Original Article

Characterizing stenosis severity of coronary heart disease by myocardial work measurement in patients with preserved ejection fraction

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Background: The novel echocardiographic parameter of myocardial work incorporates left ventricular pressure into the assessment of left ventricular systolic function and thereby corrects for afterload. We sought to investigate the diagnostic value of myocardial work to identify different grades of stenosis severity in coronary heart disease (CHD) patients with preserved left ventricular ejection fraction and without regional wall motion abnormalities.

Methods: One hundred and seventeen consecutive subjects with preserved ejection fraction referred for coronary angiography were randomized and prospectively included in this study. Forty-six in the control group, and 25, 24, and 22 in each of the grade-1, grade-2, and grade-3 CHD groups as classified by the Gensini score. The following indices of myocardial work were assessed with a Vivid E95 Version 203 instrument: global work index (GWI), global constructive work (GCW), global wasted work (GWW), global work efficiency (GWE).

Results: Both GWI (P<0.001) and GCW (P<0.001) decreased significantly in CHD grade-1, increased slightly in CHD grade-2 compared with CHD grade-1, and decreased significantly in CHD grade-3. GWW (P<0.001) increased significantly from CHD grade-1 to CHD grade-3, while GWE (P<0.001) decreased significantly from CHD grade-1 to CHD grade-3. Receiver operating characteristic curves analysis revealed good discrimination between the control group and CHD grade-3 for GWI [area under the curve (AUC): 0.810; 95% confidence interval (CI): 0.691–0.930], GCW (AUC: 0.758; 95% CI: 0.631–0.885), GWW (AUC: 0.754; 95% CI: 0.624–0.885) and GWE (AUC: 0.817; 95% CI: 0.709–0.926). The assessment of intraobserver and interobserver variability in the MW echocardiographic data documented good interclass correlation coefficients (all >0.85).

Conclusions: Myocardial work incorporates left ventricular pressure into the assessment of left ventricular systolic function and thereby corrects for afterload. It identifies patients with incipient left ventricular dysfunction caused by chronic ischemia due to CHD. A gradual worsening of myocardial work parameters was observed when comparing patients with higher degrees of stenosis severity. Therefore, adding myocardial work when evaluating patients with suspected CHD may help increase diagnostic accuracy.

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Introduction

Coronary artery stenosis can lead to incipient myocardial dysfunction even before the first clinical adverse cardiac events, such as myocardial ischemia or infarction (1). Therefore, patients with complex coronary heart disease (CHD) can still present with preserved ejection fraction and without wall motion abnormalities. Speckle tracking echocardiography (STE) revolutionizes the assessment of left ventricular (LV) dysfunction, allowing modestly angle-independent quantification of myocardial deformation. Nevertheless, the main parameter global longitudinal strain (GLS) which is dependency on loading conditions, makes it difficult to distinguish between abnormal GLS due to intrinsic reduced LV contractility or increased LV afterload (2,3).

A technique of myocardial work (MW) estimation has been introduced as a valuable method to assess myocardial performance. However, MW assessment was initially calculated using invasive pressure measurements, which limited its widespread use in clinical practices (4). The STE based parameter of MW has recently been introduced. It allows non-invasive assessment of pressure-strain loops and therefore the analysis of afterload-independent LV contractility. The software analyzes GLS in combination with noninvasively measured arterial blood pressure, potentially offering incremental value to dynamic myocardial function assessment more well directed and accurately quantified (5,6).

The objective of this current study was to investigate the value of this novel MW technique to detect early LV dysfunction in CHD patients with normal LV ejection fraction and without wall motion abnormalities but with different grades of stenosis severity as defined by the Gensini score. We present this article in accordance with the STARD reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-22-955/rc).

Methods

Study population

One hundred and seventeen consecutive individuals were randomized and prospectively included in 2021–2022, comprising control subjects and CHD patients. The enrolled patients with coronary artery stenosis were divided into grade-1 (N=25), grade-2 (N=24), and grade-3 (N=22) according to the Gensini score. The control group consisted of 46 sex- and age-matched controls with normal coronary angiography outcomes recruited within hospital staff. All the individuals had preserved left ventricular ejection fraction (LVEF) and no regional wall motion abnormalities (RWMAs). None of them had bundle branch block on ECG or other known myocardial diseases. All the individuals had normal current systolic/diastolic blood pressure. Exclusion criteria were: severe arterial hypertension, evidence or history of atrial arrhythmia, LVEF less than 52% (determined using the biplane Simpson method, according to the recommendations from current guidelines) (7,8), moderate or severe valvular regurgitation, acute or chronic renal disease, dilated or hypertrophic cardiomyopathy, and congenital heart disease. The selection process is shown with a flow diagram (*Figure 1*). All the data were collected in both of the inpatient and outpatient departments of echocardiography. No missing data and indeterminate results were shown in our study.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The research protocol was approved by the regional ethics committee of Nanjing First Hospital, and all included individuals provided written informed consent.

