

SPECKLE TRACKING DOBUTAMINE STRESS ECHOCARDIOGRAPHY DIAGNOSTIC ACCURACY IN PRIMARY CORONARY ARTERIES DISEASE DIAGNOSIS

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ABSTRACT

The aim of the work was to evaluate STE feasibility as DSE visualization method and its accuracy compared to coronary angiography (CAG) in the patients with moderate-to-high coronary arteries disease (CAD) risk.

Materials and methods: We prospectively examined 140 pts (84 (60.0%) men) with suspected CAD in order to verify diagnosis and evaluate myocardial viability and coronary reserve.

Results: Mean LV EF was $54.4 \pm 15.8\%$. All pts had normal BP and HR during the test. There were no significant hemodynamics alterations during the test. There were no significant complications during DSE – 15 (12.9%) cases of different relatively low-grade supraventricular and ventricular arrhythmia, mainly transitory without interventions. There were 116 (82.9%) positive DSE results, of which 2 (1.72%) were false-positive. In 2 (8.3%) pts with negative DSE results CAG revealed 1-vessel insignificant (50 – 70%) lesions with developed collaterals (false-negative results). According to DSE and CAG results, 96 (82.3%) pts underwent revascularization interventions – 86 (89.6%) PCI's and (10.4%) CABG surgeries.

Sensitivity and specificity of DSE with STE for primary CAD diagnosis according to "golden standard" CAG results were 98.3% and 91.7%, respectively, with identical positive and negative predictive value and very high method overall accuracy (AUC = 0.98) and OR = 627.0 ($p < 0.0001$). Sensitivity and specificity of DSE with STE for defining indications for intervention and revascularization were 97.9% and 91.7%, respectively, with high overall accuracy (AUC = 0.95; OR = 564.0, $p < 0.0001$). Combined quantification of Δ GLS and Δ WMSI for primary CAD diagnosis showed significantly lower sensitivity 86.2% ($p = 0.0002$) and specificity 80.4% ($p = 0.0064$) with significantly lower integral method accuracy (AUC 0.83, $p < 0.0001$).

Conclusions: DSE with STE as a visualization method is a safe and optimal method for ischemia diagnosis and myocardial viability and coronary reserve evaluation in the pts with CAD suspicion. Given the lower Δ GLS and Δ WMSI accuracy compared to integral DSE with STE result evaluation, as well as frequent GLS growth in significant amount of patients with definite positive test result, authors recommend evaluating integral test result rather than strain value.

KEY WORDS: coronary heart disease, speckle tracking, stress echo

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INTRODUCTION

Timely and urgent diagnosis of coronary arteries disease (CAD) and coronary artery territory plays the key role in managing patients (pts) in daily cardiology practice, including those having acute coronary syndromes (ACS) or revascularization procedures history, namely percutaneous (PCI) and surgeon venous and mammary grafts (CABG). Indications for revascularization is the main dilemma facing cardiologist and cardiovascular surgeon, while reliable ischemia verification and myocardial viability evaluation, especially in the pts with multivessel disease and ischemic cardiomyopathy (ICM) largely determines patient management tactics and scope of intervention. Prompt primary CAD diagnosis is also of big importance, especially in large centers with big pts flow.

Conventional routine echocardiography (EchoCG) is not reliable enough for CAD diagnosis expertise even with tissue Doppler imaging (TDI). Stress EchoCG with dobutamine (DSE) is an acknowledged today noninvasive method for such purposes with acceptable diagnostic accuracy. Still, visual regional contractility abnormalities evaluation during DSE remains rather subjective, since evaluation largely depends on operator's experience in acquiring images and pharmacological stress results interpretation [1,2].

Speckle tracking EchoCG in B-mode (STE) or myocardial deformation study is a widely spreading method for global and regional left (LV) and right (RV) ventricles function evaluation. STE provides important information about myocardial

strain by its quantification with those advantages over TDI that strain does not depend on angle between angle between ultrasound (US) beam and myocardial strain vectors during contraction or relaxation [1-4]. Today STE is being actively verified by many centers and used in diagnosis and treatment efficacy verification in many coronary and non-coronary myocardial diseases, having high sensitivity in detecting pre-clinical myocardial dysfunction even with normal results of traditional resting EchoCG in B-mode [1-7]. High diagnostic accuracy of STE was proven for verifying coronary territory of lesions with its high correlation with coronary angiography (CAG) results regarding levels of lesions in different CAD forms [8-11], including acute coronary syndrome (ACS) with or without ST segment elevation [12-15].

