

Assessment of the left ventricular function in patients with uremia using layer-specific 2-dimensional speckle tracking echocardiography

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Abstract

The aim of this research is to evaluate the longitudinal and circumferential systolic function of the left ventricle with different configurations from endocardium, midmyocardium, and epicardium, respectively, in patients with uremia using layer-specific 2-dimensional speckle tracking echocardiography (2D-STE).

According to the different left ventricular (LV) configurations, 119 patients with uremia were divided into 2 groups: LV normal group (LVN group, $n=63$) and LV hypertrophy group (LVH group, $n=56$). In all, 66 healthy volunteers were selected as controls. High-frame rate 2-dimensional images were recorded from the apical 4-chamber view, apical 2-chamber view, parasternal LV long-axis view, and mitral annulus, papillary muscle, and apical levels of the parasternal LV short-axis view during 3 consecutive cardiac cycles. The peak systolic longitudinal strain (LS) and circumferential strain (CS) were measured in the endocardium, midmyocardium, and epicardium.

In the 3 groups, the endocardium had the highest LS and CS, whereas the epicardium had the lowest LS and CS; the LS and CS of each group gradually decreased from the endocardium to the epicardium in all the 3 sections; the LS and CS of the myocardial layers were kept gradient features, namely, endocardium > midmyocardium > epicardium. The LS of the endocardium in the LVN and LVH groups was significantly lower than that in the control group ($P < .05$). The LS of the midmyocardium and epicardium in the LVH group were significantly lower than those in the control group ($P < .05$). The LS of the endocardium significantly decreased in the LVH group compared with that in the LVN group ($P < .05$). The CS of the endocardium and midmyocardium in the LVH group significantly decreased compared with those in the control and LVN groups ($P < .05$). There were no significant differences in the CS between the LVN and control groups ($P > .05$).

In patients with uremia, the longitudinal and circumferential systolic function in 3 myocardial layers of the LVH group, and the longitudinal systolic function in endocardium of the LVN group were found significantly impaired by layer-specific 2D-STE.

Abbreviations: 2D-STE = 2-dimensional speckle tracking echocardiography, CS = circumferential strain, EF = ejection fraction, FS = fractional shortening, IVSTd = interventricular septum diastolic thickness diameter, LAD = left atrial end-systolic diameter, LS = longitudinal strain, LV = left ventricular, LVDd = LV end-diastolic diameter, LVEF = LV ejection fraction, LVH = LV hypertrophy, LVM = LV mass, LVMI = LVM index, LVN = LV normal, LVPWTd = end-diastolic thickness of the LV posterior wall, SCr = serum creatinine.

Keywords: 2-dimensional speckle tracking echocardiography, circumferential strain, longitudinal strain, uremia

1. Introduction

The persistent increase in the prevalence of kidney diseases is a growing public health problem worldwide and is associated with an increased risk of cardiovascular diseases in many popula-

tions.^[1,2] It is well known that uremia, which is an end-stage condition in kidney diseases, will impair the heart mainly. Uremic cardiomyopathy is a critical problem in affected patients and is reportedly the leading cause of high morbidity and mortality rates among patients with uremia.^[3–5] Therefore, it is very important to timely and accurately evaluate the impaired left ventricular (LV) function to help to reduce and/or postpone further damage. Previous studies have suggested that the primary manifestation of uremic cardiomyopathy is left ventricular hypertrophy (LVH).^[6–8] Conventional echocardiography is a useful and noninvasive method to study both structural and functional cardiac status in patients with uremia. Measurements of endocardial fractional shortening (FS) and LV ejection fraction (LVEF) are widely used to evaluate LV function, but fail to identify early impaired LV function in patients with uremia who may already have LVH.^[9–11]

Two-dimensional speckle tracking echocardiography (2D-STE)—a new, semiautomated quantitative echocardiographic technique—could angle-independently quantify the LV strain. It could track the myocardial movement in all directions (longitudinal, circumferential, radial, and torsional movements) and quantitatively evaluate the regional myocardial function by discerning the myocardial echo speckles.^[12–14] Also, it has been

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proven to be an accurate method of evaluating regional and global LV myocardial movement and function than conventional echocardiography.^[15–17] A normal left ventricle has 3 layers: endocardium, midmyocardium, and epicardium; 75% of the endocardium and epicardium mainly consist of longitudinal fibers, whereas 25% of the middle layer mainly comprises circumferential fibers.^[18] Layer-specific 2D-STE, which is an advanced technology derived from 2D-STE, could, respectively, obtain longitudinal strain (LS) and circumferential strain (CS) of the 3 myocardial layers of the left ventricle to evaluate the layer-specific myocardial function.^[19,20] Previous studies have reported that uremic cardiomyopathy cases exhibited a lower global longitudinal, circumferential, and radial myocardial strain in patients with uremia who have a normal LVEF than the healthy volunteers group^[21–23]; however, no studies focus on the LS and CS of 3 layers of the left ventricle in patients with uremia.

