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Altered spatial distribution of the diastolic left ventricular pressure difference in heart failure

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Abstract

Background—The left ventricle (LV) fills in early diastole due to a progressive intraventricular pressure difference (IVPD) that extends from the left atrium (LA) to the LV apex. We hypothesized that, in symptomatic heart failure (HF) regardless of LV ejection fraction (EF), an increase in LA pressure maintains early diastolic filling due to a preserved IVPD from the LA to the mid LV, while the IVPD from the mid LV to the apex is diminished due to reduced LV suction.

Methods—One hundred fifty and one HF patients (50 with preserved EF (EF ≥ 0.50, HFpEF) and 101 with reduced EF (EF < 0.50, HFrEF)) and 28 normal controls were prospectively enrolled. The IVPD from LA to the LV apex (total IVPD), LA to mid LV (basilar IVPD), and mid LV to the apex (apical IVPD) were determined using color M-mode Doppler (CMMD) echocardiographic data to integrate the Euler equation. The propagation of early diastolic filling was also assessed by CMMD.

Results—LVEF was 0.63 ± 0.07 in HFpEF, 0.32 ± 0.09 in HFrEF, and 0.64 ± 0.06 in controls. Peak early diastolic transmitral flow velocity (E) were similar among the groups and the basilar IVPD were maintained in HFpEF and HFrEF (HFpEF: 1.59 ± 0.62 mmHg, HFrEF: 1.49 ± 0.75 mmHg, controls: 1.80 ± 0.61 mmHg, ANOVA NS). However, the apical IVPD was decreased in both HF groups (HFpEF: 1.18 ± 0.56 mmHg, $P < 0.01$ vs controls; HFrEF: 0.87 ± 0.48 mmHg, $P < 0.01$ vs controls; controls: 1.65 ± 0.62 mmHg), resulting in a decreased total IVPD in HF (HFpEF: 2.55 ± 0.80 mmHg, $P < 0.01$ vs controls; HFrEF: 2.16 ± 0.80 mmHg, $P < 0.01$ vs controls; controls: 3.17 ± 0.91 mmHg). E/e' was increased in HF consistent with elevated LA pressure. In HF, E

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Disclosures

Drs. Hiroyuki Iwano, Daisuke Kaimimura, Ervin Fox, Michael Hall, and William Little are employed by University of Mississippi Medical Center. Dr. Pavlos Vlachos is employed by Purdue University. Dr. Little has served as a consultant for CorAssist Cardiovascular, Ltd., Medtronic, Inc., Bio-Control Medical, CorNova Inc, and CVRx, Inc.

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correlated with basilar IVPD but not with apical IVPD whereas the propagation of the filling correlated with the apical IVPD but not with the basilar IVPD.

Conclusion—In both HFpEF and HFrEF, the apical IVPD is reduced while the basilar IVPD was maintained by elevated LA pressure resulting in preserved E.

Keywords

Left ventricular diastolic function; Heart failure; Intra left ventricular pressure difference; Color M-mode Doppler imaging

Introduction

The left ventricle (LV) fills in early diastole due to a progressive pressure difference from the left atrium (LA) to LV apex.¹ Normally, the intraventricular pressure difference (IVPD) is generated as rapid myocardial relaxation and recoil of elastic elements compressed during ejection causes LV pressure to fall below LA pressure. This results in a progressive IVPD that extends from the LA to the LV apex driving brisk early diastolic filling that rapidly propagates to the apex.² Normally, a reduction of early diastolic pressures at the LV apex during exercise allows enhanced LV filling without an elevation of LA pressure.^{3, 4} This process is altered with diastolic dysfunction. In the presence of impaired relaxation, the pressure fall in LV apex is diminished resulting in a reduced IVPD and decreased early diastolic filling.⁵ In an animal model of progressively impaired LV function, an increase in LA pressure maintains or even increases the early diastolic IVPD and filling despite higher LV diastolic pressures.⁵ Although, there is the normal or even increased E (pseudo-normalized or restricted filling pattern) in most symptomatic patients with HF, the total IVPD from the LA to the LV apex has been reported to be reduced in these patients.^{6–8} To explain this apparent paradox, we hypothesized that, in patients with symptomatic HF regardless of LV ejection fraction (EF), increased LA pressure maintains the basilar IVPD from the LA to the mid LV, while the apical IVPD from mid LV to the apex is diminished resulting in reduced total IVPD. The basilar IVPD from the LA to mid LV accounts for the preserved or increased E wave in symptomatic HF patients.

