Left Ventricular Mechanical Dispersion and Global Longitudinal Strain and Ventricular Arrhythmias in Predialysis and Dialysis Patients

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Background: Patients with advanced chronic kidney disease (CKD) have high risk for sudden cardiac death (SCD) and may benefit from implantable cardioverter-defibrillators (ICDs). However, the risk for ICD-related complications is also high in this population. Therefore, there is an unmet need for accurate risk stratification tools to identify patients with CKD at risk for ventricular arrhythmias (VAs), who may benefit from ICD implantation. The aim of this hypothesis-generating study was to investigate the association between left ventricular (LV) mechanical dispersion and LV global longitudinal strain (GLS) measured using two-dimensional speckle-tracking echocardiography and VA and SCD in patients with CKD.

Methods: Patients with CKD stages 3b to 5 (estimated glomerular filtration rate < 45 mL/min/1.73 m^2 or on dialysis) were included and were divided into two groups according to the occurrence of VA or SCD during follow-up. LV mechanical dispersion, as a measure of the temporal heterogeneity of the LV deformation, was measured as the SD of time to peak longitudinal strain of 17 LV segments. The ability of LV mechanical dispersion, LV ejection fraction, and LV GLS to discriminate patients with VA or SCD during follow-up was evaluated using receiver operating characteristic curve analysis.

Results: Of 250 patients (66% men; mean age, 61 ± 14 years), 16 (6%) experienced VA or SCD during a median follow-up duration of 28 months (interquartile range, 16–53 months). Using receiver operating characteristic curve analyses, LV GLS (area under the curve = 0.79; 95% CI, 0.68–0.89) and LV mechanical dispersion (area under the curve = 0.71; 95% CI, 0.61–0.82) showed modest discrimination to identify patients at risk for VA or SCD. In contrast, LV ejection fraction showed poor discrimination (area under the curve = 0.60; 95% CI, 0.41–0.78).

Conclusions: LV mechanical dispersion along with LV GLS may be an additional valuable risk marker of VA and SCD in predialysis and dialysis patients. (J Am Soc Echocardiogr 2018;■:■-■.)

Keywords: Chronic kidney disease, Sudden cardiac death, Strain, LV mechanical dispersion

Patients with advanced chronic kidney disease (CKD), particularly dialysis patients, have a high mortality rate.[1] Cardiac disease is the major cause of death, and sudden cardiac death (SCD) is the most frequent cause.[1] The enhanced arrhythmogenicity in patients with advanced CKD is due to the increased prevalence of cardiac risk factors, such as coronary artery disease, left ventricular (LV) hypertrophy and myocardial fibrosis, as well as noncardiac (CKD-specific) risk factors such as electrolyte alterations, sympathetic hyperactivity, uremia, and anemia.[2] Patients with advanced CKD may benefit from implantable cardioverter-defibrillators (ICDs) for prevention of SCD. However, they also show an increased risk for ICD-related complications.[3-5] Therefore, there is an unmet need for accurate risk stratification tools to identify patients with CKD at risk for ventricular arrhythmias (VAs) and SCD. LV mechanical dispersion and LV global longitudinal strain (GLS), measured using two-dimensional speckle-tracking echocardiography, have been shown to be associated with VA in several cardiomyopathies.[6-8] The aim of this hypothesis-generating study was to investigate the association between LV mechanical dispersion and LV GLS (measured using speckle-tracking echocardiography) and VA and SCD in predialysis and dialysis patients.

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Abbreviations
AUC = Area under the curve
CKD = Chronic kidney disease
GLS = Global longitudinal strain
ICD = Implantable cardioverter-defibrillator
LV = Left ventricular
LVEF = Left ventricular ejection fraction
SCD = Sudden cardiac death
VA = Ventricular arrhythmia

METHODS

Patient Population and Protocol

In this retrospective study, predialysis and dialysis patients from an ongoing registry at the Leiden University Medical Centre were included.[9] All patients were diagnosed with CKD stages 3b to 5 (estimated glomerular filtration rate of <45 mL/min/1.73 m^2 or on dialysis) according to the classification of the 2012 clinical practice guideline for the evaluation and management of CKD from Kidney Disease: Improving Global Outcomes.[10] Patients <18 years of age with inadequate echocardiographic image quality for offline analysis or with limited echocardiographic examination were excluded. From the departmental cardiology information system (EPD-vision; Leiden University Medical Centre, Leiden, The Netherlands) and electronic medical records (HiX; ChipSoft, Amsterdam, The Netherlands), clinical data (demographics, cardiovascular risk factors, medication use and laboratory results) were collected and retrospectively analyzed. Estimated glomerular filtration rate was calculated using the CKD Epidemiology Collaboration equation.[10] Residual renal function in dialysis patients was calculated using the predialysis plasma creatinine concentration and the concentration of creatinine in a 24-hour urine specimen.[11] QT interval was corrected for heart rate using Bazett's formula.[12] The present retrospective evaluation of clinically acquired data was approved by the institutional review board.