The aim of this study is to evaluate the longitudinal and circumferential myocardial strains in the 3 myocardial layers of the left ventricle with different configurations in patients with uremia using layer-specific 2D-STE, focusing on the clinical applications of layer-specific 2D-STE for the evaluation of early lesions of the heart, and detect subtle impairments in the LV systolic function of these patients with normal LVEF.

2. Materials and methods

2.1. Study participants

In all, 155 patients who were diagnosed with uremia were recruited at the Second Affiliated Hospital of Dalian Medical University from December, 2014 to December, 2017; 119 (62 men and 57 women; age range 20–72 years; mean age 45.3 ± 10.5 years) of them were finally included in this study.

The eligibility criteria were as follows:

1. Renal disease as the primary disease
2. Serum creatinine (SCr) level >707 μmol/L
3. LVEF >50%
4. No pericardial effusion
5. Age >18 years; entire hemodialysis duration of at least 6 months; and hemodialysis schedule of thrice a week for 4 hours using low-flux dialysis filters, polysulfone membranes, reverse osmosis purified water, and bicarbonate-based hemodialysis solution

The exclusion criteria were as follows:

1. Cardiovascular diseases: any history of congenital heart disease, ischemic heart disease, valvular heart disease, rhythm problems, pulmonary hypertension, primary hypertension, and so on (each patient has no corresponding conventional echocardiography abnormalities and electrocardiogram abnormalities, and has no associated clinical symptoms)
2. Endocrine and metabolic diseases, such as diabetes mellitus, systemic lupus erythematosus, and hyperthyroidism
3. Any history of cardiovascular treatment, such as cardiopulmonary surgery or cardiovascular-related medications
4. Other reasons, such as missed cases or transfer to other hospitals, refusal to participate, and poor image quality

According to the LV mass (LVM) index (LVMI),^[24] all 119 patients were divided into 2 groups:

1. LV normal (LVN) group: 63 patients (men: 33, LVMI of ≤115 g/m²; women: 30, LVMI of ≤95 g/m²; age range 25–68 years, mean age 45.9 ± 9.6 years)

2. LV hypertrophy (LVH) group: 56 patients (men: 29, LVMI of >115 g/m²; women: 27, LVMI of >95 g/m²; age range 40–72 years, mean age 48.0 ± 8.4 years)

In all, 66 age and sex-matched healthy individuals (men: 37, women: 29; age range 25–70 years, mean age 44.9 ± 8.7 years) were included in the control group. All healthy individuals did not have any histories of kidney, cardiovascular, endocrine, and metabolic diseases, and their physical examination, electrocardiogram, echocardiography, and X-ray findings were all normal. All the subjects provided their informed consent, and the Ethics Committee of the Second Affiliated Hospital of Dalian Medical University approved this study.

2.2. Image acquisition and analysis

2.2.1. Conventional echocardiography assessment. Trans-thoracic echocardiography was performed on the participants at rest in the left lateral decubitus position by a doctor who had no knowledge of the clinical data and the group assignments using GE Vingmed Vivid 7 (GE Vingmed Ultrasound, Horten, Norway) equipped with a 1.5 to 4.3 MHz transducer (M3S probe); each subject was connected with electrocardiogram.

According to the recommendations of the American Society of Echocardiography, the parameters were measured via conventional echocardiography, including left atrial end-systolic diameter (LADs), LV end-diastolic dimension (LVDD), interventricular septum diastolic thickness diameter (IVSTd), and end-diastolic thickness of the LV posterior wall (LVPWTd). The early diastolic mitral inflow velocity (E) and late diastolic mitral inflow velocity (A) were measured from the apical 4-chamber view using pulsed Doppler, and the E/A ratio was also calculated; the LVEF was measured using biplane Simpson method.

The LVMI was measured using the M-mode echocardiography and calculated using the following equation: $LVMI = LVM / \text{body surface area}$; the LVM was calculated using the Devereux-modified method: $LVM = 0.8 \times (1.04 \{ [LVDD + LVPWTD + IVSTd]^3 - [LVDD]^3 \}) + 0.6$.^[25]

2.2.2. 2D-STE assessment. The images were recorded and stored for offline analysis on EchoPAC workstation, which were obtained during three consecutive cardiac cycles with a frame rate of 50 to 70 Hz/s from the apical 4-chamber view, apical 2-chamber view, parasternal LV long-axis view, and the parasternal LV short-axis view (including mitral annulus, papillary muscle, and apical levels). The LV endocardium was traced manually when the endocardium and epicardium were clearly shown, and the software would then delineate the curve of the LV epicardium automatically. Thereafter, the curves of the endocardium and epicardium were adjusted to ensure consistency with the LV wall thickness; the myocardium was divided into the endocardium, midmyocardium, and epicardium automatically by the system. The 3 layers of the left ventricle obtained from the LV apical views and parasternal LV short-axis view were analyzed using 2D-STE. The myocardial LS curves and CS curves of the 3 layers were created automatically, and the average value of the data from the 3 cardiac cycles was adopted.