Echocardiography assessment

Transthoracic echocardiographic examinations were

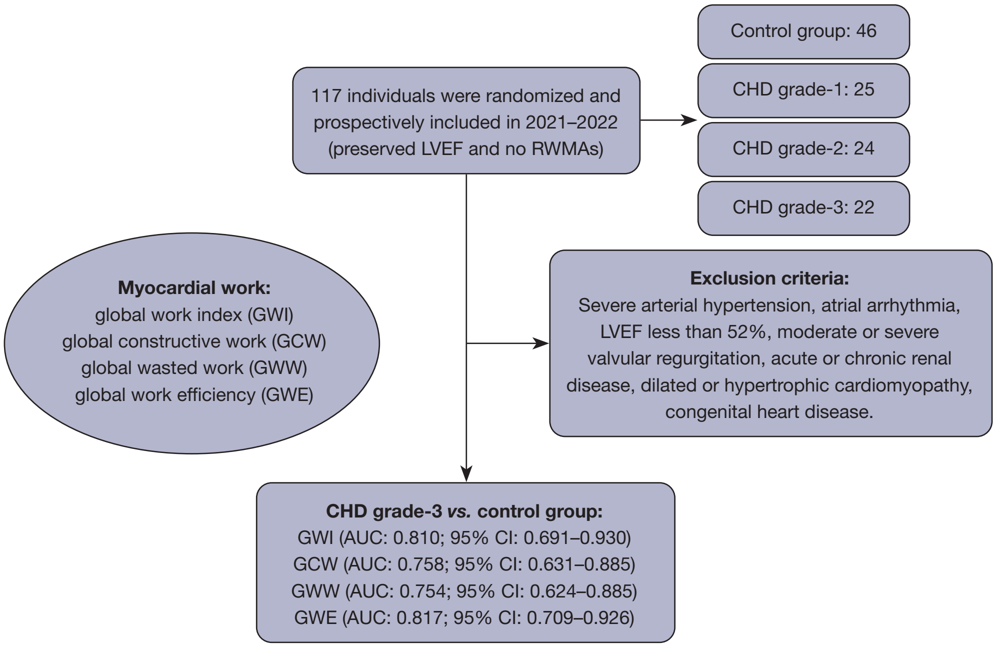


Figure 1 A flow diagram indicating the selection process for the present echocardiographic study (i.e., GWI, GCW, GWW, GWE). CHD, coronary heart disease; LVEF, left ventricular ejection fraction; RWMAs, regional wall motion abnormalities; AUC, area under the curve; CI, confidence interval; GWI, global work index; GCW, global constructive work; GWW, global wasted work; GWE, global work efficiency.

performed at rest and in the left lateral recumbent position using a Vivid E95 Version 203 (GE Medical Systems, Horten, Norway) ultrasound machine and a 2–4.5 MHz M5Sc 2D transducer. Optimal electrocardiogram (ECG) signal with a clear definition of the QRS-complex and P-wave was obtained ensuring a consistent ECG-triggering during the examination. Images were stored digitally and were analyzed offline using EchoPAC software (GE Healthcare, Milwaukee, Wisconsin, USA).

Traditional two-dimensional echocardiography

Standardized 2D evaluation was performed on the stored images according to the current recommendations (7,8). This included measurement of left ventricular end-diastolic and end-systolic volumes (LVEDV/LVESV) and calculation of LVEF by the modified biplane Simpson's method, measurement of left atrial volume index (LAVI), peak early diastolic ($E_{velocity}$) and late diastolic ($A_{velocity}$) filling velocities as well as peak early diastolic and late diastolic tissue velocities of mitral septal and lateral annular velocities ($E'_{septal/lateral}$ and $A'_{septal/lateral}$).

Novel myocardial work echocardiography

Immediately before the start of the examination, blood pressure was measured by sphygmomanometer. As part of the examination, apical 4-, 3-, and 2-chamber views were acquired with a particular focus on the LV myocardium. Using these images, global longitudinal strain was measured by manually tracing the LV endocardial border. Strain in the apical two-, three-, and four-chamber views was recorded with the bull's-eye plots, as previously described (9,10). The MW software used the measured blood pressure and the GLS results to construct LV pressure volume curves, as pressure strain loops (11).

