Evaluation of left atrial function using four-dimensional volume-strain in end-stage renal disease patients with preserved left ventricular ejection fraction

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Abstract

Objective: The purpose of this study was to investigate alterations in routine echocardiographic parameters and left atrial(LA) strains in normal LA and large LA groups in end-stage renal disease(ESRD) patients. **Methods:** Thirty-five age-matched healthy individuals and 82 patients with ESRD, including 52 with LA maximum volume index(LAVmax I)<34 ml/m2 (normal LA group)and 30 with LAVmax I[?]34 ml/m2 (large LA group), were enrolled. LA volumes and longitudinal and circumferential strains were measured using 4-dimensional(D) volume-strain technology. **Results:** Left ventricular(LV) wall thickness, the Left ventricular mass index(LVMI), peak early diastolic trans-mitral flow velocity/average peak early diastolic mitral annular velocity(E/ E'), and peak systolic dispersion(PSD) were higher in normal LA and large LA group compared with the control group. Mitral valve early diastolic velocity/mitral valve late diastolic velocity(E/A), the early diastolic velocity at the septal mitral annulus(E' septal), the early diastolic velocity at the lateral mitral annulus (E' lateral), global longitudinal strain(GLS), left atrial peak longitudinal strain of reservoir function (LASr) and left atrial peak longitudinal strain of conduit function(LAScd) were lower in normal LA and large LA group compared with the control group. Left atrial peak circumferential strain of reservoir function(LASr-c) and left atrial peak circumferential strain of contractile function(LASct-c) were lower in the large LA group compared with the control group. In ESRD patients, LASr-c and LASct-c showed a good correlation with LAVmax I. **Conclusions:** This study showed that LA longitudinal strains had decreased before LA enlargement. When LA enlargement occurred, the circumferential strains decreased. This may indicate that longitudinal strain changed earlier than circumferential strain in ESRD patients.

INTRODUCTION

Patients with ESRD often have severe reductions in life quality and life expectancy, which are related to the increasing cardiovascular (CV) risk factors, such as cardiac structural and functional changes[1-2]. Previous studies found that left atrial volume(LAV) enlargement often existed in ESRD patients and may be used to predict LV diastolic dysfunction[3]. LAV might also be possible to stratify risk and guide early treatment in ESRD patients[4].

LA function was traditionally assessed by the LA size or volume, trans-mitral tissue Doppler measurements, pulmonary venous flow evaluations, and two-dimensional(2D) LA strain. It is well known that the LA myocardium includes longitudinal and circumferential layers which are predominately arranged in inner and outer layers, respectively. 2D LA strain could only reflect the longitudinal strain of the LA myocardium. LA 4D echocardiography could evaluate the longitudinal strain combined with circumferential strain in 4D space. Several studies demonstrated that the 2D LA strain deteriorated in ESRD patients[5,6]. However, 4D

LA strains in ESRD patients have never been assessed. Therefore, the objective of our study was to measure values of longitudinal and circumferential LA strains using 4D echocardiography in ESRD patients.

METHODS

Study population

Eighty-two consecutive ESRD patients receiving dialysis at the Nephrology Department of Wuxi No.2 hospital between January 2021 and December 2021 were enrolled. The enrolled patients were divided into normal LA(LAVmax I<34 ml/m2) and large LA(LAVmax I[?]34 ml/m2) groups according to LAVmax I[7]. Inclusion criteria included age[?]18 years, renal dialysis for at least three months, LVEF[?]50%, normal sinus rhythm, without other systemic or organic diseases. Exclusion criteria were as follows: age<18 years, low LVEF<50%, patient history, physical examination, electrocardiography and echocardiography diagnosed suspected coronary artery disease (CAD), angiographically proven CAD, history of coronary angioplasty, moderate or severe valvular regurgitation or stenosis, pericarditis, medium or massive pericardial effusion, cardiac arrhythmia, metabolic diseases, systemic diseases, poor quality of echocardiographic images. Thirty-five age- and gender-matched healthy individuals, without the classic CV risk factors or any systemic diseases, were recruited as the control group.

Data collection

Routine biochemical tests including a lipid profile, blood glucose level, and renal function parameters were performed in all patients. Weight and height measurements were used to calculate body surface area(BSA).