The IVPD can be analyzed noninvasively by integrating the Euler equation from the echocardiographic color M mode Doppler (CMMD) imaging providing a non-invasive method to test our hypothesis.^{6, 9} Accordingly, the aim of the present study was to determine the difference of the spatial distribution of the IVPD between the patients with HF and normal controls.

Methods

Study Population

The study protocol was approved by the institutional review board of the University of Mississippi Medical Center (#2013-0254). Between November 2013 and June 2014, we prospectively evaluated 608 consecutive patients who underwent clinically indicated transthoracic echocardiography and had a documented history of symptomatic HF based on the Framingham criteria.¹⁰ Exclusion criteria were non-sinus rhythm, left bundle branch

block, fusion of early and late diastolic mitral inflow, significant left-side valvular disease, prosthetic valve, and LV assist device. From the 334 patients who were eligible for the study inclusion, 183 patients with insufficient two-dimensional or CMMD echocardiographic images were also excluded before the image analysis. Accordingly, the remaining 151 HF patients were included in the final analysis. The HF patients were divided into HF with preserved LVEF (HFpEF) and HF with reduced LVEF (HFrEF) with a partition value of an LVEF of 0.50. Twenty-eight subjects without any previous history of cardiovascular risk factors who underwent transthoracic echocardiography for the assessment of cardiac function (due to other organ disease: 13, screening: 5, atrial arrhythmia: 4, syncope: 4, palpitation: 2) and had not any echocardiographic abnormal findings served as the normal controls.

Echocardiography

Echocardiography was performed by using an iE33 ultrasound system with a multiple frequency transducer (Phillips Medical Systems, Andover, Massachusetts). Digital 2-dimensional cine loops were obtained in the apical 4-chamber, 2-chamber, and long-axis views and short-axis views of basal, mid-ventricular, and apical level at a frame rate of 72 ± 17 (range 40 to 140) s^{-1} .

LV volumes and left atrial volume were measured according to the recommendations of the American Society of Echocardiography.¹¹ LV mass was calculated according to Devereux formula and indexed to the body surface area.¹² Transmitral Doppler flow was recorded in the apical 4-chamber view, and peak early diastolic velocity (E), peak atrial velocity (A), and E/A ratio were measured. Septal and lateral peak systolic annular velocities (s') as well as early diastolic peak of mitral annular velocities (e') were measured from the apical 4-chamber view by using pulsed-wave tissue Doppler imaging and average of the septal and lateral velocities were used for the subsequent analysis. The ratio of E to e' (E/e') was calculated. CMMD images were recorded with a cursor parallel to LV inflow in the apical 4-chamber view. Diastolic function was graded as normal, impaired relaxation (grade I), pseudo-normal (grade II), and restrictive filling (grade III) using e' , E/A, and E/e' as previously described.¹³

Myocardial function was also assessed by speckle-tracking method by using QLAB Advanced Quantification Software version 9.0 (Phillips Medical Systems, Andover, Massachusetts) as previously reported.^{14, 15} Briefly, the longitudinal parameters were obtained from three apical views and the circumferential parameters were from mid-ventricular short-axis view. The global strain/strain rate curves were extracted with the use of entire LV wall in the image and peak global strain, peak systolic global strain rate (SR_{sys}), and early diastolic peak of global strain rate (SR_E) were measured. Longitudinal indices from three apical views were averaged and used for the final analysis. In addition to the global strain, peak segmental longitudinal strain was measured from each segmental strain curves and averaged for the basal and apical levels. LV rotation was measured at basal and apical short-axis views and LV twist was calculated as the apical rotation relative to the basal rotation at each corresponding time point which was normalized to the percentage of systolic duration.

