

Quantitative assessment of the rotation and twist of the left ventricle during dobutamine stress echocardiography: a comparison of patients with and without significant coronary artery disease

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KEY WORDS

apical rotation, basal rotation, coronary artery disease, left ventricular rotation, speckle tracking

ABSTRACT

BACKGROUND The rotation and twist of the left ventricle (LV) have been comprehensively evaluated at rest. However, little is known about rotational mechanics during dobutamine stress echocardiography (DSE).

AIMS We aimed to quantify and compare the basal and apical rotation and twist of the LV at rest as well as at the peak and recovery stages of DSE in patients with and without coronary artery disease (CAD).

METHODS We enrolled 91 patients, including 48 patients with CAD and 43 patients without CAD (mean [SD] age, 62 [9] years and 61 [10] years, respectively). Coronary artery disease was defined as the presence of stenoses of 50% or more in the left main coronary artery and/or stenoses of 70% or more in other epicardial arteries. Rotation was measured by 2-dimensional speckle-tracking echocardiography, and twist was calculated as the difference between the basal and apical rotation.

RESULTS Neither rotation nor twist differed between patients with and without CAD at rest, although apical rotation was significantly greater in the CAD group at peak DSE (mean [SD], 5.43° [3.45°] vs 3.71° [3.52°], $P = 0.01$) and at recovery (mean [SD], 5.05° [3.65°] vs 2.87° [2.73°], $P < 0.01$). On the contrary, the absolute value for basal rotation at recovery was higher in patients without CAD (mean [SD], 3.87° [3.37°] vs 2.63° [2.43°], $P = 0.03$). In both groups, the rotation and twist did not change significantly during the dobutamine challenge.

CONCLUSIONS During DSE, we observed differences in LV rotation between patients with and without CAD, revealing the effect of ischemia on deformation parameters.

INTRODUCTION As ischemic heart disease is the leading cause of death in the Western world, the accuracy and safety of diagnostic methods play a vital role in clinical practice.¹ Dobutamine stress echocardiography (DSE) is a noninvasive method with an established diagnostic value. According to the European Society of Cardiology Guidelines on myocardial revascularization, DSE is a class I diagnostic test in patients with an intermediate probability of coronary artery

disease (CAD) and stable symptoms.^{2,3} However, the accuracy of DSE depends on the expertise of the echocardiographer.⁴ The subjective visual assessment of left ventricular (LV) contractility has a significant percentage of false-positive or negative results, prompting the search for quantitative parameters to support its diagnostic value.

Speckle-tracking echocardiography is a novel method of angle-independent quantitative

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WHAT'S NEW?

Our study revealed that apical rotation of the left ventricle (LV) is higher in patients with coronary artery disease (CAD) during the peak and recovery stages of dobutamine stress echocardiography (DSE), which is in accordance with the limited data available in the literature. Moreover, we observed that basal rotation during the recovery stage is higher in patients without CAD, which, to our knowledge, is a novel finding. We conclude that DSE can reveal differences in the global rotational function of the LV, which is related to the presence of significant stenoses in the coronary arteries. This could help improve the diagnosis of CAD during stress echocardiography in the future. However, it is important to incorporate the recovery stage of DSE into daily clinical practice as well as to further evaluate the ischemic criteria.