2.2.3. Observer reliability and repeatability. For the interobserver and intraobserver reproducibilities, all parameters were measured again for 35 randomly selected participants from the 185 study participants according to the above mentioned methods 2 weeks later. The intraobserver (SMY) and interobserver (HDM) variabilities were calculated and assessed using the intraclass correlation coefficient.

Table 1
Demographic and clinical characteristics.

Variables	LVN group (n = 63)	LVH group (n = 56)	Control group (n = 66)
Sex (man/women)	33/30	29/27	37/29
Age (y)	45.9 ± 9.6	48.0 ± 8.4	44.9 ± 8.7
BMI (kg/m ²)	26.4 ± 2.6	26.2 ± 2.1	26.3 ± 1.9
Heart rate (beats/min)	70 ± 10	71 ± 11	73 ± 9
SBP (mm Hg)	145 ± 21*	152 ± 25*	104 ± 16
DBP (mm Hg)	84 ± 13*	90 ± 12*	72 ± 12
SCr (μmol/L)	902.85 ± 324.08*	846.37 ± 367.10*	75.23 ± 19.20
BUN (mmol/L)	22.53 ± 15.36*	19.64 ± 13.65*	6.80 ± 1.35
iPTH (pg/mL)	485.26 ± 287.11*	430.81 ± 325.35*	41.35 ± 13.49

Data are expressed as number of patients or mean value ± SD.

BMI=body mass index, BUN=blood urea nitrogen, DBP=diastolic blood pressure, iPTH=immunoreactive parathyroid hormone, LVH=left ventricular hypertrophy, LVN=left ventricular normal, SBP=systolic blood pressure, SCr=serum creatinine.

* $P < .05$ versus control group.

2.3. Statistical analysis

All statistical calculations were performed using the computer program SPSS 17.0 for Windows (SPSS 17.0, Inc., Chicago, IL). Numeric variables were presented as mean ± standard deviation (SD). One-way analysis of variance was performed to test for statistically significant differences among the 3 groups. Continuous data were compared among individual groups using the Student-Newman-Keuls post-test. All statistical tests were 2-sided, and $P < .05$ was considered statistically significant.

2.4. Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Dalian Medical University on human research, and all patients provided their informed consent to participate in this research.

All authors consent for the publication in Medicine.

3. Results

3.1. Demographic and clinical characteristics

There were no significant differences among the 3 groups with respect to age, sex, heart rate, and body mass index ($P > .05$; Table 1). The SCr level, blood urea nitrogen level, immunoreactive parathyroid hormone level, the systolic and diastolic blood pressures of the LVN and LVH groups were significantly higher than those of the control group ($P < .05$; Table 1).

3.2. Conventional echocardiographic parameters

There were no significant differences between the control and LVN groups ($P > .05$; Table 2). There were no significant differences among the 3 groups with respect to LVDd and LVEF ($P > .05$; Table 2). The LADs, LVPWTd, and IVSTd of the LVH group were significantly higher than those of the control and LVN groups ($P < .05$; Table 2). The E/A ratio of the LVH group was significantly lower than that of the control and LVN groups ($P < .05$; Table 2).

3.3. 2D-STE parameters

In the 3 groups, the endocardium had the highest LS and CS in the same section, whereas the epicardium had the lowest LS and CS.

Table 2
Conventional echocardiographic parameters.

Variables	LVN group (n = 63)	LVH group (n = 56)	Control group (n = 66)
LVDd (mm)	44.77 ± 4.79	46.26 ± 5.27	43.18 ± 4.60
IVSTd (mm)	9.36 ± 0.72	12.31 ± 0.91*	9.71 ± 0.89
LVPWTd (mm)	9.66 ± 0.73	11.83 ± 1.07*	9.13 ± 0.80
LADs (mm)	32.73 ± 4.39	38.89 ± 5.39*	29.41 ± 3.87
E/A ratio	1.16 ± 0.41	0.67 ± 0.69*	1.19 ± 0.22
LVEF (%)	64.21 ± 4.87	63.85 ± 4.63	63.63 ± 3.82

Data are expressed as mean value ± SD.

E/A ratio=the ratio of the early (E) to late (A) ventricular filling velocities; IVSTd=interventricular septum diastolic thickness diameter; LADs=left atrial end-systolic diameter; LVDd=left ventricular diastolic diameter; LVEF=left ventricular ejection fraction; LVH=left ventricular hypertrophy; LVN=left ventricular normal; LVPWTd=end-diastolic thickness of the left ventricular posterior wall.

* $P < .05$ versus control group and LVN group.

