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Clinical study on feasibility and repeatability of left ventricular systolic function assessment in patients with chronic kidney disease using artificial intelligence-based automatic strain technique

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Abstract

Background: Studies have shown that cardiovascular damage is a common complication in patients with chronic kidney disease (CKD), and left ventricular longitudinal strain measurement (GLS) is superior to LVEF in evaluating left ventricular systolic function. However, it has not yet been widely accepted as a routine clinical examination because it requires proficiency and is time-consuming. Therefore, the aim of this study is to investigate the feasibility, reproducibility and its predictive value of automated GLS measurement compared with standard manual measurement of GLS, so as to provide an important reference for clinical treatment and reduction of cardiovascular events in CKD patients.

Methods: A total of 285 CKD patients (aged 52 ± 12.85) were selected from Hainan Provincial People's Hospital, all of whom had not received dialysis treatment. All CKD patients were measured by three different GLS evaluation methods using the same apical three-cavity, two-cavity and four-cavity heart images. (1) Entirely automatic GLS, directly analyzed by on-machine functions, (2) Semi-automatic GLS, corrected by experienced researchers on the basis of fully automatic measurements, and (3) manual GLS, standard manual measurements made by experienced researchers. Five patients were excluded due to poor image quality and could not be automatically measured and analyzed. Clinical outcomes were followed up with patients by telephone and outpatient review.

Results: After automatic GLS measurement, about 35% of the measurements were considered to need manual correction, and there was a statistically significant difference between automated, semi-automated and manual GLS (P <0.01). The correlation and consistency between semi-automated GLS and manual GLS were higher than automated GLS (P <0.01). At 2-year follow-up, 55 CKD patients (19.6%) experienced adverse cardiovascular events. Automated GLS was able to predict adverse cardiovascular events, but its predictive value was lower than semi-automated GLS. The automatic measurement and analysis time (15.23±0.75s/patient) and the semi-automatic measurement and analysis time (75.06±19.01s/patient) were significantly shorter than that of manual group (236.81±45.41s/patient). (P <0.01).

Conclusions: Automatic GLS assessment of left ventricular systolic function in CKD patients is feasible and reproducible. However, there are still some images that require manual correction at this stage, so a semi-automated approach using this new automated software to evaluate left ventricular systolic function in CKD patients and provide predictive value seems to be a superior option...

Keywords: Echocardiography, two-dimensional speckle tracking imaging, longitudinal strain, automatic measurement

Introduction

Cardiovascular damage is a common complication in patients with chronic kidney disease (CKD) [1]. Routine two-dimensional echocardiography mainly applies ejection fraction (LVEF) to evaluate the systolic function of the heart. However, LVEF in most CKD patients is within the normal range clinically, so the sensitivity and specificity of LVEF in evaluating heart damage in CKD patients are low. Previous

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studies have shown that left ventricular global longitudinal strain (LVGLS) can detect early myocardial systolic function impairment and is associated with cardiovascular adverse events in patients with CKD, and has a higher predictive value than LVEF in risk stratification [2-5]. However, LVGLS manually delineated by two-dimensional speckle tracking technology (2D-STI) are still limited by the professional requirements and the time-consuming manual analysis, and have not been widely used in the clinic. Artificial intelligence-based automatic strain measurement software can automatically track endocardial boundaries and measure GLS on the basis of machine learning, providing a rapid and repeatable strain parameter measurement method for clinical use. However, the feasibility, repeatability and prognostic value of using artificial intelligence-based automatic strain measurement software to evaluate GLS in patients with chronic kidney disease have not been established. Therefore, the aim of this study is to determine the feasibility and reproducibility of automatic GLS measurement compared with standard manual GLS measurement, and to determine the predictive value of automatic GLS measurement, so as to provide an important reference for clinical treatment and reducing the occurrence of cardiovascular events in CKD patients

1 Research methods

1.1 Objects

A total of 280 patients with CKD who were treated in Hainan Provincial People's Hospital from July 2020 to January 2022 were selected (15 patients with CKD2, 65 patients with CKD3, 90 patients with CKD4 and 110 patients with CKD5), all of whom did not receive dialysis treatment. Patients who have congenital heart disease, valvular disease, cardiomyopathy, coronary heart disease and other serious heart disease, severe pulmonary hypertension, emergency hemodialysis indications, malignant tumors or other life expectancy of less than two years were excluded. All objects had follow-up data and echocardiographic images for strain analysis. All the included patients gave informed consent and this research was approved by the hospital ethics committee. At the beginning of the study, general clinical data such as age, gender, body surface area, heart rate, blood pressure, blood glucose and blood lipid were collected. All objects of research were followed up for 2 years by telephone and outpatient review. The primary ending at 2 years was death, and secondary endings included admitted for heart failure, stroke, and nonfatal myocardial infarction.