TABLE 1 Characteristics of the study groups

Parameter	CAD (n = 48)	No CAD (n = 43)	P value
Male, n (%)	31 (64.6)	14 (32.6)	0.01
Age, y	62.3 (9.4)	61.6 (9.9)	0.702
Age >65 years, n (%)	12 (25)	15 (34.9)	0.42
Body weight, kg	79.4 (14.7)	77.5 (12.8)	0.52
Height, cm	167.7 (9.9)	165.6 (7.2)	0.26
SBP, mm Hg	132.3 (17.5)	126.8 (17.1)	0.13
DBP, mm Hg	69.7 (9.1)	70.0 (9.7)	0.87
Type 2 diabetes, n (%)	11 (22.9)	10 (23.3)	0.83
Smoking, n (%)	25 (52.1)	19 (44.2)	0.04
Hyperlipidemia, n (%)	45 (93.8)	34 (79.1)	0.08
TC, mg/dl	187.5 (42.8)	209.8 (42.3)	0.02
LDL-C, mg/dl	104.6 (37.4)	121.2 (33.4)	0.03
HDL-C, mg/dl	55.4 (25.6)	59.9 (13.1)	0.29
Triglycerides, mg/dl	148.9 (103.2)	132.8 (48.4)	0.34
Hypertension, n (%)	46 (95.8)	34 (79.1)	0.033
LAD, n (%)	23 (47.9)	-	-
Cx, n (%)	19 (39.6)	-	-
RCA, n (%)	18 (37.5)	-	-
1-vessel CAD	36 (75)	-	-
2- or 3-vessel CAD	12 (25)	-	-
Previous MI	19 (44)	0	<0.01

Data are presented as mean (SD) unless otherwise indicated.

SI conversion factors: to convert TC, HDL-C, and LDL-C to mmol/l, multiply by 0.0259; triglycerides to mmol/l, multiply by 0.0113.

Abbreviations: CAD, coronary artery disease; Cx, circumflex artery; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LAD, left anterior descending artery; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; RCA, right coronary artery; SBP, systolic blood pressure, TC, total cholesterol

estimation of global and regional LV function,⁵⁻⁷ which may, in turn, improve the accuracy of DSE.^{8,9} Aside from global longitudinal strain, which is frequently used to assess LV function, 2-dimensional speckle-tracking echocardiography is used for the quantification of apical and basal rotations as well as the twist.¹⁰ The helical orientation of the myocardial fibers determines the counterclockwise rotation of the apex and clockwise rotation of the base, with the mean normal rotation values of 6.9° for the base and 13° for the apex, and the mean normal value of 20° for LV twist.¹¹⁻¹³ Left ventricular twist is the net difference between the LV apex and base rotation.¹⁴ Subtle LV dysfunction in patients with CAD can be detected by a systolic twist and diastolic untwist of the LV around its long axis during the cardiac cycle.¹⁵ Cardiac rotation around the long axis represents an important component of LV global systolic function.^{16,17}

Data concerning the significance of novel parameters of LV function are limited, especially in the DSE setting.

METHODS The aim of this study was to assess the value of LV rotation and twist as additional quantitative parameters during DSE for the detection of CAD. We calculated and compared LV rotation at basal and apical levels, as well as LV twist at rest, at peak stage, and at recovery stage of DSE in patients with stable CAD and those without CAD. Additionally, in the CAD group, we assessed separately the subgroups with and without a history of myocardial infarction (MI).

Study population We analyzed a group of 250 patients with angina referred for DSE and then, within a 12-week timeframe, for coronary angiography or computed tomography. The final study sample included 91 patients. For each patient, DSE was performed, followed by invasive angiography.

Patients were divided into 2 groups based on the results of coronary angiography and visually assessed DSE: 43 patients with negative results of DSE who did not have significant coronary stenosis and 48 patients with positive DSE and stenosis of 50% or more in the left main coronary artery and/or stenosis of 70% or more in other epicardial arteries. The clinical characteristics of patients are presented in **TABLE 1**.

The exclusion criteria were any of the following: left bundle branch block, severe valvular disease, hypertrophic cardiomyopathy, or atrial fibrillation.

All patients filled out an informed consent form to participate in the study. Approval for the study was obtained from the local Bioethics Committee (RNN/119/10/KE).