Strain indices do not so much depend on neighbor segments “translational” motion and injured segments “pulling-up” which may lead to misinterpreting of segments kinetics during qualitative visual evaluation of regional evaluation of segments during DSE. Today there are quite a lot of recent publications evaluating clinical application of STE during STE in different pts groups with CAD [2,7,8,10-12], allowing to view STE for DSE as a highly trustworthy quantitative method for ischemia diagnosis and myocardial viability evaluation, but they usually describe small pts cohorts. In our center, we performed about 500 DSE procedures using STE in various clinical situations, and may conclude it to become a routine clinical practice. Still, there were no evidence-based studies of the matter in our country.

THE AIM

Aim of this study was to assess the diagnostic value of STE at rest and during DSE in primary CAD diagnosis and diagnostic accuracy of B-mode longitudinal strain evaluation as a method indicative of CAG and revascularization necessity.

MATERIALS AND METHODS

We prospectively examined 140 pts (84 (60.0%) men and 56 (40.0%) women) aged 57.6 ± 11.3 years with CAD suspicion admitted for diagnosis verification and defining indications for coronary interventions. All pts underwent DSE with longitudinal strain study as per STE. Exclusion criteria were significant valvular heart disease, history of any cardiac pacemaker implanted, and permanent atrial fibrillation (AF). Pts with complete left hemiblock were included into the study since our experience shows that strain dynamics during pharmacological stress is usually obvious in asynchronous segments, too. Amosov National Institute of Cardiovascular Surgery (NICVS) of NAMS of Ukraine local ethics committee approved study protocol. All patients gave written informed consent. Authors declare no conflicts of interest.

IMAGING

All examinations were performed using Vivid E9 (General Electric, USA) ultrasound equipment with M5S-D probe.

Images for strain studies were acquired in patients' left decubitus position from parasternal and apical windows (4-, 2-, and 3-chambers) with video records at rest and at every stage of pharmacological dobutamine stress, and at restitution. 2D greyscale videos were recorded at 60 – 70 Hz frame rate in order to optimize speckle-tracking quality with their sequential off-line analysis. Quantitative longitudinal strain analysis was performed using Vivid E9 software package.

DOBUTAMINE STRESS ECHOCG

DSE was performed before CAG for primary ischemia diagnosis in coronary territories of interest.

All patients were asked to withdraw nitrates for at least 48 h before test. In the beginning, we also asked to withdraw beta-blockers (BB) 48 h before test, but in the process of our work and experience accumulation, we made a conclusion that BB withdrawal is not necessary for ischemia diagnosis and myocardial viability and coronary reserve estimation by means of ST for the following reasons. Despite their negative chronotropic and inotropic effects BB are unable to influence ischemic or non-ischemic myocardial deformation changes due to dobutamine stress significantly. In addition, abrupt BB withdrawal in the pts with confirmed CAD, heart arrhythmia or arterial hypertension (AH) is relatively contraindicated.

DSE was performed according to standard protocol [2,10,13,16]. Dobutamine infusion was infused via intravenous line in four 3-min stages with dobutamine dose increase: (5)-10-20-30-40 mcg/kg/min under heart rate (HR) and blood pressure (BP) control with every tree min. dose increase and consecutive analysis of regional strains changes on a “bull’s eye” LV model. Giving additional atropine for achieving age-adjusted target HF was considered inappropriate in the pts with confirmed CAD and ACS history, since our experience shows that STE is sensible enough to ischemic strain changes even if target HR is not reached.

With experience accumulation, we concluded that primary ischemia diagnosis requires start dobutamine dose of 10 mcg/kg/min, since 5 mcg/kg/min is not enough to provoke ischemia where STE did not reveal it at rest.