Also, the LS and CS of the myocardial layers were kept the same gradient features, namely, endocardium > midmyocardium > epicardium (Tables 3 and 4; Figs. 1 and 2).

3.3.1. LS obtained via 2D-STE. The LS of the endocardium in the LVH and LVN groups was significantly lower than that in the control group ($P < .05$), and the LS of the endocardium in the LVH was significantly reduced compared with the LVN group ($P < .05$). In addition, the LS of the midmyocardium and epicardium in the LVH group were both significantly decreased compared with the control group ($P < .05$). However, there were no significant differences in the LS of the midmyocardium and epicardium between the LVN and control groups ($P > .05$) (Table 3; Figs. 1 and 3).

3.3.2. CS Obtained via 2D-STE. The CS of the endocardium and midmyocardium in the mitral annulus and papillary muscles levels of the LVH group were significantly lower than those in same section of the LVN and control groups ($P < .05$). However, compared with the LVN and control groups, there was no significant difference in the CS of the endocardium in the apical level of the LVH group ($P > .05$). Apart from this, there were no

Table 3
The longitudinal strain of myocardium of left ventricle.

Variables	LVN group (n = 63)	LVH group (n = 56)	Control group (n = 66)
Apical 4-chamber view			
Endocardium (%)	-24.41 ± 3.82*	-19.10 ± 4.69* [†]	-28.71 ± 3.53
Midmyocardium (%)	-22.28 ± 3.71	-17.26 ± 4.13*	-24.79 ± 3.86
Epicardium (%)	-21.47 ± 4.14	-15.12 ± 4.63*	-21.73 ± 3.56
Apical 2-chamber view			
Endocardium (%)	-22.74 ± 5.28*	-17.61 ± 5.12* [†]	-27.89 ± 3.33
Midmyocardium (%)	-22.09 ± 4.45	-16.36 ± 4.31*	-24.61 ± 3.91
Epicardium (%)	-20.51 ± 4.34	-15.11 ± 4.63*	-22.69 ± 3.70
LV long-axis view			
Endocardium (%)	-21.76 ± 3.53*	-16.36 ± 5.59* [†]	-27.57 ± 3.22
Midmyocardium (%)	-21.04 ± 3.87	-15.88 ± 4.35*	-23.86 ± 3.39
Epicardium (%)	-20.24 ± 4.10	-14.30 ± 5.26*	-20.19 ± 3.30

Data are expressed as mean value ± SD percentage.

LVH=left ventricular hypertrophy; LVN=left ventricular normal.

* $P < .05$ versus control group.

[†] $P < .05$ versus LVN group.

Table 4**The circumferential strain of myocardium of left ventricle.**

Variables	LVN group (n=63)	LVH group (n=56)	Control group (n=66)
Mitral annulus level			
Endocardium (%)	-29.18 ± 5.61	-23.69 ± 6.22*	-32.69 ± 5.40
Midmyocardium (%)	-19.09 ± 5.47	-13.77 ± 6.82*	-20.42 ± 4.81
Epicardium (%)	-12.10 ± 3.91	-10.48 ± 4.98	-13.29 ± 4.11
Papillary muscles level			
Endocardium (%)	-31.51 ± 6.11	-24.88 ± 6.60*	-32.76 ± 5.20
Midmyocardium (%)	-18.76 ± 5.69	-13.37 ± 4.25*	-20.13 ± 4.37
Epicardium (%)	-9.91 ± 3.39	-7.74 ± 3.68	-11.15 ± 3.88
Apical level			
Endocardium (%)	-31.57 ± 4.98	-30.43 ± 5.59	-33.60 ± 5.16
Midmyocardium (%)	-21.74 ± 3.91	-15.79 ± 4.37	-22.41 ± 4.40
Epicardium (%)	-13.93 ± 3.82	-13.58 ± 4.89	-15.61 ± 4.19

Data are expressed as mean value ± SD percentage.

LVH=left ventricular hypertrophy; LVN=left ventricular normal.

* $P < .05$ versus control group and LVN group.

significant differences in the CS of the epicardium among the 3 groups ($P > .05$), and there were no significant differences in the CS of the endocardium and midmyocardium between the LVN and control groups ($P > .05$) (Table 4; Figs. 2 and 4).

3.4. Interobserver and intraobserver reproducibilities and repeatabilities

The analysis revealed good inter and intraobserver reproducibilities, and small inter and intraobserver variabilities using layer-specific 2D-STE in the evaluation of the patients with uremia (Table 5).

4. Discussion

Most studies found normal LV function in patients with early stage of uremia using conventional echocardiographic indices of

cardiac function, such as LVEF and FS.^[9–11] Surprisingly, 2D-STE could early detect global LV systolic dysfunction in patients with chronic kidney disease with normal LVEF.^[21–23,26,27] In addition, it is reported that layer-specific 2D-STE could evaluate the longitudinal and circumferential systolic function of the left ventricle for the early detection of cardiotoxicity in postoperative breast cancer patients.^[28] In this study, we used layer-specific 2D-STE to early evaluate the longitudinal and circumferential systolic function in 3 myocardial layers of the left ventricle in patients with uremia with normal LVEF to provide more clinical information.