Echocardiographic assessment Echocardiography was performed using a commercially

TABLE 2 Echocardiographic parameters at rest and comparison of heart rate at all stress test stages between patients with and without coronary artery disease

Parameter	CAD	No CAD	P value
LVEF, %	53.5 (8.9)	59.7 (4.2)	<0.001
E/A	0.88 (0.38)	0.96 (90.33)	0.27
LVEDd, mm	48.1 (5.3)	45.8 (4.6)	0.03
LVESd, mm	34.4 (6.4)	30.6 (4.7)	0.002
LA, mm	41.7 (3.7)	39.3 (4.2)	0.004
IVSd, mm	12.1 (1.8)	11.0 (1.6)	0.002
IVSs, mm	15.1 (1.8)	14.1 (1.6)	0.01
PWd, mm	11.6 (1.4)	10.8 (1.5)	0.01
PWs, mm	14.2 (1.8)	14.0 (1.4)	0.42
HR rest, bpm	70 (13)	68 (10)	0.64
HR peak, bpm	132 (16)	134 (13)	0.71
HR recovery, bpm	92 (11)	91 (12)	0.69
WMSI rest	1.06 (0.1)	1	0.89
WMSI peak	1.17 (0.07)	1	0.79

Data are presented as mean (SD).

Abbreviations: E/A, mitral valve early filling/mitral valve atrial filling; HR, heart rate; IVSd, interventricular septum diameter; IVSs, interventricular septum systolic diameter; LA, left atrium; LVEDd, left ventricular end-diastolic diameter; LVESd, left ventricular end-systolic diameter, LVEF, left ventricular ejection fraction; NS, nonsignificant; PWd, diastolic posterior wall thickness; PWS, systolic posterior wall thickness; WMSI, wall motion score index

TABLE 3 Comparison of rotation and twist at all stress test stages between patients with and without coronary artery disease

Parameter	No CAD	CAD	P value	
Rest	R basal segments, °	-2.91 (3.33)	-2.47 (2.20)	NS
	R apical segments, °	3.62 (3.33)	4.83 (3.16)	NS
	T, °	6.38 (4.48)	7.3 (3.87)	NS
Peak stage	R basal segments, °	-3.17 (3.94)	-2.79 (3.25)	NS
	R apical segments, °	3.71 (3.52)	5.43 (3.45)	0.01
	T, °	6.73 (5.32)	8.22 (5.13)	NS
Recovery stage	R basal segments, °	-3.87 (3.37)	-2.63 (2.42)	0.03
	R apical segments, °	2.87 (2.73)	5.05 (3.65)	<0.01
	T, °	6.27 (4.01)	7.68 (4.72)	NS

Data are presented as mean (SD).

Abbreviations: R, rotation; T, twist; others, see TABLE 1

available echocardiographic system, Vivid 7 and E9 (General Electric Company, Boston, Massachusetts, United States). Images were obtained in the parasternal short-axis view at 3 LV levels: basal, mid, and apical, and in apical 4-, 3-, and 2-chamber views, with images taken at rest, at peak dobutamine infusion, and during recovery. The echocardiographic assessment was done using the highest possible frame rate and

achieving an average of 83 frames per second. Next, a quantitative analysis of LV deformation was performed with an ECHO PAC workstation (General Electric Company), using 2-dimensional speckle-tracking echocardiography. The 18-segment model of the LV was used for analysis.

We calculated and compared LV rotation at basal and apical levels, and LV twist at rest, at peak stage, and at recovery stage of DSE. Left ventricular rotation was measured at the aortic valve closure as an end-systolic parameter. Twist was calculated as the difference between basal and apical rotation according to the guidelines.

Dobutamine stress echocardiography

A dobutamine-atropine stress echocardiography protocol was used. Dobutamine was infused intravenously in four 3-minute stages, with gradual dose titration from 10, 20, 30, up to 40 µg/kg/min. Atropine was added up to a maximum dose of 2 mg until the age-adjusted target heart rate was reached, calculated as $0.9 \times (220 - \text{age})$.

The stress protocol was terminated when wall motion abnormality, chest pain, abnormal blood pressure reaction, ischemic changes, or arrhythmia was observed.

Coronary angiography

All patients also underwent invasive coronary angiography within 12 weeks of performing the DSE. Significant coronary stenosis was defined as a narrowing of at least 50% in the left main coronary artery and/or a narrowing of at least 70% in other epicardial arteries.