Echocardiography

All transthoracic echocardiographic examinations, using a Vivid E95 Version 203 instrument(GE Medical Systems, Horten, Norway) were performed at rest in the left lateral decubitus position. The ultrasound investigation started with an optimal ECG signal with a clear definition of the QRS complex and P wave. Images were obtained using Vivid Dimension with a 2-to 4.5-MHz M5Sc 2D transducer and a 2.5-to 4-MHz 4Vc 4D transducer. Images were stored digitally and were analyzed offline using EchoPAC software(GE Healthcare, Milwaukee, WI, USA).

Two-Dimensional and Doppler Assessment

Interventricular septum thickness (IVST) at the end of the diastolic phase, left ventricular posterior wall thickness (LVPWT) at the end of the diastolic phase, and LV end-diastolic diameter(LVEDD) were measured in parasternal long-axis view. LV mass(LVM) was calculated from the l long-axis view using the following formula: LVM=0.8×[1.04x(LVEDD+IVST+LVPWT)3-(LVEDD)3]+0.6. The LVM index(LVMI)=LVM/BSA. LV ejection fraction(LVEF) was measured by the modified biplane Simpson's method.

Pulse-Doppler ultrasound of the mitral inflow was obtained to measure peak early diastolic velocity(E), late diastolic velocity(A), E wave deceleration time(E-DT), and E/A ratio. Pulsed tissue Doppler ultrasound of mitral annular was used in the apical 4-chamber view to measure the septal and lateral mitral annular early diastolic velocity(E'septal and E'lateral). E/E' ratio was the average value of E/ E'septal and E/ E'lateral.

Two-Dimensional Speckle Strain Assessment

Two-dimensional speckle tracking strain technology was used to measure LV global longitudinal strain(GLS) and peak systolic dispersion(PSD). The endocardial borders were delineated in the end-systolic frame of the 2D images from apical 4-,3-, and 2-chamber views. Segments that failed to track were manually adjusted by the operator.

GLS was calculated as the mean strain of all apical views. PSD was calculated as the standard deviation(SD) of LV 17 segment time to peak longitudinal strain.

Four-Dimensional Volume and Strain Assessment

4D volume transducer was used to obtain images in an apical 4-chamber view which displayed LA walls clearly. Images of 3 cardiac cycles were obtained with a 4D frame rate >40% of the heart rate(HR). The patients were asked to hold their breath when the 4D model was performed. The volume 4D auto LAQ measurement model was used to analyze the LA function. Setting landmarks and adjusting the mitral valve center on every plane at end-systole clearly displayed the mitral annulus and LA walls. The software presented the following standard 4D parameters: LAVmin (minimal volume, mL), LAVmax (maximum volume, mL), LAVpreA (volume at pretrial contraction, mL), LAEV(emptying volume, mL), LAEF (emptying fraction, %), LASr (peak longitudinal strain of reservoir function, %), LAScd (peak longitudinal strain of conduit function, %), LASct (peak longitudinal strain of contractile function,%), LASr-c (peak circumferential strain of reservoir function), LAScd-c (peak circumferential strain of conduit function, %), LASct-c (peak circumferential strain of contractile function, %).

Statistics

Data were expressed as mean+-SD for continuous variables and as percentages for categorical variables. Differences between the three groups were tested by analysis of variance(ANOVA) after having verified the normal distribution of variables. Categorical variables were compared using the "chi-square" test. Correlation between LAVmax I and LA 4D strain parameters was tested by the Pearson correlation. A P value <0.05 was considered to be statistically significant. Statistical analyses were calculated using SAS 9.4 software.

RESULTS

Clinical characteristics

Clinical characteristics of the control, normal LA ESRD, and large LA ESRD groups were detailed in Table 1. The normal LA ESRD and large LA ESRD groups had higher systolic BP, diastolic BP, CRE, and BNU compare to the control group, whereas age, gender, HR, BSA, and other biochemical data did not differ between the three groups.

Two-dimensional echocardiographic analysis

Parameters derived from two-dimensional echocardiography were shown in Table 2. Pulsed Doppler and tissue Doppler echocardiography presented E/A ratio, E' septal, E' lateral, and E/E' ratio of LV diastolic function. These parameters were impaired in normal LA ESRD and large LA ESRD groups, whereas LVEF was preserved (P<0.05).