1.2 Echocardiography

Standard Two-dimensional Transthoracic and Doppler Echocardiography is performed by two experienced sonographers who have worked for more than 5 years using the same equipment (Epic CvX; Philips Medical Systems, Andover, MA) were measured. The examinee was placed in the left lateral position and electrocardiogram was attached. To ensure the quality of image, patients were asked to breathe calmly and hold their breath if necessary. Measurements included left atrial diameter, left ventricular diameter, interventricular septal thickness, left ventricular posterior wall thickness, left ventricular mass index, and left ventricular ejection fraction function. Dynamic images of the left ventricular long axis, four-cavity and two-cavity were obtained during three cardiac cycles. In full volume mode, the left ventricle endocardium was clearly displayed, and apical four-cavity three-dimensional echocardiography image was obtained. All 2D (two-dimensional) and 3D (three-dimensional) echocardiographic images were obtained according to guidelines issued by the American Society of Echocardiography [6], and the examining physician was unaware of the clinical characteristics of the subjects.

GLS values from three different measurements were obtained by an experienced sonographer without knowledge of the client's clinical features from images of the same apical left ventricle long axis, four- and two-cavity incisor. According to the European Association of Cardiovascular Imaging/American Society of Echocardiography/Industry Task Force to Standardize Deformation Imaging [7], entirely automated measurement operators of GLS analysis for two-, three-, and four-cavity image, after selecting the on-machine function AutoStrain LV, the software automatically tracks endocardial boundaries and calculates GLS without manual adjustment by the operator. As for semi-automated GLS, after automatic GLS measurement and tracking mass review, the operator manually corrects the endocardial boundary until sufficient tracking mass is obtained. For manual GLS measurement, the on-machine function aCMQ was used to analyze the long axis of the left ventricular apex first, manually select the mitral ring and the inner membrane of the apex tricycle at the end of systole, and the software automatically generates the area of interest, adjusts the width of the area of interest to make it consistent with the thickness of the myocardium, and accurately select the closing time point of the aortic valve. The software automatically tracks the myocardium movement in the area of interest frame by frame to get the results. The apical four-cavity and apical two-cavity were analyzed in the same way, and the endocardial boundary was modified manually if necessary.

GLS calculation's time: Fifty patients were randomly selected to measure the time required for each GLS measurement. We define the GLS's time of measurement as the time taken to measure GLS for each measurement method from the initial selection of the three sectional views to the timepoint that GLS results are calculated.

Fifty patients with CKD were randomly selected to evaluate the variation of intra-observer and inter-observer in the same images. The intra-observer variation between the first and second measurements (30 days later) was calculated by the same researcher, who was unaware of the results of the previous measurements. Inter-observer differences between the first measurements of two independent investigators were calculated, and both investigators were unaware of each result. All GLS measurements were performed by an experienced sonographer.

1.3 Statistical analysis

Continuous variables are expressed as mean ± standard deviation or median (IQR). Categorical variables are expressed as numbers (percentages). The normal distribution of the data was tested by Kolmogorov-Smirnov. One-way ANOVA and Tukey post Hoc test were applied to compare GLS obtained from three different measurement methods, and Bonferroni was used to correct multiple comparisons. Intra-observer and inter-observer repeatability tests were performed applying the repeated measures ANOVA, as expressed by the intra-group correlation coefficient (ICCs). Pearson correlation analysis was used to evaluate the correlation between GLS obtained by three different measurements. Bias and limits of agreement (LOA) between the two different measurements were assessed using Bland-Altman analysis. Receiver operating characteristic (ROC) curve analysis was used to calculate the area under the curve (AUC) for GLS measured by each method, and the best cutoff value for each variable to distinguish between cardiovascular adverse events was obtained from the ROC curve. The area of ROC curve was compared using Medcalc Version 22.0.2 (Medcalc Software, Ostend, Belgium), and the remaining statistical analysis was performed using SPSS version 27.0 (SPSS, Chicago, IL). The data was considered statistically significant if bilateral P value <0.05.