Analysis of the CMMD

The CMMD image was analyzed using an in-house developed automated analysis algorithm based on MATLAB (The Mathworks, Natick, Massachusetts). A more detailed description of this algorithm has been published.² The isovelocity contours between 45% and 55% of the peak E was detected and an ensemble contour was fit to the series of isovelocity contours (Figure 1). The conventional flow propagation velocity of early diastolic mitral inflow (Vp) was automatically measured by tracing the isovelocity contour between 45% and 55% of the peak E from mitral annulus to 4 cm into the LV cavity. In addition, the extent of propagation of the early diastolic filling into the LV was assessed by measuring the distance from the mitral annulus to the deceleration point of the initial E wave propagation velocity (Figure 1) by using a statistical change-point analysis method.² The initial propagation velocity from mitral annulus to the deceleration point (initial Vp) and after the terminal point (terminal Vp) were also measured.²

The IVPD was estimated by using the CMMD data to integrate the one-dimensional Euler equation as previously described.^{2, 13} The pressure difference at each point along with the scan line was measured relative to LA just above the mitral valve at the mitral annulus just before mitral valve opening by calculating the line integral between them.^{6, 9} From the temporal profile of the IVPD, the peak total IVPD from the LA to LV apex was calculated.^{7, 9} This method has been validated by comparison to direct measurements with micromanometers.^{6, 9} In addition to the total IVPD from LA to LV apex, the basilar IVPD from the LA to mid LV (2 cm from the mitral annulus) and the apical IVPD from the mid LV to LV apex were also measured (Figure 2).⁸

Statistical Analysis

Continuous variables were expressed as mean $\pm$ SD and compared by 2-tailed unpaired *t* test between HFpEF and HFrEF or by using one-way analysis of variance (ANOVA) among the groups, and post hoc analysis was then performed by using Turkey-Kramer's test. Proportions were compared using chi-square analysis. Linear regression analysis was used for the detection of correlation between two continuous variables. For all tests, a *P* value of <0.05 was considered significant. All data were analyzed using JMP software by SAS Institute Inc.

Results

Patient characteristics

The clinical characteristics of the study subjects are presented in Table 1. Among the 151 HF patients, 50 patients had a preserved LVEF (HFpEF) and 101 patients had a reduced LVEF (HFrEF). Both of HFpEF and HFrEF were older and had a higher systolic blood pressure than normal controls. HFrEF tended to have worse HF symptoms, more non-ischemic cardiomyopathy, and less hypertensive heart disease than HFpEF. The use of angiotensin converting enzyme inhibitor or angiotensin II receptor blockers and beta blockers were less frequent and that of calcium antagonists was more frequent in HFpEF than in HFrEF.

Comparison of the echocardiographic parameters

The echocardiographic parameters are summarized in Table 2. LV end-diastolic and end-systolic volumes were larger and EF was lower in HFrEF than in controls and HFpEF whereas they were comparable between HFpEF and controls. LA volume index was enlarged in HFpEF compared to the controls and further enlarged in HFrEF.

Vp was significantly slower in HFrEF compared to the controls and tended to be slower in HFpEF than in controls, which did not reach statistical significance. Although, e' was similarly decreased in HFpEF and HFrEF, s' was lower in HFrEF than in HFpEF. E/e' was higher both in HFpEF and HFrEF than in controls, consistent with an elevation of LA pressure in the HF groups. Global longitudinal strain and SR_{Sys} were reduced in HFpEF than in controls and further reduced in HFrEF. In contrast, global circumferential strain and SR_{Sys} were relatively preserved in HFpEF ($P=0.08$ and $P=0.64$ vs controls, respectively) and significantly reduced in HFrEF. Similarly, LV twist was preserved in HFpEF compared to the controls and reduced in HFrEF. In addition, basal and apical longitudinal strains were reduced both in HFpEF and HFrEF than in normal controls as global longitudinal strain did.