Our study showed that there was a gradient feature of the LS and CS from the endocardium to the epicardium among the 3 groups, namely endocardium > midmyocardium > epicardium. These gradient characteristics were consistent with the previous studies using layer-specific 2D-STE.^[29–31] There might be several reasons. First, the LV wall is inhomogeneous, and the myocardial fibers in the 3 layers are arranged in a different orientation.^[32,33] Second, the wall stress in the 3 layers are different; it is characterized by increases in end-diastolic wall stress toward the endocardium, leading to an increase in the shortening of the systolic endocardial fibers.^[34] Third, the coronary perfusion and metabolism of endocardium are higher than other 2 myocardial layers.^[35] Apart from these, the more decrease in circumferential radius of curvature during systole in endocardium than that in epicardium is another possible reason for gradient characteristics of CS.^[36]

The LS of the endocardium, midmyocardium, and epicardium in the LVH group significantly decreased compared with the control group ($P < .05$). The changes in the LV configuration were used as the basis of impaired LV function. The prevalence of LVH is high in patients with uremia and is an important manifestation of uremic cardiomyopathy.^[6–8] Hypertension, anemia, phosphorus metabolic abnormalities, and so on could cause LVH. Chronic hypertension could increase the LV loop resistance and cause cardiomyocyte hypertrophy and interstitial fibroblast proliferation. These 2 factors constitute the

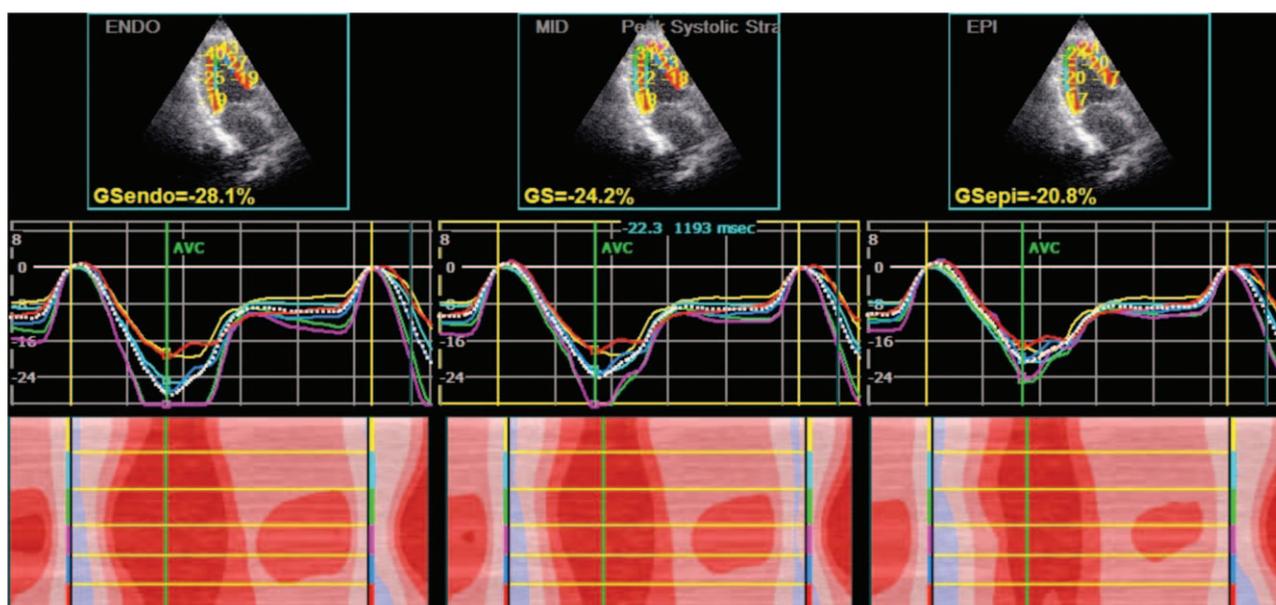


Figure 1. Left ventricular (LV) longitudinal strain curves of endocardium, midmyocardium, and epicardium in the LVH group from LV long-axis view. LVH=left ventricular hypertrophy.