Two-dimensional speckle tracking echocardiography presented GLS and PSD. GLS was decreased and PSD was increased in both ESRD groups, whereas LVEF was preserved (P<0.05). ESRD patients in both groups had significantly higher IVST, LVPWT, and LVMI than controls(P<0.05).

Four-dimensional echocardiographic analysis

The 4D LA echocardiography results of the controls and normal LA ESRD and large LA ESRD groups were presented in Table 3. Large LA ESRD patients had reduced LAEF compared with control subjects(P<0.05). Large LA ESRD patients had increased LA Vmin, LA Vmin I, LA Vmax, LA Vmax I, LA VpreA, LA VpreA I, LA EV, LA EV I and significantly decreased strain values with lower LASr, LAScd, LASr-c, and LASct-c than the controls(P<0.05). Increased LA volumes, impaired longitudinal reservoir and conduit functions, and impaired circumferential reservoir and contractile functions were revealed. Normal LA ESRD patients had significantly decreased strain values with lower LASr and LAScd than the controls(P<0.05). Declined LA longitudinal reservoir and conduit functions were indicated.

Correlation analysis between LAVmax I and LA 4D strain were presented in Table 4 and figure1. Correlation analysis indicated a significant relation between LAVmax I and LA 4D circumferential strain(LASr-c [r= -0.266, p = 0.0169], LASct-c [r = 0.422, p<.0001]).

DISCUSSION

The main findings of the current study can be summarized as follows: (1) Both large and normal LA ESRD patients had significant reduction of LA longitudinal reservoir and conduit functions according to LA 4D strains; (2) In large ESRD patients, there was also a decrease in LA circumferential reservoir and contrast functions. (3) Correlation analysis indicated a significant relation between LAVmax I with LASr-c and LASct-c in ESRD patients.

Various echocardiographic methods for ESRD assessment had been used, including conventional and new echocardiographic techniques [8,9]. In this study, IVST, LVPWT, and LVMI were increased in both ESRD patients. It was suggested that LV remodeling existed in ESRD patients. In ESRD patients, myocardial hypertrophy may compensate for an increase in the cardiac afterload, and maintain normal systolic function. When the compensation mechanism deteriorates, LV EF will reduce. We found that both large and normal LA ESRD patients presented impaired LV diastolic function and increased LV filling pressure measured by E/A ratio, E' septal, E' lateral, and E/E' ratio. This may be related to LV compensatory hypertrophy. Some studies revealed that GLS is reproducible, stable, and used as a load-independent measure of LV systolic function[9,10]. GLS is correlated with LVEF and more sensitive to evaluating early LV systolic dysfunction than LVEF. This study showed that GLS decreased in large and normal LA ESRD patients compared with the normal subjects, indicating that these patients had early systolic dysfunction, while LVEF is still in the normal range; this is consistent with the results of previous studies[8,9,11]. PSD is the standard deviation of the peak of the 17 segments of the myocardium. In this study, PSD was significantly increased in both ESRD patients, suggesting that LV systolic dyssynchrony existed at the early stage of ESRD. LV systolic dyssynchrony reduces ventricular pump function with increased oxygen consumption and may result in arrhythmia susceptibility[12]. Patients with left ventricular mechanical dyssynchrony (LVMD) have a higher mortality rate and poorer survival[13].