Comparison of the IVPD

The IVPD was compared among the groups for the total IVPD from the LA to LV apex, as well as the basilar and apical IVPDs (Figures 3 and 4). The basilar IVPD was comparable among the groups. However, the apical IVPD was reduced both in HFpEF and HFrEF compared to the controls, resulting in a significant reduction of the total IVPD from LA to the apex in both HFpEF and HFrEF.

When the IVPDs were compared among the different diastolic grades, the apical IVPD was similarly reduced in grade I, grade II, and grade III than in normal (normal: 1.60 ± 0.10 mmHg; grade I: 0.84 ± 0.51 , $P < 0.01$ vs normal; grade II: 1.02 ± 0.42 mmHg, $P < 0.01$ vs normal; grade III: 0.99 ± 0.54 mmHg, $P < 0.01$ vs normal; ANOVA $P < 0.001$) whereas basilar IVPD was reduced in grade I and grade II but not in grade III (normal: 1.86 ± 0.72 mmHg; grade I: 1.04 ± 0.32 , $P < 0.01$ vs normal; grade II: 1.16 ± 0.46 mmHg, $P < 0.01$ vs normal; grade III: 1.65 ± 0.72 mmHg, $P = 0.44$ vs normal; ANOVA $P < 0.001$).

Correlations of LV myocardial function to the IVPD

In overall subjects, all parameters significantly correlated with the apical IVPD with the absolute R values of 0.31 to 0.50 (Table 3).

Correlations of the early diastolic filling to the IVPD

The correlations within HF patients between the IVPD and early diastolic LV filling are shown in Figure 5. In HF, peak E did not correlate with the apical IVPD from mid LV to the apex, whereas peak E did correlate with the basilar IVPD from LA to mid LV. In contrast, the deceleration point of the E wave propagation velocity correlated with the apical IVPD but not basilar IVPD.

Reproducibility analysis

The reproducibility of the IVPD was assessed in 20 of the study subjects. Two independent observers analyzed the same CMMD images and one blinded observer repeated the analysis on a separate day. Intra- and inter-observer variabilities of total, basilar, and apical IVPD were 0.18 mmHg (7%) and 0.19 mmHg (8%), 0.10 mmHg (8%) and 0.15 mmHg (12%), and 0.10 mmHg (8%) and 0.15 mmHg (12%), respectively.

Discussion

The early diastolic filling (E) of the LV is driven by the IVPD.^{3, 6, 16} However, in patients with symptomatic HF, E is typically normal or increased, while the total IVPD from the LA to the LV apex may be reduced.⁶ Our study confirmed that the IVPD from the LA to the apex was reduced in symptomatic patients with HF regardless of LV EF. This reduction of the total IVPD was due to a reduction of the apical IVPD from mid LV to the apex which was associated with reduced longitudinal LV function and is consistent with diminished LV suction. The reduced apical IVPD was associated with reduced early diastolic flow propagation towards the apex in patients with HF. In contrast, the basilar IVPD from the LA to the mid LV was preserved due to an increase in LA pressure. This basilar IVPD maintains the early diastolic filling despite reduced LV suction and the reduced total IVPD from LA to LV apex.

Spatial distribution of the IVPD in heart failure

We found a clear correlation between the basilar IVPD and peak E, whereas there was no correlation between the apical IVPD and peak E in HF. This indicates that early diastolic LV filling is determined by the LA pressure and the basilar IVPD but not by the apical IVPD in HF. Although a decreased total IVPD assessed by the same method we used has been observed in patients with dilated cardiomyopathy,⁶ hypertrophic cardiomyopathy,⁷ and diastolic dysfunction,⁸ ours is the first study to determine that the lower total IVPD in HF regardless of EF is due to a reduced apical IVPD while early diastolic filling is preserved by the basilar IVPD.