Statistical analysis

For categorical variables, data were presented as percentages and as means (SD), while continuous variables were presented as the median and interquartile range, depending on distribution. Data distribution was tested using the d'Agostino test. The *t* test for independent variables or the Mann-Whitney test was applied to assess differences between groups. Categorical variables were analyzed using the χ^2 test, χ^2 test with Yates correction, or the Fisher exact probability test. A *P* value of less than 0.05 was considered significant. All statistical analyses were performed using MedCalc version 12.0 (MedCalc, Mariakerke, Belgium) and STATISTICA version 10.0 (Statsoft, Tulsa, Oklahoma, United States).

RESULTS Clinical and echocardiographic characteristics

There were no differences in age, body weight, or the prevalence of diabetes or dyslipidemia between patients with CAD (48 patients; mean [SD] age, 62 [9] years; men, 64.6%) and those without CAD (43 patients; mean [SD] age, 62 [10] years; men, 32.6%). Smoking and hypertension were more frequent in the CAD group (TABLE 1).

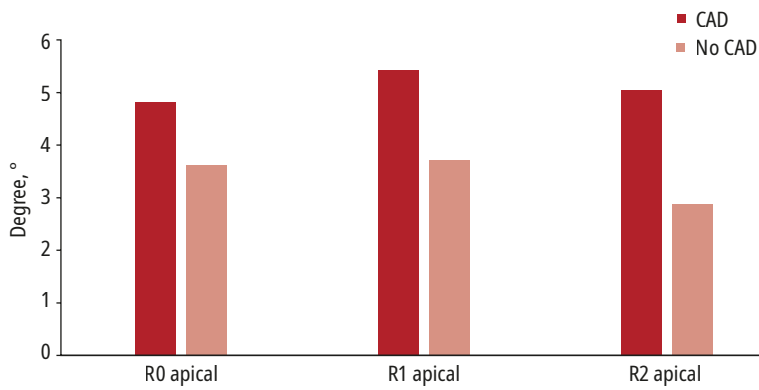


FIGURE 1 Apical rotation during different stages of dobutamine stress echocardiography in patients with and without coronary artery disease (CAD)

Abbreviations: R0, baseline (rest); R1, peak stage; R2, recovery stage

TABLE 4 Comparison of rotational parameters between subsequent stress test stages

Parameter	Group	Rest	Peak stage	Recovery stage	<i>P</i> value ^a
Basal rotation	CAD	-2.47 (2.20)	-2.79 (3.25)	-2.63 (2.42)	0.25
	No CAD	-2.91 (3.33)	-3.17 (3.94)	-3.87 (3.37)	0.24
Apical rotation	CAD	4.83 (3.16)	5.43 (3.45)	5.05 (3.65)	0.23
	No CAD	3.62 (3.33)	3.71 (3.52)	2.87 (2.73)	0.21
Twist	CAD	7.3 (3.87)	8.22 (5.13)	7.68 (4.72)	0.1
	No CAD	6.38 (4.48)	6.73 (5.3)	6.27 (4.01)	0.69

Data are presented as mean (SD).

^a Changes during dobutamine stress test within the group

Abbreviations: see TABLE 1

Patients with CAD had lower LV ejection fraction than those without CAD (53.5% vs 59.7%, $P < 0.001$), but had a larger left atrium (42 mm vs 39 mm, $P = 0.004$; TABLE 2).

Impact of coronary artery disease on left ventricular rotation and twist during dobutamine stress echocardiography

All deformation parameters at rest were similar in both groups. Apical rotation was higher in patients with CAD at the peak stage of DSE (mean [SD], 5.43° [3.45°] vs 3.71° [3.51°], $P = 0.01$; TABLE 3, FIGURES 1 and 2) as well as at the recovery stage (mean [SD], 5.05° [3.65°] vs 2.87° [2.73°]; FIGURES 1 and 2). As concerning the basal parameters, higher absolute values of rotation were detected only during the recovery stage of DSE in patients without CAD (TABLE 3, FIGURE 3). The comparison of deformation parameters between subsequent DSE stages within each group did not reveal any significant differences for rotation or twist (TABLE 4).