2 Results

2.1 General clinical data and baseline echocardiographic data are shown in Table 1.

Table 1 General clinical data and baseline echocardiographic data

Age (years of age)	51.10±12.62
Gender (male/female, n)	182/98
Body surface area (BSA, m^2)	1.63±1.72
Heart rate (times/min)	77.49±8.93
Systolic pressure (mmHg)	147.76±23.50
Diastolic pressure (mmHg)	87.15±15.13
Blood glucose (mmol/L)	6.35±3.13
Blood fat (mmol/L)	1.64±1.33
Left ventricular internal diameter (mm)	49.25±5.60
Left atrial diameter (mm)	37.84±5.44
Interventricular septal thickness (mm)	12.55±1.73
Left ventricular posterior wall thickness (mm)	12.25±1.7
Left ventricular mass index (LVMI, g/m^2)	102.49±24.82
left ventricular ejection fraction (LVEF, %)	59.63±7.08
Automatic GLS	-16.37±3.39
Semi-automatic GLS	-17.04±3.41
Manual GLS	-18.18±4.13

2.2 Comparison of correlation and consistency between automatic, semi-automatic GLS and manual GLS three measurement methods is shown in Table 2.

Table 2 Correlation and consistency comparison between automatic, semi-automatic GLS and manual GLS measurement methods

	r	*p*	Bias±LOA
Automatic and manual GLS	0.865	＜0.001	0.71±3.4
Semi-automatic and manual GLS	0.720	＜0.001	1.81±5.7
Semi-automatic and automatic GLS	0.769	＜0.001	1.1±5.2

2.3 Comparison of area under ROC curve between automatic and semi-automatic GLS and manual GLS: automatic GLS and manual GLS:P=0.0235, P < 0.05; Semi-automatic GLS and manual GLS: p=0.1331, p > 0.05; Automatic GLS and semi-automatic GLS: p=0.0007, P < 0.05, as shown in Table 3.

Table 3 Area under ROC curve of automatic GLS, semi-automatic GLS and manual GLS measurement methods

	AUC (95%CI)	GLS cutoff value (%)	Sensitivity (%)	Specificity (%)
Automatic GLS	0.753 (0.683-0.823)	-17.6	83.0	65.2
Semi-automatic GLS	0.858 (0.809-0.906)	-15.7	83.0	76.7
Manual GLS	9.828 (0.774-0.883)	-15.0	73.1	79.2

2.4 The comparison of repeatability between automatic and semi-automatic GLS and manual GLS three measurement methods is shown in Table 4.

Table 4 Comparison of repeatability of automatic GLS, semi-automatic GLS and manual GLS measurement methods

	Intraclass correlation coefficient (ICC)	95% CI	*P value*
Intra-observer			
Automatic GLS	1	1.000-1.000	*P=0.000*
Semi-automatic GLS	0.958	0.928-0.976	*P=0.000*
Manual GLS	0.908	0.843-0.947	*P=0.000*
Inter-observer			
Automatic GLS	1	1.000-1.000	*P=0.000*
Semi-automatic GLS	0.912	0.851-0.949	*P=0.000*
Manual GLS	0.868	0.778-0.923	*P＜0.001*

3 Discussion

In this study, we validated the feasibility, repeatability, and prognostic value of automated GLS measurement in patients with CKD using AI-based automated software. The main results of this study are as follows: (1) The automated and semi-automated methods for accessing GLS in CKD patients have short analysis time and good repeatability; (2) The correlation and consistency between semi-automated GLS and manual GLS are higher than automated GLS; (3) About 35% of cases require manual correction, so there is a difference between automated, semi-automated and manual GLS; (4) Automated and semi-automated GLS can predict cardiovascular adverse events in patients with CKD, but the predictive value of automated GLS is lower than that of semi-automated GLS.