Transthoracic Echocardiography

Images were obtained from two-dimensional transthoracic echocardiography with patients lying in the left lateral decubitus position, using commercially available systems (Vivid 7 or E9; GE Vingmed Ultrasound, Horten, Norway) equipped with 3.5-MHz or M5S transducers. The echocardiographic data were digitally stored in cine-loop format for offline analysis (EchoPAC version 112.0.1; GE Vingmed Ultrasound). Linear dimensions of the left ventricle were measured from the parasternal long-axis view on M-mode recordings, and LV mass index was calculated and indexed to body surface area.[13] LV ejection fraction (LVEF) was measured using LV end-diastolic and end-systolic volumes from the apical four- and two-chamber views, according to the biplane Simpson method.[13] To measure wall motion score index, the left ventricle was divided into 16 segments, and the sum of the segment scores divided by 16 was calculated.[13] Left atrial volume was measured using the disk summation technique in the apical four-chamber view and indexed to body surface area.[13] By measuring the width of the vena contracta in the parasternal long-axis view, the severity of mitral regurgitation was graded semiquantitatively.[14] Aortic regurgitation was graded according to an integrative approach that includes qualitative (valve morphology, regurgitant jet characteristics, presence of diastolic flow reversal in descending aorta), semiquantitative (vena contracta width and pressure half-time of the continuous-wave spectral signal of aortic regurgitation jet), and quantitative parameters (effective regurgitant orifice area and regurgitant volume) as well as LV dimensions.[14] The aortic valve stenosis grade was based on aortic valve area, aortic jet peak velocity, and the mean transvalvular gradient measured according to current recommendations.[15] LV diastolic parameters, including peak early diastolic (E) wave and late diastolic (A) wave, were measured using pulsed-wave Doppler recordings of mitral inflow, and the E/A ratio was calculated. Septal and lateral e′ mitral annular velocities were measured using tissue Doppler imaging at the septal and lateral side of the mitral annulus in the apical four-chamber view.[16] The e′ velocity was calculated by averaging the septal and lateral e′ mitral annular velocities. The E/e′ ratio as a measure of LV filling pressures was calculated.[16] Tricuspid regurgitation gradient was measured on continuous-wave Doppler tracings of the tricuspid valve, and tricuspid regurgitation velocity was calculated.[16]

Two-dimensional speckle-tracking echocardiography was used to measure LV GLS on standard routine grayscale images of the apical four-chamber, two-chamber, and long-axis views.[17] LV GLS was derived from the average peak systolic longitudinal strain value of the three apical views. LV GLS is normally presented as negative values because it indicates the shortening of the myocardium relative to the original length.[17] However, in the present study, the absolute value of LV GLS is presented. LV mechanical dispersion was measured as the SD of time to peak longitudinal strain of 17 LV segments (including the apex) and represents the temporal heterogeneity of the LV deformation (Figure 1).[7] The onset of the Q/R wave on the surface electrocardiogram was considered to measure the time to peak longitudinal strain.[7] The interobserver variability of LV mechanical dispersion measurements was evaluated using Bland-Altman analysis, which showed a mean bias of −6.6 msec (95% limits of agreement, −42.5 to 29.4 msec).

Follow-Up

The occurrence of VA or SCD during follow-up was registered through case record review. VA was defined as aborted cardiac arrest, documented sustained ventricular tachycardia, or ventricular fibrillation. Ventricular tachycardia was defined as sustained when lasting >30 sec or requiring earlier intervention because of hemodynamic instability.[18] SCD was diagnosed when a congenital or acquired potentially fatal cardiac condition was known to be present during life, or autopsy had identified a cardiac or vascular anomaly as the probable cause of the event, or no obvious extracardiac causes had been identified on postmortem examination and therefore an arrhythmic event was a likely cause of death.[19]

Statistical Analysis

Categorical data are presented as frequencies and percentages and continuous data as mean ± SD or median (interquartile range), as appropriate. Patients were divided into two groups according to the occurrence of VA or SCD during follow-up. Student's *t* test or the Mann-Whitney *U* test was used to analyze differences between the two groups for continuous data and the χ^2 test or Fisher exact test for categorical data, as appropriate. The ability of LV mechanical dispersion, LVEF, and LV GLS to discriminate between patients with and those without VA or SCD during follow-up was assessed using receiver operating characteristic curves, and area under the curve (AUC) is reported. Comparisons between receiver operating characteristic curves of LV mechanical dispersion, LVEF, and LV GLS were performed using MedCalc version 16.2.1 (MedCalc Software, Ostend, Belgium) using the method of DeLong *et al.*[20] All statistical tests were two