No significant differences were observed when the changes (Δ values) in apical and basal rotation and twist were compared between patients with and without CAD for all 3 stages of DSE (TABLE 5).

The analysis of the CAD subgroups with and without history of MI (19 and 29 patients, respectively) showed higher basal rotation at peak DSE in patients without MI (mean [SD], -3.8 [3.47] vs -1.25 [2.3], $P < 0.01$). However, other deformation parameters did not change (Supplementary material, Table S1). A comparison of patients without CAD to patients with CAD without history of MI revealed higher apical rotation

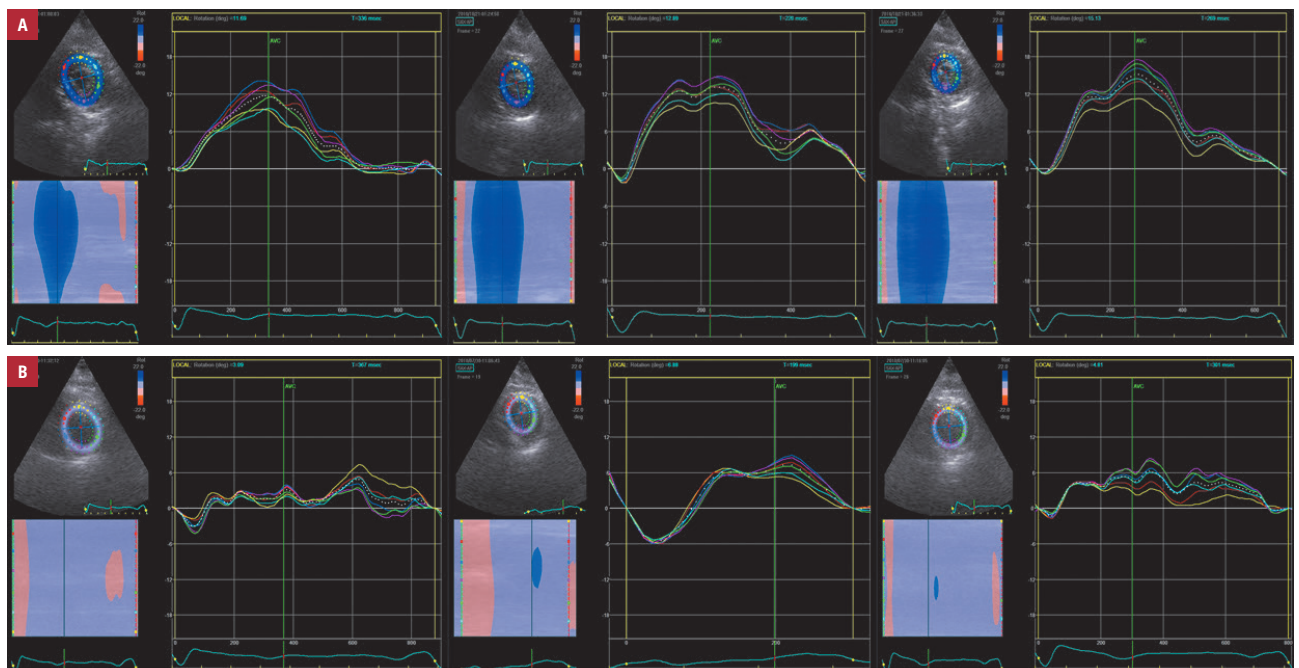


FIGURE 2 Apical rotation at rest, at peak stage, and at recovery stage of dobutamine stress echocardiography: **A** – patients with coronary artery disease (CAD); **B** – patients without CAD