Different parameters of MW were reported by the software as published in previous works (12-14):

- ❖ Myocardial work index: the area of pressure strain loops as strain and pressure data were synchronized using the onset of R wave on the ECG.
- ❖ Myocardial constructive work: adequate work performed during segmental shortening in systole or during lengthening in isovolumic relaxation.
- ❖ Myocardial wasted work: inadequate work

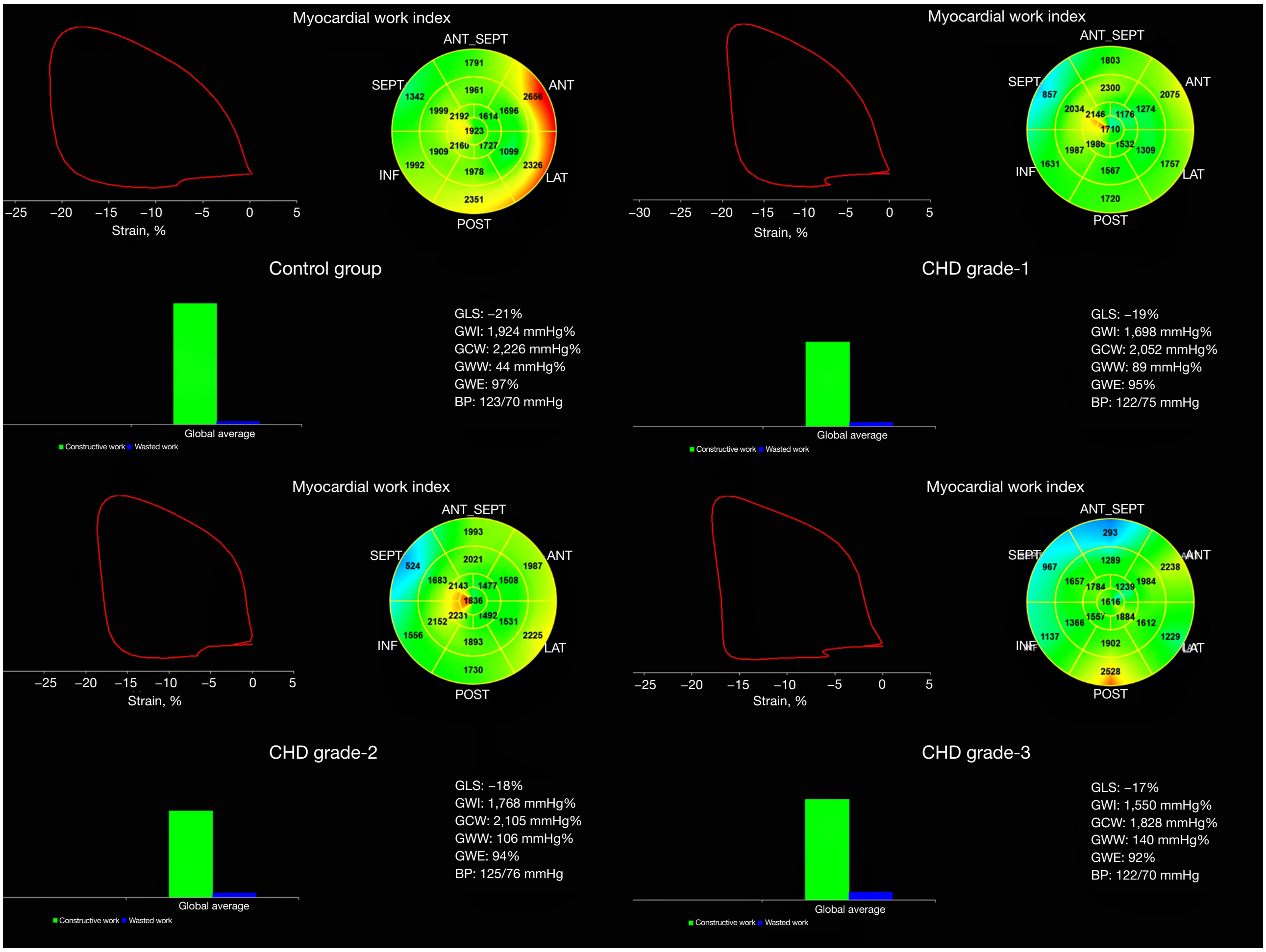


Figure 2 Four examples of myocardial work analysis, showing a control subject and one subject out of each of the three CHD grades (i.e., GWI, GCW, GWW, GWE). CHD, coronary heart disease; GLS, global longitudinal strain; BP, blood pressure; SEPT, septal; ANT-SEPT, anterior-septal; ANT, anterior; LAT, lateral; POST, posterior; INF, inferior; GWI, global work index, GCW, global constructive work, GWW, global wasted work; GWE, global work efficiency.

performed during segmental lengthening in systole or during segmental shortening in isovolumic relaxation.

- ❖ Myocardial work efficiency: calculated as a percentage expressing the ratio of constructive and wasted work in all segments.

All MW parameters are given as global values, averaged from the segmental values (*Figure 2*). [i.e., global work index (GWI), global constructive work (GCW), global wasted work (GWW), global work efficiency (GWE)].