With the development of mechanical and transducer technology, the automated 4D LA volume-strain echocardiography allows for a more accurate assumption of the geometry of LA with a higher temporal resolution and spatial resolution and may provide more useful quantitative and objective data in the diagnosis of LA dysfunction[14]. Previous studies showed that increased LA size is linked to atrial fibrillation(AF), obstructive sleep apnea(OSA), adverse cardiac events, elevated mortality in patients with ESRD[14,15]. LA strain provided a detailed analysis of LA dysfunction and LV filling pressures and was divided into three phases: reservoir strain: pulmonary venous blood return into LA during LV systole; conduit strain, the passage of blood to LV through diastasis until the onset of contraction; Contraction strain: the passage of blood to LV during late ventricular diastole[16]. Previous studies on LA strain (LAS) were based on two-dimensional speckle-tracking echocardiography(STE). Compared with 4D LA volume-strain echocardiography, the main limitation of two-dimensional STE can be partial displacement of speckles outside the image plane. 4D LA volume-strain echocardiography may overcome this limitation due to its volumetric dataset. LAS was described in lots of diseases such as atrial fibrillation (AF), heart failure, coronary artery disease, cardiac amyloidosis, valvular heart disease, and breast cancer[17].LAS may identify LA dysfunction before anatomical changes occur[18]. As we know, LA consists of two layers, including longitudinal and circumferential fibers. The 4D LA volume-strain echocardiography automatically calculates longitudinal and circumferential LA strain values and phasic volumes. In this study, both large and normal LA ESRD patients had a significant reduction of LA longitudinal reservoir and conduit functions compared with the control group. Large LA ESRD patients also had significantly lower circumferential reservoir and contractile strain values than the control group. Previous studies had indicated that LA strain is impaired before changes in volume appear, thus being able to predict LA dysfunction in chronic kidney disease patients[19]. This study showed that LA longitudinal strains had decreased before LA enlargement. When LA enlargement occurred, the circumferential strains decreased. This may indicate that longitudinal strain changed earlier than circumferential strain in ESRD patients. This may be related to the position of longitudinal myocardial fibers which are mainly arranged in the deep layer. In the stratified strain of the left ventricle, it was found that the endocardium strain changed earlier than the other two layers[20]. The mechanism may be similar to that of left atrial strain, that is, the endocardium of the heart cavity is first affected. In normal LA ESRD patients, the longitudinal strain changes were mainly in reservoir and conduit function, but no change in contractile function. In large LA ESRD patients, the longitudinal strain changes were mainly in reservoir and conduit function, while the circumferential strain changes were mainly in the reservoir and contractile function. More research is needed to clarify the possible causes. This study hypothesized that it may be related to the characteristics of LA longitudinal and circumferential myocardium. The correlation analysis between LA Vmax I and LA strains showed that LA circumferential reservoir and contractile strain were correlated with LA Vmax I. It also explained, to a certain extent, the change of LA circumferential strain in ESRD patients with LA enlargement.

There were still a few limitations in this study. The sample size of this study was not very large, and the results of this study needed to be confirmed by large sample studies in the future. Reduced left atrial strain may be associated with left atrial fibrosis[21], but was not further evaluated by magnetic resonance imaging(MRI). Further study on the mechanism of left atrial dysfunction is needed.

Conclusion

LA longitudinal strains had decreased before LA enlargement in ESRD patients. When LA enlargement occurred, the circumferential strains decreased. This may indicate that LA longitudinal strain changed earlier than the circumferential strain in ESRD patients. 4D volume-strain analysis can detect the early changes of left atrial dysfunction in ESRD patients and may provide evidence for early clinical intervention.

DECLARATIONS

Ethics approval and consent to participate

Written informed ethics approval and consent to participate were obtained from our patient.

Consent for publication

Written informed consent for publication was obtained from our patient.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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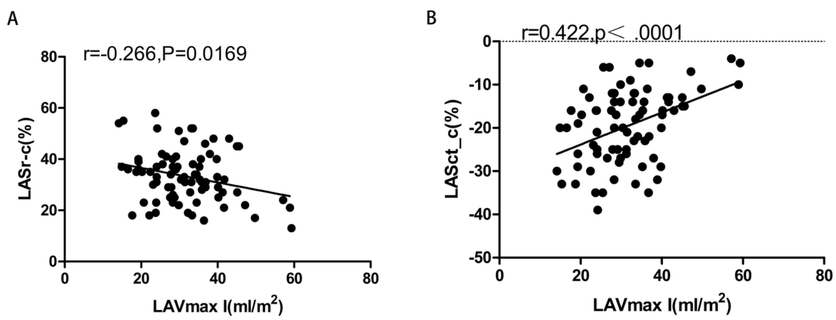
Table1 Baseline characteristics of the study populations

Table2 2D Echocardiographic characteristics of the study populations

Table3 Four-dimensional echocardiographic parameter with functional evaluation of the study populations

Table 4 Correlation of LA strains with LAVmax I in ESRD patients

Fig.1 Scatter plots and Pearson correlations between left atrial maximum volume index(LAVmax I)with peak circumferential strain of reservoir function (LASr-c)and peak circumferential strain of contractile function (LASct-c) in end-stage renal disease(ESRD) patients



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