Cardiovascular complications can occur at all stages of CKD. Clinically, some patients with CKD may die from cardiovascular complications before the disease progresses to end-stage kidney disease. Therefore, the diagnosis and intervention of cardiovascular damage in patients with CKD are of great significance. GLS has emerged as a powerful marker of subclinical left ventricular (LV) dysfunction, detecting early changes in LV function more sensitively than LVEF. GLS can provide important predictive value for the occurrence of adverse cardiovascular events in patients with CKD, and has better predictive value than LVEF in terms of risk stratification [8]. However, because the measurement of GLS is time-consuming and requires a certain degree of professional knowledge, patients with CKD cannot obtain GLS in a timely and effective manner during their busy daily work. Therefore, the automatic measurement of GLS is a clinical demand. Tetsuji Kitano et al. [9] found that automated measurement of GLS provided effective prognostic information for asymptomatic aortic valve patients. The results of Gonzalez-Manzanares et al suggest that automatic GLS is superior to conventional echocardiography in early detection of cardiotoxicity and can be an effective indicator for long-term cardiac monitoring of childhood leukemia survivors. However, the feasibility and repeatability of entirely automated GLS measurements have not been studied in CKD patients.

The problem of reproducibility of GLS is very important in the clinical management of patients with various heart diseases. Kitano et al. [10] used automatic 2D strain software to study the prognostic value of GLS in patients with asymptomatic aortic stenosis, and the results showed that the test-retest ICC of automatic GLS was 0.95(0.90-0.98). Kawakami et al. [11] revealed in their study of 558 patients with asymptomatic heart failure that the ICCs of intra-observer of automatic GLS, semi-automatic GLS and manual GLS were 1.00 (95%CI, 1.00-1.00) and 0.97 (95%CI, 1.00-1.00), 0.95-0.98) and 0.94 (95%CI, 0.90-0.97). The cv of automated, semi-automated and manual GLS were 0.46%, 1.64% and 2.23%, respectively. The inter-observer ICC for automatic, semi-automated, and manual GLS were 1.00 (95%CI, 1.00-1.00), 0.90 (95%CI, 0.84-0.95), and 0.92 (95%CI, 0.87-0.96). This is similar to our findings, which showed high reproducibility and consistency in the results of automatic, semi-automatic and manual evaluations. If different researchers use the same images, the automated approach will often produce the same results because the machine will perform the exact same process each time using the same machine learning algorithm. The finding has important clinical implications for patients with CKD, enabling real changes in left ventricular systolic function to be detected during follow-up. In this study, 35% of patients were considered to need manual correction after automatic GLS assessment, which is similar to about 40% reported by Kawakami H et al. [11].

Unsatisfactory quality of images is an unavoidable factor, limiting the accuracy that can be achieved by manual and automatic measurement [12, 13]. Therefore, our data show that there is a difference between automated, semi-automated, and manual GLS, so although automatic, semi-automatic, and manual GLS are significantly associated with adverse cardiovascular events, semi-automatic GLS is more predictive of adverse cardiovascular events than automatic GLS. In this study, the automatic evaluation time is 15.23±0.75s and the semi-automatic evaluation time is 75.06±19.01s, which is significantly shorter than the manual evaluation time (236.81±45.41s). This result is similar to the results of the recent study on the feasibility and reproducibility of semi-automatic longitudinal strain analysis by Peng et al. [14]. The rapid analysis and reproducibility of automated assessments contribute to the widespread use of GLS in patients with CKD, and given that semi-automated GLS has a high predictive value of cardiovascular adverse events and requires less time than manual approaches, semi-automated approaches seem to provide a better balance between feasibility and clinical relevance at this stage.

The study has several potential limitations. First, this study is a single-center retrospective study, and the results may be affected by selection bias. Second, CKD patients with sinus rhythm were selected in this study, and patients with arrhythmia were not selected. Further studies are still required to clarify the clinical significance of this automatic assessment in CKD patients with arrhythmia. Third, subgroup analysis of CKD patients with different configurations has not been conducted, and whether different configurations will affect the results of automated measurement is still unknown. Fourth, the fact that semi-automated methods are more accurate than fully automated methods for GLS measurement shows that there is room for improvement and improvement of automated algorithms in the future.

4 Conclusion

Automated GLS assessment of left ventricular systolic function in patients with CKD is feasible and reproducible. However, there are still some images that need manual correction at this stage, so using the semi-automated method of this new automated software to evaluate left ventricular systolic function in CKD patients and provide predictive value seems to be a prior choice.

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