Gensini score assessment

All angiograms were performed within three days after echocardiography for all individuals and were evaluated by two ten-year work experienced interventional cardiologists who were blinded to the baseline characteristics of the patients. We ensured that the procedure was performed in an ethical and equitable manner, with a view to maintaining the highest standards of patient care and safety.

The severity of coronary artery lesions was assessed by the Gensini scoring system as published in previous manuscripts (15,16). In brief, each coronary stenosis was given a severity score: 1 point for 1–25% stenosis, 2 points for 26–50% stenosis, 4 points for 51–75% stenosis, 8 points for 76–90% stenosis, 16 points for 91–99% stenosis, and 32 points for 100% occlusion. Afterwards, each lesion score is multiplied by a coefficient that takes into account the importance of the lesion's position from 5 for the left main (LM) coronary artery to 0.5 for the posterolateral branch.

Statistics analysis

The software IBM SPSS Statistics 26.0 was used for statistical analysis. Continuous variables were expressed as mean value ± standard deviation and categorical variables as percentages. In case of normal distribution of variables, the independent *t*-test was used for comparison of two groups. Differences among more than two groups were analyzed by one-way analysis of variance (ANOVA). Receiver operating characteristic (ROC) curves were plotted to examine the ability of MW indicators to differentiate the three CHD grades and control subjects. Statistical significance was defined as P<0.05.

Reproducibility

To evaluate reproducibility, interclass correlation coefficients (ICCs) were calculated. For this analysis, 15 randomly selected patients were analyzed twice on two different days by the same observer, as well as by a second observer, who was blinded to the values obtained by the first observer.

Results

Baseline characteristics and general data

A flow diagram of the selection process is shown in *Figure 1*. In our study, patients were classified into three stenosis severity grades according to the quartile of Gensini score: CHD grade-1 with <22 points; CHD grade-2 with ≥22 points and <48 points; CHD grade-3 with ≥48 points. The study population consisted of 117 individuals: 25 CHD grade-1 patients, 24 CHD grade-2 patients, 22 CHD grade-3 patients, and 46 control subjects. The baseline and clinical characteristics of the control and the CHD groups are shown in *Table 1*. No differences were observed among all groups and CHD groups regarding sex, age, heart rate, and body surface area, as well as current systolic blood pressure. Differences were observed among all groups and CHD groups regarding current diastolic blood pressure but based on the normal values. Considering the cardiovascular risk factors smoking, diabetes mellitus, and systemic arterial hypertension history there were no differences among CHD groups.

Two-dimensional parameters evaluation

Echocardiographic measurements of the left atrium and the left ventricle are presented in *Table 1*. While there were no differences in LAVI among all groups and CHD groups, LVEDV was observed differences among all groups and CHD groups, LVESV was observed differences among CHD groups. LVEF was preserved in all patients and in the controls. Diastolic function was impaired in CHD patients.

Myocardial work parameters evaluation

GLS value was significantly lower in CHD grade-3 than in controls (P<0.001), but there was no significant difference among the three CHD groups. However, both GWI (P<0.001) and GCW (P<0.001) decreased significantly in CHD grade-1, increased slightly in CHD grade-2 compared with CHD grade-1, and decreased significantly in CHD grade-3. GWW (P<0.001) increased significantly from CHD grade-1 to CHD grade-3, while GWE (P<0.001) decreased significantly from CHD grade-1 to CHD grade-3 (*Table 2*, *Figure 3*). In ROC curves analysis, the area under the curve (AUC) and 95% confidence interval (CI) were revealed. GWI (AUC: 0.810; 95% CI: 0.691–0.930), GCW (AUC: 0.758; 95% CI: 0.631–0.885), GWW (AUC: 0.754; 95% CI: 0.624–0.885), and GWE (AUC: 0.817; 95% CI: 0.709–0.926) separated CHD grade-3 patients from the control group (*Figure 4*). With the cut-off values of 1,824.5 mmHg%, 2124.5 mmHg%, 137.0 mmHg%, 94.5%, the sensitivities compared CHD grade-3 with control group of GWI, GCW, GWW, GWE were 81.8%, 72.7%, 54.5%, 72.7%, respectively, while the specificities compared CHD grade-3 with control group of GWI, GCW, GWW, GWE were 69.9%, 69.9%, 95.7%, 73.9%, respectively.

Intraobserver and interobserver variability

Regarding intraobserver and interobserver variability good ICCs were shown in all measurements (all: ICCs >0.85, P<0.001) (*Table 3*).