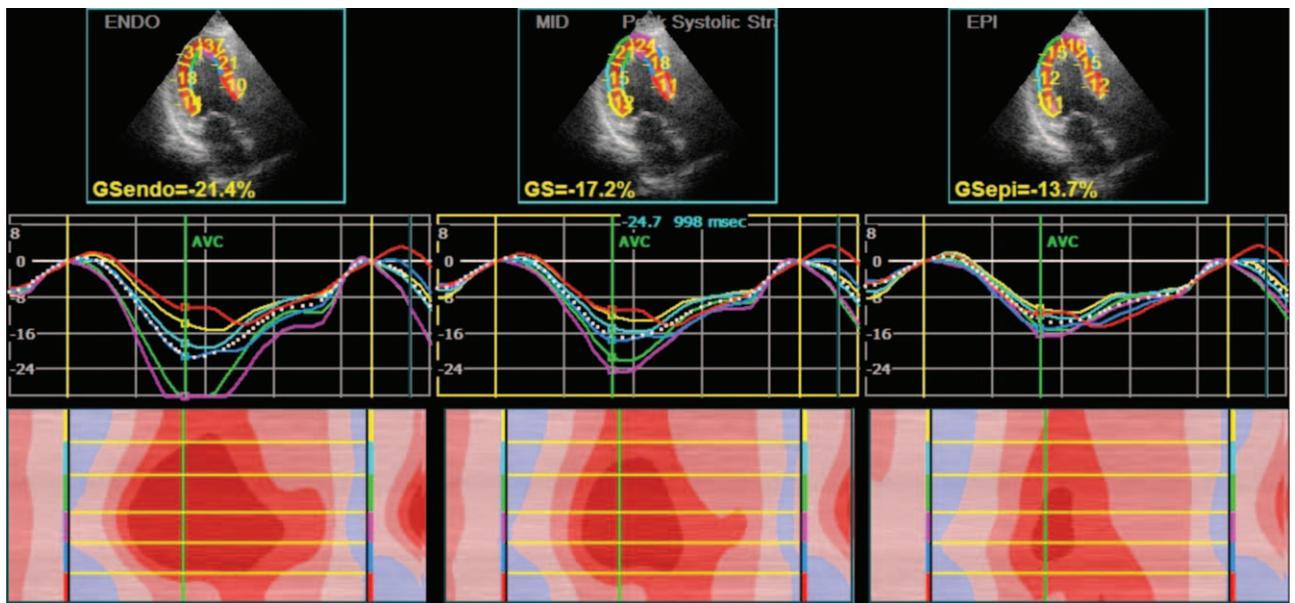


Figure 2. Left ventricular circumferential strain curves of endocardium, midmyocardium, and epicardium in the LVH group from papillary muscles level. LVH=left ventricular hypertrophy.

important pathological basis of LVH in patients with uremia.^[37,38] Myocardial fibrosis could aggravate LVH and impair the cardiac function of patients with uremia with LVH. At the same time, LVH could reduce the length and density of the myocardial capillary, and reduce the blood supply to the myocardium.^[38] The scope and degree of lesion of the LV myocardium in the LVH group is heavier than that in the LVN group; the hypertrophic endocardial fibers are rearranged and the structure is disordered^[39]; thus the systolic function of 3 layers of myocardium were all impaired in the LVH group. In addition, the LS of the endocardium in the 3 groups was

significantly different ($P<.05$). This finding suggests that longitudinal systolic function of the endocardium was impaired not only in the LVH group but also in the LVN group, which presents a high sensitivity of layer-specific 2D-STE in detecting subclinical myocardial injury in patients with uremia; the causes may include the following:

1. The fractional contributions to total wall thickening of the endocardium, midmyocardium, and epicardium were 58%, 25% and 17%, respectively. Meanwhile, endocardium mainly consists of longitudinal fibers that play an important role in cardiac systolic movement.^[18,40]