Physiological determinants of the IVPD

During systole, both intramyocardial and extra-cellular elastic components are compressed storing some of the energy of contraction. The subsequent elastic recoil of these elements contributes to LV suction.¹⁷ Consistent with this concept, the IVPD is associated with LV systolic^{18, 19} and diastolic function.¹⁹ Our results in which all parameters of LV systolic and diastolic function were associated with the apical IVPD (Table 3) similarly support this concept. Furthermore, consistent with other observations,²⁰ circumferential shortening and LV twist were relatively preserved and longitudinal shortening was reduced in HFpEF whereas both of them were reduced in HFrEF (Table 2). A maintained circumferential shortening and LV twist despite reduced apical IVPD and longitudinal shortening in HFpEF suggests that the reduced longitudinal function plays an important role in the decreased apical IVPD. Although it is difficult to elucidate the causal-relationships between LV wall mechanics and IVPD because they occur almost simultaneously and interact with each other,

our data are consistent with the concept that decreased longitudinal LV function is a major contributor to the decreased apical IVPD in HF.

Study limitations

We did not measure invasive hemodynamics for the comparison with the echocardiographic parameters. However, the HF patients had symptoms of pulmonary congestion, enlarged LA dimensions, and increased E/e' all of which are consistent with increased LA pressure. In addition, the result of the comparison among the different diastolic grades supports the differences in the IVPDs. Because we selected the HF patients based on their history of hospitalization, this study does not include the HF patients without a hospitalization history who have the symptom only during exertion.

In this study, the normal controls were younger than the HF patients. Therefore, we selected relatively older normal controls (35 years old) and young HF patients to provide a closer age matching (Supplemental Table). This analysis produced results similar to the overall study group suggesting that the age differences are not the cause of the differences we observed.

We evaluated the IVPD only along a single scan line from the left atrium to the LV apex. Thus, we cannot assess the IVPD and flow outside of the scan line. We excluded a large proportion of the subjects (183 out of 344) because of insufficient quality of the two-dimensional or CMMD images before doing the analysis.

Conclusions

In both HFpEF and HFrEF, the total IVPD from the LA to the LV apex is reduced due to a reduction in the apical IVPD related to reduced longitudinal function. This is associated with a diminished propagation of early diastolic flow toward the apex. In contrast, the basilar IVPD from the LA to mid LV is maintained by increased LA pressure which accounts for the normal or enhanced early diastolic filling (E) in patients with symptomatic HF.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations list

IVPD	intraventricular pressure difference
CMMD	color M-mode Doppler
HFpEF	heart failure with preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction

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Figure 1.

Left: Color M-mode Doppler imaging of transmitral flow. Right: Corresponding dealiased image with initial (pink) and terminal (green) propagation velocities. Because the point where the propagation velocity turns from pink to green indicates the deceleration point, the distance from mitral annulus to the deceleration point (yellow vertical arrow) was measured as an extent of propagation of the early diastolic filling.

Figure 2.

Measurement of the IVPD. From the color-M mode Doppler imaging (**A, top**), temporal profile of the IVPD from the left atrium (LA) at the level of the mitral annulus to LV apex (**A, below**), from LA to mid LV (2 cm from the mitral annulus) (**C**), and mid LV to the apex (**D**) were calculated by integrating the one-dimensional Euler equation. The corresponding spatial profile of the IVPD at the peak timing of the IVPD from LA to the apex is also shown (**B**). From the temporal profiles of the IVPDs, the peak early diastolic IVPDs (vertical arrows) were measured for LA to the apex (black), LA to mid LV (blue), and mid LV to the apex (red), respectively. IVPD, intraventricular pressure difference.

Figure 3.

