. Barberato SH, Pecoits Filho R. Prognostic value of left atrial volume index in hemodialysis patients. Arq Bras Cardiol. 2007;88(6):643-50. doi: 10.1590/s0066-782x2007000600004.
20. Kim SJ, Han SH, Park JT, Kim JK, Oh HJ, Yoo DE, Yoo TH, Kang SW, Choi KH. Left atrial volume is an independent predictor of mortality in CAPD patients. Nephrol Dial Transplant. 2011 Nov;26(11):3732-9. doi: 10.1093/ndt/gfr118.
21. Tripepi G, Benedetto FA, Mallamaci F, Tripepi R, Malatino L, Zoccali C. Left atrial volume monitoring and cardiovascular risk in patients with end-stage renal disease: a prospective cohort study. J Am Soc Nephrol. 2007;18(4):1316-22. doi: 10.1681/ASN.2006080881.

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