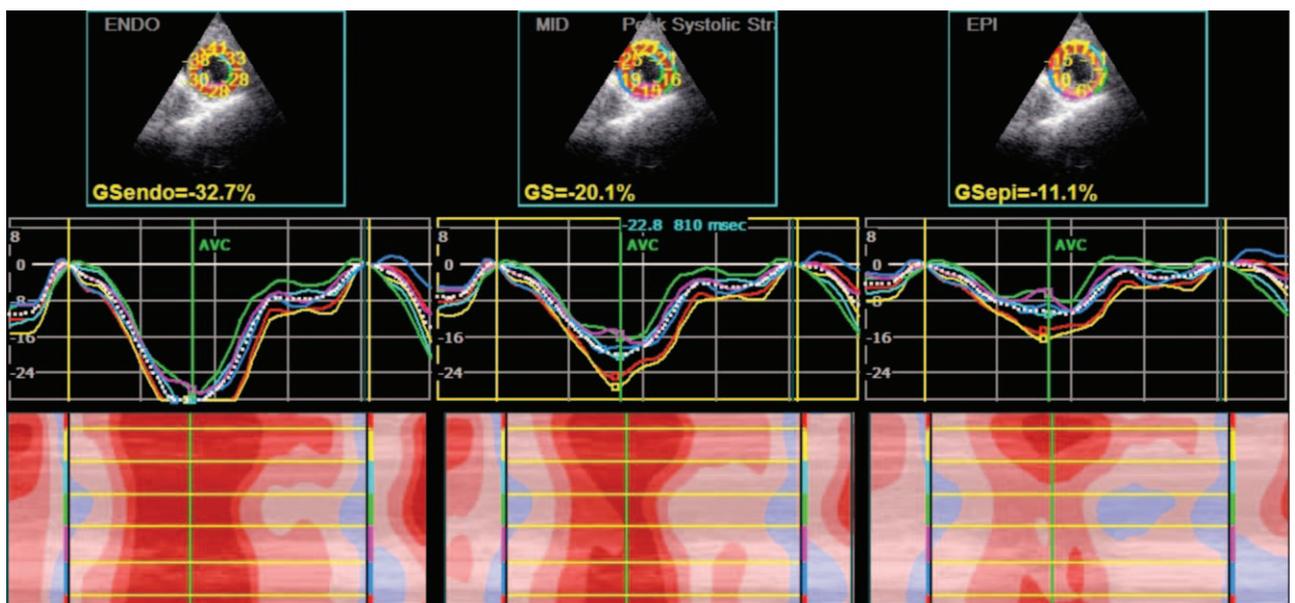


Figure 3. Left ventricular longitudinal strain curves of endocardium, midmyocardium, and epicardium in the control group from LV long-axis view. LV=left ventricular.

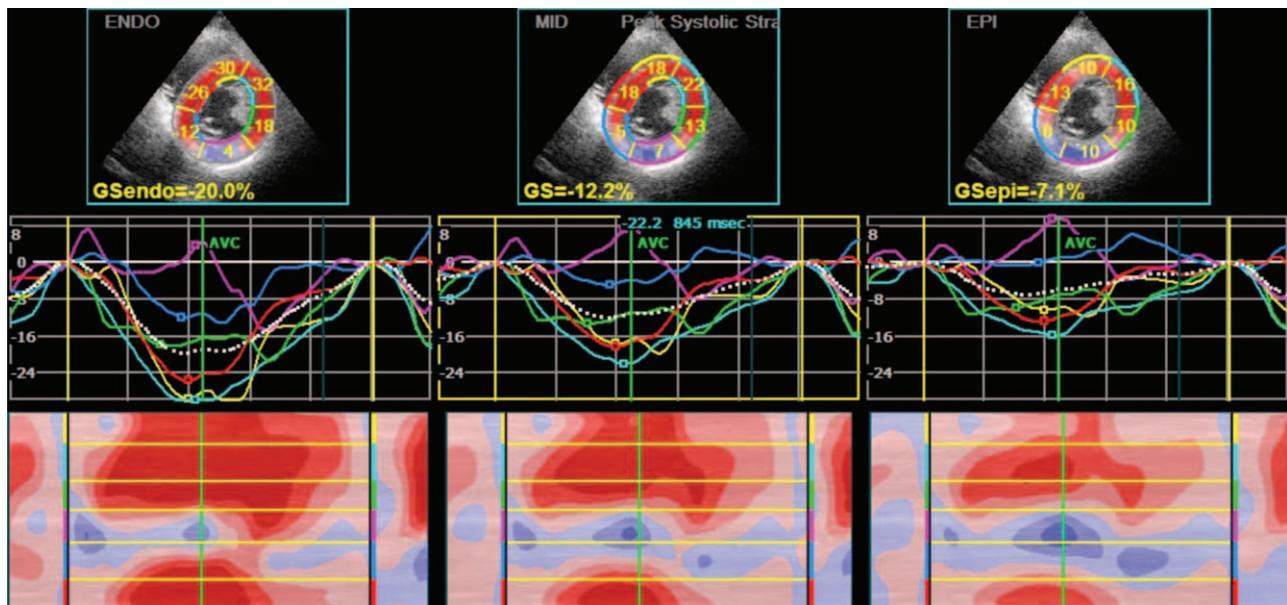


Figure 4. Left ventricular circumferential strain curves of endocardium, midmyocardium, and epicardium in the control group from papillary muscles level.

2. Because of the poor hypoxia tolerance, higher tendency for collateral blood flow, lower mean effective perfusion pressure caused by systolic extravascular compression, it needs more oxygen for thickening in endocardium than that of the 2 other layers. Therefore, the endocardium is more easily impaired.^[40,41]

A study by Scharrenbroich et al^[42] indicated that assessment of layer-specific strain by 2D-STE might identify myocardial injury in acute myocardial infarction patients, the global longitudinal systolic function of the endocardium was more affected in patients with acute myocardial infarction compared with epicardial function and LVEF. A study by Luo et al^[28] showed that epirubicin-induced cardiotoxicity had a significant impact on the pattern of global LS of the endocardium in breast cancer patients with epirubicin treatment. These previous studies have all presented a high sensitivity of layer-specific 2D-STE in detecting subclinical myocardial injury.