Examples of the apical IVPD from mid LV to the apex (middle line), basilar IVPD from the LA to mid LV (bottom line), and the corresponding color M-mode Doppler images (Top line) are shown. In HFpEF and HFrEF, the apical IVPD from mid LV to the apex is reduced compared to the normal while the basilar IVPD from the LA to mid LV is preserved. LV, left ventricular; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction. Other abbreviations are the same as Figure 2.

Figure 4.

Comparisons of the total, basilar, and apical IVPD among normal controls (dense colors), HFpEF (light colors), and HFrEF (white). [†] $P < 0.05$ vs normal controls, [‡] $P < 0.05$ vs HFpEF. Abbreviations are the same as Figures 2 and 3.

Figure 5.

A: Correlations of peak early diastolic LV filling velocity (E) to the IVPD in heart failure.

B: Correlations of the deceleration point of E wave propagation from mitral annulus to the IVPD in heart failure. Abbreviations are the same as Figure 2.

Table 1

Clinical characteristics of the study subjects

	Control (N=28)	HFpEF (N=50)	HFREF (N=101)	P value
Age, years	36±15	60±16 [†]	55±13 [†]	<0.001
Female, n (%)	15 (52)	28 (56)	35 (35)	0.027
Body surface area, m ²	1.85±0.25	1.98±0.28	2.01±0.24 [†]	0.013
Systolic blood pressure, mmHg	119±19	142±24 [†]	132±26 [†]	<0.001
Diastolic blood pressure, mmHg	69±10	74±18	80±19 [†]	0.020
Heart rate, bpm	73±17	77±14	79±14	0.11
Duration from HF worsening, days	NA	28±67	75±141 [‡]	
NYHA functional class				0.006
I	NA	0 (0)	0 (0)	
II	NA	33 (66)	43 (43)	
III or IV	NA	17 (34)	58 (57)	
Cardiac disease, n (%)				<0.001
Ischemic heart disease	NA	10 (20)	30 (30)	
Non-ischemic dilated cardiomyopathy	NA	1 (2)	36 (36)	
Hypertensive heart disease	NA	31 (62)	18 (18)	
Undefined	NA	6 (12)	16 (16)	
Others	NA	2 (4)	1 (1)	
Comorbidity, n (%)				
Hypertension	NA	47 (94)	81 (80)	0.018
Diabetes Mellitus	NA	22 (44)	48 (48)	0.68
Dyslipidemia	NA	8 (16)	17 (17)	0.90
Medication, n (%)				
ACE-I or ARB	NA	23 (46)	71 (70)	0.004
Beta blockers	NA	32 (64)	84 (83)	0.010
Calcium antagonists	NA	16 (32)	13 (13)	0.006
Diuretics	NA	31 (62)	60 (59)	0.76
Aspirin	NA	23 (46)	47 (47)	0.91
Statin	NA	21 (42)	57 (56)	0.09

P values are for the analysis of variance (ANOVA) or chi-square test.

[†]P<0.05 vs normal group by Turkey-Kramer's post-hoc test,

[‡]P<0.05 vs HFpEF by paired t test.

NA, not applicable for controls; HF, heart failure; New York Heart Association; ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker, HFpEF, heart failure with preserved ejection fraction; HFREF, heart failure with reduced ejection fraction.