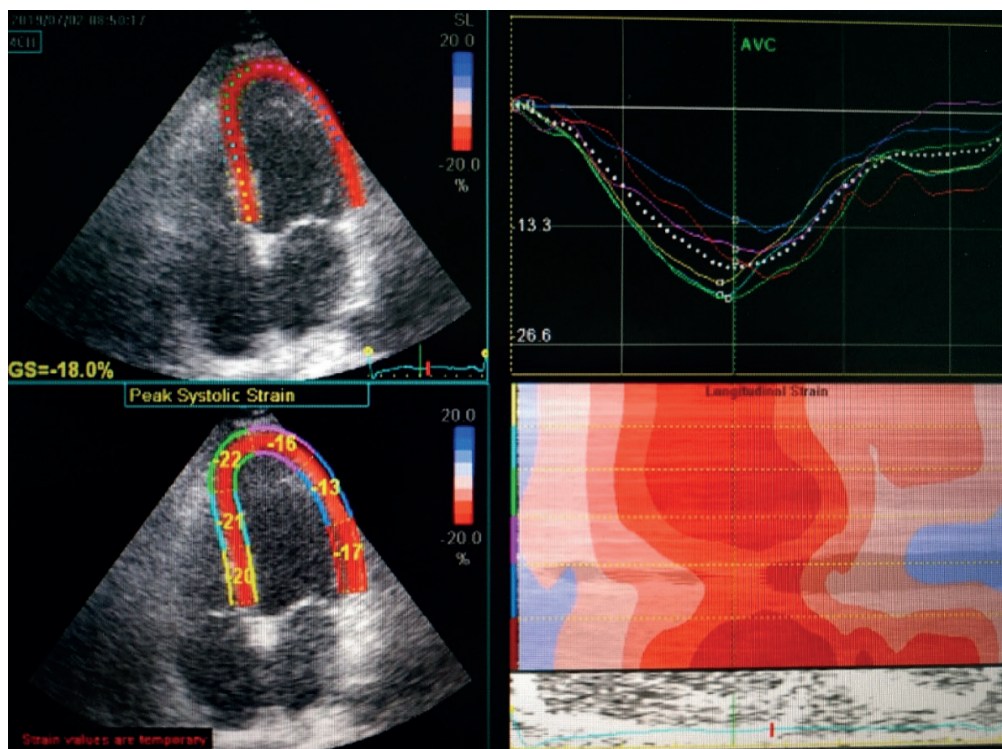
Test was performed with present anesthesiologist with necessary equipment for possible complications management (Ambu bag, intubation equipment, and cardioverter-defibrillator). In the test beginning 12-lead ECG was registered and rest EchoCG was performed with recording of rest (“native”) longitudinal strain pattern (bull’s eye) and global longitudinal strain (GLS) quantification. After that bull’s eye pattern was quantified and qualified after every 3 min of each following dose increase stage, and after 3 min of restitution. HR normalization was reached in 3 to 5 min after infusion stop and did not require additional BB administration.

Stress protocol termination criteria were as follows:

- 1) age-adjusted submaximal HR was achieved as per formula $[220 - \text{age (years)}] \times 0.85$ [2,10];

Table I. Criteria for STE dynamics during DSE qualitative assessment

Data at rest	Dynamics	Interpretation
Normal strain	Continuous growth or stable high / normal strain	Territory without ischemia
Normal strain	Continuous strain drop	Ischemia / low coronary reserve
Normal strain	Growth at low doses and drop at higher doses	Ischemia («two phased» answer) / insufficient coronary reserve
Normal strain	Drop at low doses and growth at higher doses	Ischemia with high / sufficient coronary reserve
Mild-to-moderate strain decrease	Continuous strain growth at all stages	Moderate ischemia of viable myocardium at rest with sufficient coronary reserve / non-ischemic cardiomyopathy
Moderate-to-severe strain decrease / inverted strain	Strain growth at different stress stages	Severe ischemia of viable myocardium at rest (hibernation), including postinfarction scar zone
Severe strain decrease/ inverted strain	Absent strain reaction to stress	Scar / unviable myocardium

**Fig. 1.** Example of automatically plotted in time vs. strain graphs in apical 4-chamber (A4C) position in the patient with later approved moderate middle segment Cx lesion – decreased distal lateral segments strain.

- 2) signs of ischemia as per strain drop in neighbor 4 or more myocardial LV and RV segments;
- 3) patient reported intense angina-like pain;
- 4) ECG-signs of clinically relevant arrhythmia: atrial fibrillation (AF), “runs” of ventricular tachycardia (VT), ventricular bigeminy or trigemini or multiform or frequent premature ventricular complexes (VES), including pairs;
- 5) >2 adverse events of any other grade, including frequent premature supraventricular complexes (SVES), bradycardia or HR decrease compared to previous stress stages.

LV and RV kinetics were assessed by expert operators. 17-segment LV model was used [1,12,14,17]. Myocardial segments motion was graded according to kinetics type at each stage of stress as normo- (grade 1), hypo- (grade 2),

a- (grade 3) or dyskinesia (grade 4). Any motion abnormality or deterioration by one or more grade was indicative of ischemia. Wall motion score index (WMSI) was calculated at rest and at peak stress stage for gradient Δ WMSI calculation.