Table 1 Clinical and basic echocardiographic parameters evaluation of the study population

Baseline	Control group [1]	CHD grade-1 [2]	CHD grade-2 [3]	CHD grade-3 [4]	P value (4 *vs.* 1)	P value (4 *vs.* 2)	P value (4 *vs.* 3)	P value ANOVA-a	P value ANOVA-b
Patient characteristics									
Number of patients	46	25	24	22					
Male sex	17 (37%)	14 (56%)	15 (63%)	13 (59%)	0.088	0.835	0.818	0.128	0.902
Age, mean years	57.93±8.88	60.44±10.24	57.79±9.51	62.55±9.80	0.057	0.477	0.102	0.219	0.267
Heart rate, bpm	69.65±10.15	70.72±8.40	66.92±11.85	67.95±11.14	0.534	0.338	0.762	0.562	0.430
Body surface area, m^2	1.69±0.12	1.73±0.13	1.79±0.15	1.73±0.13	0.253	0.930	0.194	0.060	0.272
Cardiovascular risk factors									
Smoking	2 (4%)	8 (32%)	6 (25%)	9 (41%)	0.003*	0.536	0.263	0.002†	0.526
Drinking	2 (4%)	5 (20%)	4 (17%)	5 (23%)	0.068	0.824	0.614	0.116	0.879
Diabetes mellitus	0 (0)	7 (28%)	6 (25%)	7 (32%)	0.005*	0.781	0.617	0.001†	0.881
Systemic arterial hypertension history	0 (0)	14 (56%)	9 (38%)	11 (50%)	<0.001*	0.689	0.404	<0.001†	0.431
Current systolic blood pressure, mmHg	122.65±8.16	122.64±8.59	128.08±9.47	126.36±11.56	0.132	0.213	0.582	0.067	0.151
Current diastolic blood pressure, mmHg	76.52±7.03	72.20±7.31	79.08±8.04	75.41±7.58	0.554	0.147	0.119	0.014†	0.010†
Coronary angiography parameters									
Gensini score	0	8.90±6.71	36.13±7.84	92.64±24.49					
LM stenosis	0 (0)	0 (0)	1 (4%)	9 (41%)	0.001*	0.001*	0.004*	<0.001†	<0.001†
LAD stenosis	0 (0)	23 (92%)	23 (96%)	22 (100%)	<0.001*	0.161	0.344	<0.001†	0.407
LCX stenosis	0 (0)	4 (16%)	14 (58%)	16 (73%)	<0.001*	<0.001*	0.317	<0.001†	<0.001†
RCA stenosis	0 (0)	9 (36%)	11 (46%)	13 (59%)	<0.001*	0.118	0.380	<0.001†	0.294
One-vessel disease	0 (0)	14 (56%)	4 (17%)	3 (14%)	0.083	0.002*	0.781	<0.001†	0.001†
Two-vessel disease	0 (0)	10 (40%)	14 (58%)	3 (14%)	0.083	0.041*	0.001*	<0.001†	0.006†
Three-vessel disease	0 (0)	1 (4%)	6 (25%)	16 (73%)	<0.001*	<0.001*	0.001*	<0.001†	<0.001†
2D echocardiography parameters									
LAVI, mL/m^2	27.78±4.15	26.48±3.69	26.38±4.63	26.45±3.78	0.208	0.981	0.950	0.392	0.996
LVEDV-bp, mL	74.46±11.38	70.36±11.41	82.38±15.62	77.09±13.40	0.402	0.069	0.227	0.011†	0.011†
LVESV-bp, mL	23.37±5.29	21.40±4.68	25.83±7.81	24.27±5.43	0.516	0.058	0.440	0.063	0.042†
Biplane LVEF, %	68.61±5.23	69.60±5.03	68.83±5.80	68.41±5.16	0.883	0.428	0.795	0.862	0.739
$E_{velocity}/A_{velocity}$ ratio	1.05±0.32	0.83±0.33	1.00±0.29	0.77±0.16	<0.001*	0.411	0.002*	0.001†	0.014†
E'_{septal}/A'_{septal} ratio	1.02±0.42	0.74±0.19	0.79±0.26	0.68±0.14	<0.001*	0.213	0.081	<0.001†	0.197
$E'_{lateral}/A'_{lateral}$ ratio	1.28±0.47	0.79±0.29	0.97±0.32	0.84±0.33	<0.001*	0.616	0.158	<0.001†	0.114
$E'_{average}/A'_{average}$ ratio	1.15±0.41	0.77±0.21	0.88±0.25	0.76±0.21	<0.001*	0.901	0.073	<0.001†	0.105
$E_{velocity}/E'_{average}$ ratio	7.13±1.34	8.17±1.58	8.11±2.06	7.84±2.33	0.197	0.575	0.676	0.051	0.835

Data are presented as mean ± SD or n (%). *, P<0.05 *vs.* CHD grade groups and Control group with *t*-test. †, P<0.05 ANOVA indicates analysis of variances (ANOVA-a: among all groups; ANOVA-b: among CHD groups). LM, left main artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; LAVI, left atrial volume index; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction; CHD, coronary heart disease.