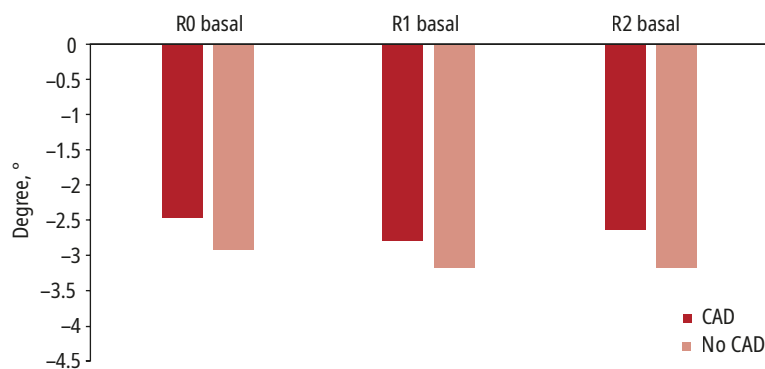


FIGURE 3 Comparison of basal rotation during dobutamine stress echocardiography in patients with and without coronary artery disease (CAD)

Abbreviations: see FIGURE 1

TABLE 5 Comparison of changes in rotation and twist at different stages of stress test between patients with and without coronary artery disease

Stage	Δ	No CAD	CAD	P value
Peak – rest	ΔR basal	0.56 (–3.3 to 2.6)	–0.63 (–2.4 to 2.04)	0.45
	ΔR apical	0.38 (–2.37 to 2.56)	0.95 (–2.38 to 3.54)	0.64
	ΔT	1.13 (–2.86 to 3.51)	2 (–3.74 to 5)	0.55
Recovery – rest	ΔR basal	–1.53 (–2.88 to 1.85)	–0.5 (–1.46 to 1.7)	0.32
	ΔR apical	–0.58 (–2.75 to 1.5)	0.44 (–1.63 to 2.19)	0.16
	ΔT	–0.13 (–1.48 to 2.05)	1.16 (–2.37 to 3.16)	0.47
Peak – recovery	ΔR basal	0.79 (–1.13 to 3.47)	0.22 (–2.47 to 2.4)	0.2
	ΔR apical	1.15 (–1.94 to 3.13)	1.03 (–1.44 to 2.69)	0.79
	ΔT	–0.51 (–4.22 to 3.75)	1.33 (–3.66 to 4.6)	0.62

Data are presented as median (interquartile range).

Abbreviations: Δ , difference between stages; others, see TABLES 1 and 3

in the CAD group at peak and recovery stages of DSE (Supplementary material, Table S2).

DISCUSSION The aim of this study was to evaluate the impact of CAD on rotational characteristics during DSE. Dobutamine stress echocardiography is an accepted clinical test for CAD detection based on visually assessed regional motion abnormalities.^{5,9,18,19} However, the contractility analysis during DSE is subjective and is highly dependent on the echocardiographer's experience.²⁰ Rotation of the LV around its long axis is an important component of global LV systolic function.⁸ Left ventricular twist is defined as the difference between rotation of the ventricular apex and base during systole.¹⁶ Previous studies have primarily focused on investigating the myocardial deformation at rest, and there are limited data about the impact of CAD on rotational parameters during a stress test.²¹

Our study demonstrated that apical rotation at the peak and recovery stages of DSE was higher in patients with CAD, whereas the basal rotation at the recovery stage was higher (in absolute values) in patients without CAD. Left ventricular twist did not differ between groups. Comparison of all deformation parameters between subsequent DSE stages for each group did not reveal any significant differences in rotation or twist.

Bansal et al²² compared patients with and without previous MI who exhibited or did not exhibit ischemia during peak DSE. They found that both ischemia and infarction had a greater impact on basal rotation than on apical rotation. In their study, the deterioration of basal rotation was correlated with infarction size, expressed as the number of infarct segments. The reduction in basal rotation was more prominent in patients with ischemia compared with those who did not exhibit ischemia at the DSE peak stage. However, similar effects were not observed for apical rotation. As with the comparison of torsion (twist divided by LV length), the resting parameters were reduced in patients who previously suffered MI when compared with patients without previous infarctions (mean [SD], 1.16°/cm [1.15°/cm] vs 3.16°/cm [1.3°/cm], $P < 0.001$), and these parameters were correlated with the infarction size. Torsion was not influenced by the induction of ischemia during DSE. Similar results were observed by Peteiro et al,^{23,24} who showed that basal rotation at peak exercise was impaired in patients with an ischemic response to exercise echocardiography on a treadmill (positive exercise test) and in whom CAD was confirmed by coronary angiography. Apical rotation and twist did not differ between patients with positive or negative exercise test results. Similar to our findings, twist did not differ between patients with and without CAD. As for basal rotation, we observed significantly higher values in patients without CAD during the recovery stage of DSE.