SPECKLE TRACKING ECHOCG

Longitudinal strain was assessed by 2D-STE as per standard protocol [1]. End-systole was identified by aortic valve (AV) closure. Operator traced endocardial borders with automated longitudinal strain quantification. Adequate tracking was verified in real time with correction, if necessary, by manual regions of interest adjustment. After tracking completion myocardial strain was automatically plotted in time vs. strain graphs for different cardiac cycle

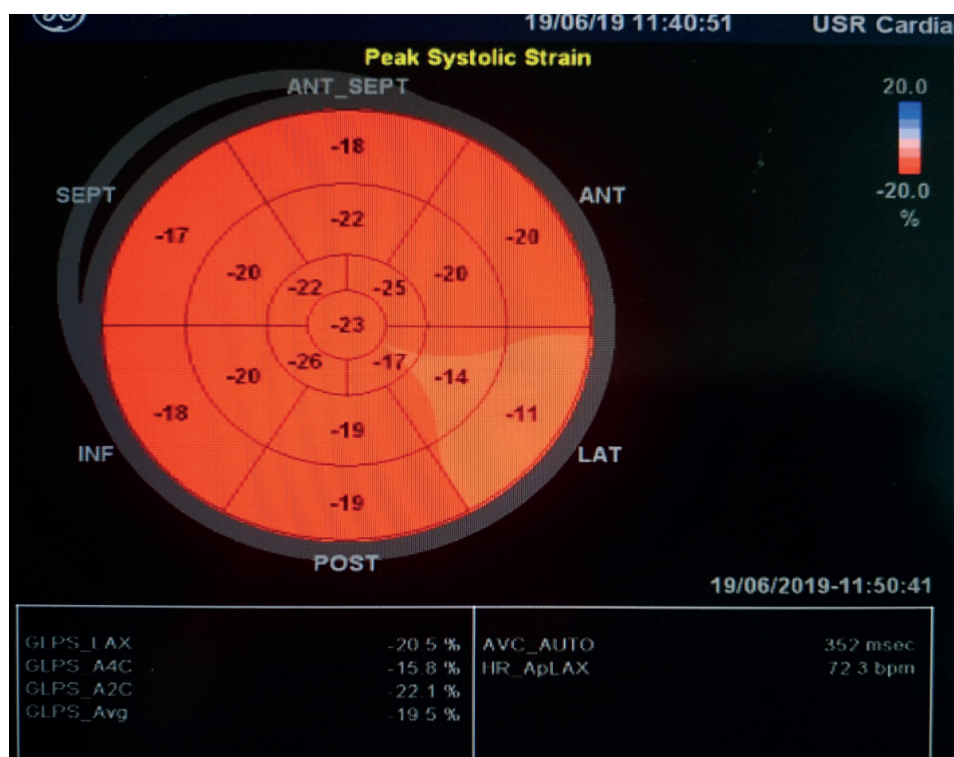


Fig. 2. 17-segments LV model (bull's eye): pattern of moderate Cx territory ischemia – moderate lateral-posterior longitudinal strain decrease with preserved global LV strain (GLS = -19,5%).

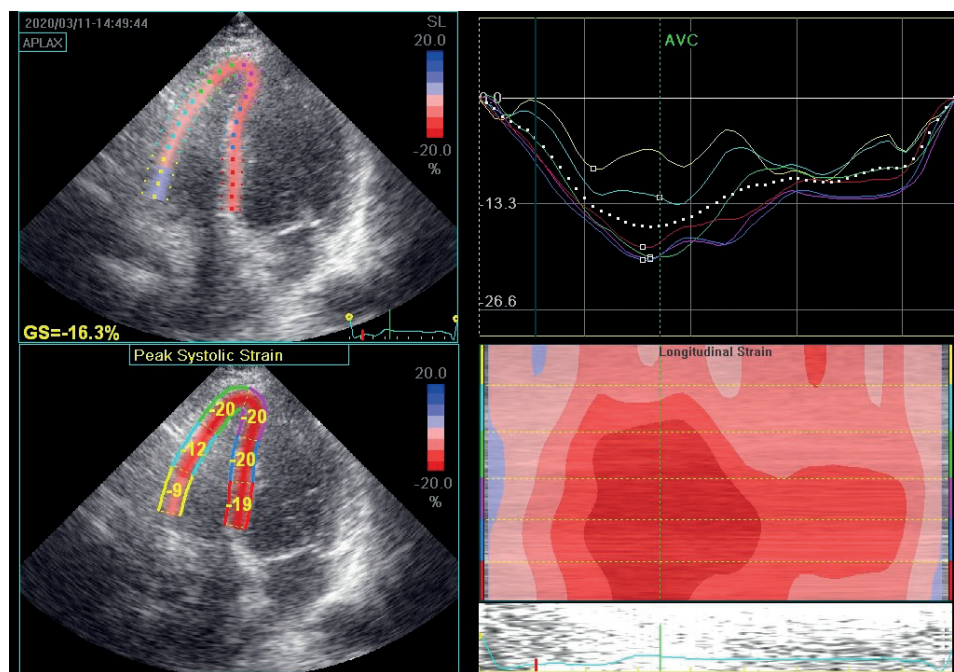


Fig. 3. Example of ischemia verification in RCA territory using RV strain quantification – moderate-to-severe basal and middle “free” strain drop (GLS = -13.7%) with preserved IVS (LAD territory) strain (GLS = -19.7%).