Table 2

Echocardiographic measurements

	Control (N=28)	HFpEF (N=50)	HFrfEF (N=101)	P value
Two-dimensional findings				
LV mass index, g/m ²	78±21	134±51 [†]	154±59 [†]	<0.001
LV end-diastolic volume, mL	86±30	103±39	170±57 ^{†‡}	<0.001
LV end-systolic volume, mL	31±13	39±16	118±49 ^{†‡}	<0.001
LV ejection fraction	0.64±0.06	0.63±0.07	0.32±0.09 ^{†‡}	<0.001
Left atrial volume index, mL/m ²	18.0±6.0	31.8±13.5 [†]	37.2±12.4 ^{†‡}	<0.001
Doppler findings				
E wave velocity, cm/s	83±16	91±28	92±27	0.25
A wave velocity, cm/s	64±16	94±31 [†]	64±26 [‡]	<0.001
E/A	1.34±0.41	1.08±0.54	1.78±1.05 ^{†‡}	<0.001
E wave deceleration time, ms	192±50	218±60	167±55 [‡]	<0.001
s', cm/s	9.5±2.3	6.8±1.3 [†]	5.0±1.1 ^{†‡}	<0.001
e', cm/s	12.3±2.4	6.4±1.6 [†]	5.9±1.7 [†]	<0.001
E/e'	6.8±1.5	14.7±4.6 [†]	16.3±5.9 [†]	<0.001
Diastolic grade, n (%)				<0.001
Normal	25 (89)	2 (4)	2 (2)	
Grade I	1 (4)	5 (10)	6 (6)	
Grade II	2 (7)	10 (20)	17 (17)	
Grade III	0 (0)	33 (66)	76 (75)	
CMMD findings				
Vp, cm/s	53.3±30.2	46.2±21.5	40.0±20.8 [†]	0.018
Initial Vp, cm/s	81.7±45.9	71.1±31.7	47.4±20.2 ^{†‡}	<0.001
Terminal Vp, cm/s	22.8±20.9	16.9±12.9	16.3±9.9	0.085
Deceleration point of initial Vp, cm	3.7±1.3	3.5±1.2	2.9±1.1 ^{†‡}	<0.001
Speckle-tracking findings				
Longitudinal global strain, %	-21.2±3.0	-16.6±3.3 [†]	-8.8±2.8 ^{†‡}	<0.001
Longitudinal basal strain, %	-20.9±5.2	-18.1±5.1 [†]	-11.5±3.8 ^{†‡}	<0.001
Longitudinal apical strain, %	-23.7±5.6	-19.6±6.0 [†]	-10.4±4.2 ^{†‡}	<0.001
Longitudinal SR _{Sys} , %	-1.2±0.2	-1.0±0.2 [†]	-0.6±0.2 ^{†‡}	<0.001
Longitudinal SR _E , %	1.5±0.4	1.0±0.3 [†]	0.6±0.2 ^{†‡}	<0.001
Circumferential global strain, %	-29.3±6.1	-26.2±7.7	-12.4±4.9 ^{†‡}	<0.001
Circumferential SR _{Sys} , %	-1.7±0.4	-1.6±0.5	-0.8±0.3 ^{†‡}	<0.001
Circumferential SR _E , %	2.2±0.6	1.7±0.6 [†]	1.0±0.4 ^{†‡}	<0.001
Left ventricular twist, degree	12.0±3.6 (N=24)	15.2±8.1 (N=33)	6.0±3.6 ^{†‡} (N=88)	<0.001

P values are for the analysis of variance (ANOVA).

[†] $P<0.05$ vs normal controls,

[‡] $P<0.05$ vs HFpEF by Turkey-Kramer's post-hoc test.

LV, Left ventricular; E, early diastolic peak of mitral inflow; A, atrial peak of mitral inflow; s', peak systolic mitral annular velocity; e', early diastolic mitral annular velocity; CMMD, color M-mode Doppler imaging; Vp, flow propagation velocity of E wave; SR_{Sys}, peak systolic global strain rate; SR_E, early diastolic peak of global strain rate. Other abbreviations are the same as Table 1.

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Table 3

Correlations to IVPD from mid LV to the apex

	R	P value
s'	0.38	<0.001
e'	0.38	<0.001
Global longitudinal strain	−0.43	<0.001
Basal longitudinal strain	−0.33	<0.001
Apical longitudinal strain	−0.41	<0.001
Longitudinal SR_{Sys}	−0.40	<0.001
Longitudinal SR_E	0.44	<0.001
Global circumferential strain	−0.50	<0.001
Circumferential SR_{Sys}	−0.42	<0.001
Circumferential SR_E	0.44	<0.001
LV twist	0.31	<0.001

Abbreviations are the same as Table 2.