Table 2 Echocardiographic myocardial work parameters evaluation of the study population

Parameters	Control group [1]	CHD grade-1 [2]	CHD grade-2 [3]	CHD grade-3 [4]	P value (4 *vs.* 1)	P value (4 *vs.* 2)	P value (4 *vs.* 3)	P value ANOVA-a	P value ANOVA-b
GLS, %	−20.91±1.76	−18.96±1.65	−18.58±2.67	−17.77±2.41	<0.001*	0.059	0.287	<0.001†	0.200
GWI, mmHg%	1,910.00±209.41	1,711.68±174.70	1,775.75±306.57	1,553.36±312.46	<0.001*	0.043*	0.019*	<0.001†	0.021†
GCW, mmHg%	2,265.17±254.98	2,010.64±202.65	2,117.25±317.49	1,939.55±356.79	0.001*	0.415	0.081	<0.001†	0.130
GWW, mmHg%	85.98±33.82	92.16±55.51	118.54±44.15	136.73±61.42	0.001*	0.012*	0.252	<0.001†	0.021†
GWE, %	95.54±1.63	94.80±2.40	93.83±1.81	92.23±3.32	<0.001*	0.004*	0.053	<0.001†	0.004†

Data are presented as mean ± SD. *, P<0.05 *vs.* CHD grade groups and Control group with *t*-test. †, P<0.05 ANOVA indicates analysis of variances (ANOVA-a: among all groups; ANOVA-b: among CHD groups). GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global wasted work; GWE, global work efficiency; CHD, coronary heart disease.

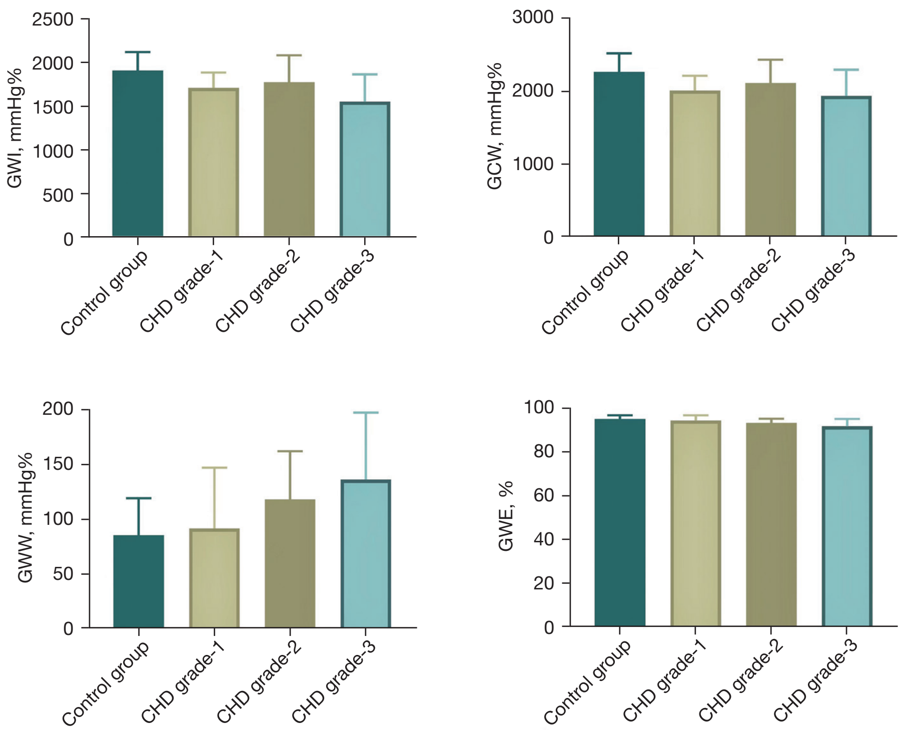
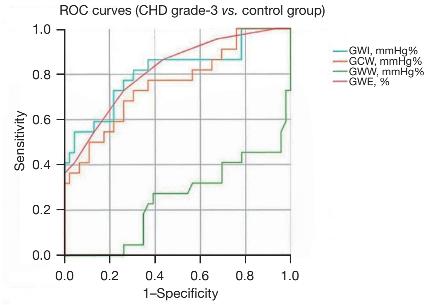


Figure 3 Myocardial work parameters comparison and value changes in the three CHD grades and control subjects (i.e., GWI, GCW, GWW, GWE). CHD, coronary heart disease; GWI, global work index; GCW, global constructive work; GWW, global wasted work; GWE, global work efficiency.