There were no significant differences in the CS of these 3 layers between the LVN and control groups ($P > .05$), suggesting that the circumferential systolic function might not be damaged or the degree of impaired circumferential systolic function was too slightly to detected via layer-specific 2D-STE in the LVN group. The circular motion occurs in the short axis of the heart and is mainly determined by the midmyocardium. The value of the CS is negative when shortened, but positive when elongated.^[43] Because of the curvature radius of the circumferential myocardial fibers is smaller than that of the longitudinal fibers, and the

tension in the circumferential fibers under deformation is lower, thus the CS on myocardial fibers is less sensitive than that of LS.^[44] The CS of the endocardium and midmyocardium in the mitral annulus and papillary muscle levels of the LVH group were significantly lower than those in same section of the LVN and control groups ($P < .05$), while there were no significant differences in the CS of the epicardium among the 3 groups ($P > .05$). The reason might be that the endocardium and midmyocardium had been damaged in the patients with uremia in the LVH group. However, compared with the LVN and control groups, there was no significant difference in the CS of the endocardium in the apical level of the LVH group ($P > .05$), suggesting that the damage progression of 3 layers of myocardium in different level is not at the same time. The reason is unclear, and a further study required. Compared with the result of LS, this could imply that the LS of myocardial fibers is more sensitive than that of CS. Leng et al^[45] also found that a decrease in LS was noted before a decrease in CS.

4.1. Study limitations and strengths

Several limitations of this study must be considered. First, this study included a relatively small number of patients. Second, long-term clinical outcome data, such as cardiovascular event rates and survival rates, were not assessed in the present study, and the prognostic significance of our findings was not evaluated. Third, some biochemical markers, such as brain natriuretic peptide, which are relevant markers for myocardial damage, were

Table 5

Inter and intraobserver analysis of LS and CS.

	Intraobserver				Interobserver			
	<i>R</i>	Bias (%)	LOA (%)	ICC	<i>R</i>	Bias (%)	LOA (%)	ICC
LS	0.88	0.93	-1.21 to 1.57	0.939	0.86	0.88	-1.67 to 2.84	0.924
CS	0.83	2.92	-6.91 to 5.76	0.856	0.82	2.61	-7.66 to 4.30	0.879

CS=circumferential strain, ICC=intraclass correlation coefficient, LOA=limit of agreement, LS=longitudinal strain, *R*=coefficient of determination.

not analyzed.^[46,47] Fourth, the quality of layer-specific 2D-STE depends highly on the spatial resolution of the image and on the frame rate of the cine loops^[12]; therefore, a number of the subjects had to be excluded from the analysis because the image quality in 1 or more segments was insufficient for layer-specific 2D-STE analysis. Fifth, in the actual myocardial structure, LV myocardium divisions in the layers are not clear-cut and the layers of the fibers are not isolated; thus each layer of the myocardium affect each other.^[48] Sixth, according to the recommendations of the ASE 2015, there are several methods that effectively calculate LVM from cube formula—truncated ellipsoid method, area-length method, and 3-dimensional based formula. We used the cube formula to calculate the LVM; the cube formula has several advantages: the method could be used fast and widely and it has wealth of published data and demonstrated prognostic value. However, the cube formula also has disadvantages: the method is based on the assumption that the left ventricle is a prolate ellipsoid with a 2:1 long-to-short axis ratio and symmetric distribution of hypertrophy; the beam orientation frequently off axis; and because linear measurements are cubed, even small measurement errors in dimensions or thickness have an impact on accuracy; apart from these, it overestimates LV mass and inaccurate in the presence of asymmetric hypertrophy, dilated ventricles, and other diseases with regional variations in wall thickness.^[49]

The strengths of this study included: the layer-specific myocardial deformation analysis provides additional information in myocardial function assessment of patients with uremia, in patients with uremia with a normal LVEF who do not manifest overt LV abnormalities; however, the myocardial function of the left ventricle may already be impaired, thus it is helpful to timely detect the abnormal myocardial function, it could help clinicians to take necessary measures to decrease the risk of morbidity and mortality. Furthermore, our findings may benefit the classified clinical management of the patients with uremia.

5. Conclusions

In patients with uremia, the longitudinal and circumferential systolic function in 3 myocardial layers of the LVH group, and the longitudinal systolic function in endocardium of the LVN group were found significantly impaired by layer-specific 2D-STE. In patients with uremia, who have a normal LVEF, layer-specific 2D-STE could quantitatively evaluate the systolic function of the left ventricle with different configurations.

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Author contributions

Dongmei Huang served as an observer in this study and guided the clinical experiment and writing of the manuscript. Prof. Li was also an observer in this study and mainly involved in the relative works, provided suggestions to this manuscript. Mengyao Sun was the other observer, wrote this manuscript and is the first author of this work. Yu Dong and Ying Wang were

mainly responsible for recruiting participants. The final manuscript is approved by all authors.

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