Some previous studies have focused on the diagnostic and prognostic role of LV twist at rest as an indicator of cardiac performance.^{6,25-27} Using resting transthoracic echocardiography, Rasalingam et al²⁸ found that apical rotation was increased in diabetic patients with significant CAD, observed by invasive angiography, compared with diabetic patients without CAD (mean [SD], 14.9° [5.1°] vs 11° [4.8°], $P < 0.001$). On the other hand, the LV ejection fraction was lower in patients with CAD but remained within the reference range. Nevertheless, in our study, resting rotational parameters did not differ between groups, but the peak and recovery stages of DSE offered additional value for the differentiation between patients with and without CAD.

In the literature, numerous studies have highlighted the valuable diagnostic and prognostic role of LV deformation parameters. In our

previous studies,^{29,30} we observed that global and regional LV peak systolic longitudinal strain was lower in all DSE stages in diabetic patients with CAD compared with nondiabetic patients. However, diabetic patients without CAD showed impaired global longitudinal strain only during the recovery stage.

Jang et al³¹ documented the effect of the extent and location of MI on LV rotational movements. Moreover, they reported that LV functional recovery after MI can be predicted by LV twist. They assessed deformation parameters at baseline, and then at 3 days and 6 months after MI. Subsequently, they divided patients into 2 groups based on the presence of LV remodeling at 3 days and 6 months. They revealed decreased LV torsion (1.9°/cm) at the initial presentation, representing a significant predictor of future remodeling, expressed as an increase in LV end-diastolic volume of greater than 20%.

Joyce et al⁸ reported that the change in LV twist during DSE could be used as a novel marker of contractile reserve. A stress-induced increase in twist during DSE was a marker of outcomes after MI, expressed as reverse LV remodeling.^{9,32} Liszka et al³² examined patients following successful percutaneous coronary intervention in patients with stable CAD who had suffered MI. Echocardiography and calculations of LV deformation parameters were performed at 3 (baseline), 30, and 90 days after the intervention. They showed that impaired LV deformation parameters such as basal and apical rotation, twist, and longitudinal and circumferential strain detected 3 and 30 days after MI may predict LV remodeling. In their study, remodeling was defined as an increase of 20% in LV end-diastolic volume, LV end-systolic volume, or both at 3-month follow-up.

Our study has several limitations. The major limitation is the small group of patients. However, although our data were primarily used to form hypotheses, we were still able to identify some significant correlations. Secondly, the assessment of deformation parameters at the peak stage was limited by the significantly elevated heart rates, which is one of the reasons why we decided to include the recovery stage in the analysis. Dobutamine, which causes significant tachycardia, may impair the signal-to-noise ratio most significantly. In our opinion, the quantitative assessment of myocardial deformation during a stress test requires further studies utilizing agents that result in a lower heart rate, such as dipyridamole. This may improve the signal-to-noise ratio at the peak stage. Finally, we assessed myocardial rotation with a single method, without the support of other imaging modalities, such as cardiac magnetic resonance. On the other hand, all patients in our study had CAD morphology confirmed by coronary angiography and its functional significance assessed by DSE.

In conclusion, end-systolic rotation and twist of the LV are both intrinsic features of LV mechanics that remain constant despite the inotropic and chronotropic challenges. However, the significant differences observed between patients with and without CAD indicate that ischemia has an impact on rotational parameters. Impaired basal rotation at recovery, together with greater apical rotation at the peak and recovery stages of DSE, may indicate significant CAD. Hence, these deformation parameters, especially when confirmed by other types of stress tests, may support the diagnosis of CAD during stress echocardiography.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/kardiologiapolska.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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