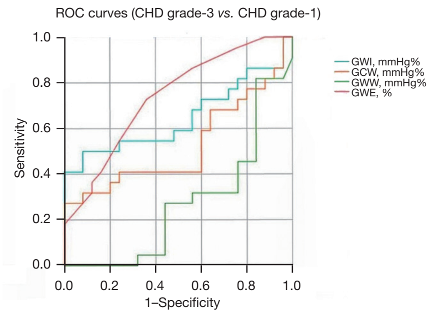
Discussion

This study characterizes noninvasive MW to provide quantifiable information for identifying different grades of stenosis severity according to Gensini score in CHD patients with preserved LVEF and without RWMAs. In summary, in patients with CHD, GWI and GCW decreased significantly in CHD grade-1, increased slightly in CHD grade-2 compared with CHD grade-1, and decreased more significantly in CHD grade-3. GWW increased significantly from CHD grade-1 to CHD grade-3, while GWE decreased significantly from CHD grade-1 to CHD grade-3. In this cohort, increased GWW and decreased GWE were superior to the established echocardiographic parameters LVEF and GLS in predicting early myocardial dysfunction. ROC analysis showed the valuable clinical

AUC (CHD grade-3 *vs.* control group)					
Parameters	Area	Standard error	Significant	95% CI	
				Lower limit	Upper limit
GWI, mmHg%	0.810	0.061	0.000	0.691	0.930
GCW, mmHg%	0.758	0.065	0.001	0.631	0.885
GWW, mmHg%	0.246	0.067	0.001	0.115	0.376
GWE, %	0.817	0.055	0.000	0.709	0.926



AUC (CHD grade-3 *vs.* CHD grade-1)					
Parameters	Area	Standard error	Significant	95% CI	
				Lower limit	Upper limit
GWI, mmHg%	0.647	0.086	0.084	0.478	0.816
GCW, mmHg%	0.525	0.090	0.765	0.349	0.701
GWW, mmHg%	0.271	0.074	0.007	0.126	0.416
GWE, %	0.738	0.072	0.005	0.597	0.879



AUC (CHD grade-3 *vs.* CHD grade-2)					
Parameters	Area	Standard error	Significant	95% CI	
				Lower limit	Upper limit
GWI, mmHg%	0.672	0.080	0.045	0.515	0.830
GCW, mmHg%	0.612	0.085	0.194	0.446	0.777
GWW, mmHg%	0.420	0.085	0.350	0.252	0.587
GWE, %	0.617	0.085	0.173	0.451	0.784

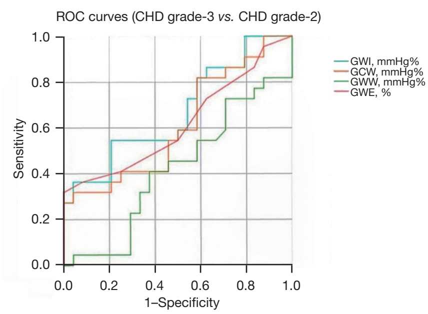


Figure 4 ROC curves for predicting the ability of myocardial work variables to differentiate three CHD grades and control subjects (i.e., GWI, GCW, GWW, GWE). The AUC and 95% CI outcomes for GWI, GCW, and GWE show with "n" when the smaller test results suggest more certainty, the AUC and 95% CI outcomes for GWW show with "1-n" when the larger test results suggest more certainty. CHD, coronary heart disease; ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; GWI, global work index, GCW, global constructive work, GWW, global wasted work; GWE, global work efficiency.

Table 3 Reproducibility assessment with interclass correlation coefficients for echocardiographic parameters of the study population

Parameters	Intraobserver variability			Interobserver variability		
	ICC	95% CI	P value	ICC	95% CI	P value
GLS, %	0.976	0.942–0.995	<0.001*	0.953	0.838–0.989	<0.001*
GWI, mmHg%	0.970	0.901–0.991	<0.001*	0.942	0.821–0.982	<0.001*
GCW, mmHg%	0.965	0.885–0.989	<0.001*	0.932	0.794–0.979	<0.001*
GWW, mmHg%	0.963	0.880–0.989	<0.001*	0.929	0.786–0.978	<0.001*
GWE, %	0.916	0.725–0.972	<0.001*	0.859	0.601–0.954	<0.001*

*, P<0.05 are statistically significant. ICC, interclass correlation coefficient; CI, confidence interval; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global wasted work; GWE, global work efficiency.

utilities of GWI, GCW, GWW and GWE. Furthermore, reproducibility of all MW parameters was verified with excellent ICCs. These findings suggest that noninvasive MW is an accurate, sensitive, and reproducible method to identify patients with incipient LV dysfunction.

LV longitudinal contractility plays an important role in overall myocardial performance throughout the cardiac cycle. This component of LV mechanics not merely contributes to the ejection phase but has considerable impact on the twisting and untwisting physiology (13,17). Reduction of LV longitudinal deformation may compromise cardiac hemodynamics. In this study, GLS values decreased gradually from CHD grade-1 to grade-3. Nevertheless, in patients with CHD grade-3 mean GLS was still above the lower limit of normality.

Adding the current blood pressure and thereby calculating MW has recently been introduced as an additional tool for studying LV systolic function in various cardiac conditions. Traditional MW assessment was dependent on invasive pressure measurements and thereby a methodology not feasible in daily clinical routine. Conventional noninvasive detection of patients with significant CHD remains a challenge despite the widespread use of imaging both at rest and during exercise (18). The new ability to calculate MW noninvasively has added a new dimension to echocardiographic evaluation of LV systolic function (6).

In patients after ST-segment elevation myocardial infarction, lower baseline values of GWI and GWE have been observed (14,19). Reduced MW in the region of the culprit vessel territory was associated with subsequent adverse LV remodeling. Global MW was also significantly reduced in patients with acute coronary artery occlusion. In a study by Boe *et al.*, the authors investigated MW in patients with non-ST-segment acute coronary syndromes. They reported that decreased MW in four neighboring myocardial segments was superior to detecting CHD when compared to GLS or LVEF (20). In another study, noninvasive global MW at rest was a more sensitive parameter than GLS to detect significant CHD in patients without RWMAs and with normal LVEF (13). Lin *et al.* could show that GWE was lower in patients with significant CHD when compared to patients with non-significant CHD. Adding peak GWE to peak endocardial GLS can provide additional diagnostic information when performing noninvasive evaluation for the presence of CHD, possibly reducing the need for further invasive examinations (21).

Our current study investigated patients with normal LVEF and various CHD grades according to the Gensini score. Abnormal MW was associated with the presence of CHD grade-3. Both GWI and GCW decreased significantly in CHD grade-1, increased slightly in CHD grade-2 compared with CHD grade-1, and decreased more significantly in CHD grade-3. GWW increased significantly from CHD grade-1 to CHD grade-3 compared with control subjects, while GWE decreased significantly from CHD grade-1 to CHD grade-3. While there were clear differences between the control group and CHD patients, differences in MW measurements among patients with CHD grade-1, grade-2, and grade-3 may be attributable to the uneven distribution of LM stenosis, complete vessel occlusion, and three-vessel disease. Differences in collateral circulation and coronary reperfusion will heavily affect MW.

This study expanded on a pilot study which had found that higher coronary stenosis severity grades were associated with lower MW indices. More three-vessel disease in CHD grade-3 with more LM stenosis compared with more one-vessel disease in CHD grade-1 without LM stenosis, which was presented with GWI and GCW statistics decreased. The significant reduction of myocardial function might reflect a pathologic adaptation of reduced metabolism in the myocardium caused by decreased blood flow in this early stage of CHD. Meanwhile, CHD grade-2 had the less LM stenosis than CHD grade-3 and the more three-vessel disease than CHD grade-1, which was presented with GWI and GCW slightly increased. The myocardial function with value fluctuation might indicate a necessary cardiac condition established with positive and effective collateral circulation and coronary reperfusion. This pathological finding becomes evident at an early stage and before prolonged myocardial ischemia leads to RWMAs and a reduction in LVEF.

The novel parameter MW considers loading conditions by combining GLS with noninvasive systemic arterial blood pressure. Significant multivessel disease exposes more myocardium to chronic ischemia, and therefore it seems reasonable that MW is abnormal in these patients. Our findings suggest that MW may identify early abnormalities in LV systolic function and might be a more sensitive parameter for an early stage of LV dysfunction in patients with significant coronary stenosis while there is still preserved LVEF and no RWMAs are present.

For further research, MW evaluation in patients undergoing stress echocardiography will be of high interest. Dynamic changes in afterload will be accounted for by the MW methodology. Stress induced ischemia may not always cause new regional wall motion abnormalities but may lead to significantly reduced global MW values. The present study lays the groundwork for such further investigations.

Limitations

Image quality is an important limiting factor of feasibility and accuracy when assessing MW. Noninvasive blood pressure measurement is imprecise when compared with invasive LV pressure measurement. Influence of diabetes and hypertension (history) as concomitant diseases has not been excluded in this project. This study included patients from a single center without a large sample size, more prospective validation is needed. MW should not be used in isolation but in conjunction with other parameters to identify patients with significant CHD to increase sensitivity and specificity.

Conclusions

This manuscript provides new insights to the diagnostic value of MW identifying patients with incipient LV dysfunction caused by chronic ischemia due to CHD. A gradual worsening of MW parameters was observed when comparing patients with higher degrees of stenosis severity. Therefore, adding MW when evaluating patients with suspected CHD may help increase diagnostic accuracy.

Furthermore, noninvasive MW as a novel method and a potential valuable clinical tool can assist the early diagnosis of CHD severity in patients with preserved LVEF and without RWMAs, particularly in patients with multivessel lesions and LM stenosis.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The research protocol was approved by the regional ethics committee of Nanjing First Hospital, and all included individuals provided written informed consent.

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