phases identification (Fig. 1) and building the strain pattern on 17-segments bull's eye model (Fig. 2) after tracking was completed in all three apical 3-, 4- and 2-chambers positions. RV longitudinal strain quantification for “free” wall and interventricular septum (IVS) right side was electively performed for additional ischemia diagnosis verification in right coronary artery (RCA) territory (Fig. 3) identically to LV segments.

Dobutamine stress results were assessed in every separate coronary territory by evaluating longitudinal strain dynamics in the territories of left anterior descending (LAD) and circumflex (Cx) left coronary artery (LCA)

branches, and RCA (Fig. 4). The absolute numerical GLS value was calculated at rest and at every stress stage with dynamics quantification Δ GLS. In addition, criteria of myocardial viability and coronary reserve were qualified (Table I).

CORONARY ANGIOGRAPHY

All pts underwent CAG according to the Judkins technique after DSE. Images and video were assessed by expert operators with significant CAD definition of >70% luminary diameter stenosis.

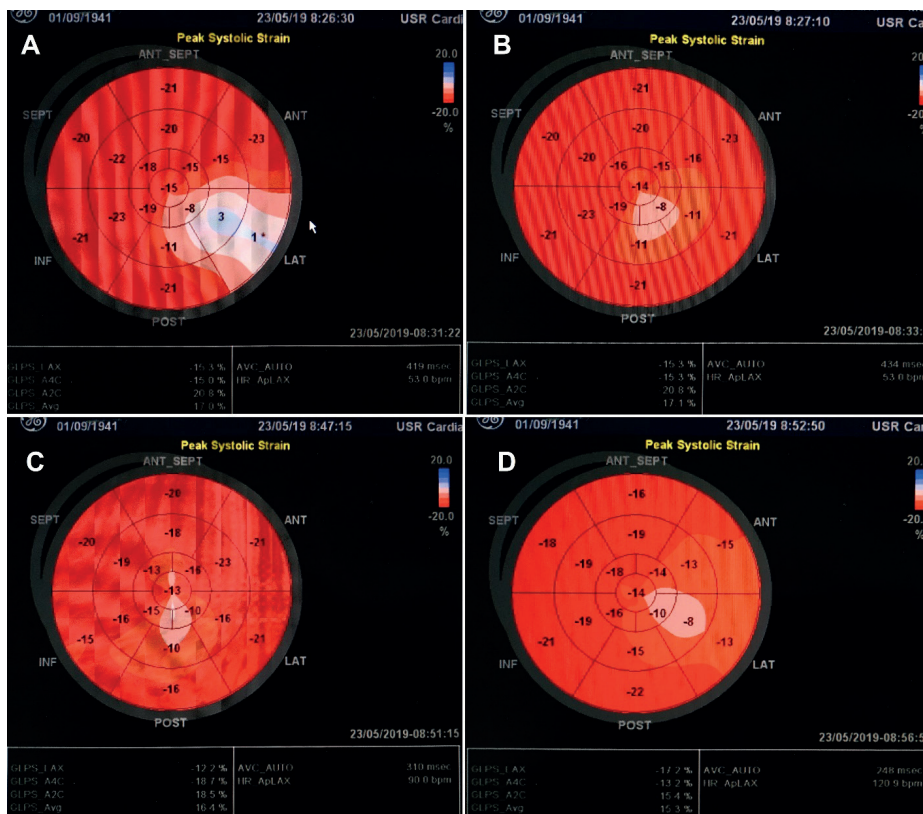


Fig. 4. A – D: continuous registration of strain patterns in bull's eye 17-segments model at rest and at 10, 20 and 40 mcg/kg/min dobutamine stress, respectively, in the patient with functional class 2 angina pectoris with ischemia in distal LAD territory (later proved by CAG). A: At rest, there is severe LV lateral wall strain decrease with local strain inversion. B: At 10 mcg/kg/min stress marked strain growth of previously compromised segments with preserved moderate decrease of apical anterior-lateral and posterior-lateral strains (ischemia with sufficient coronary reserve) without significant strains dynamics at the dose of 20 mcg/kg/min. C: Given targeted HR not reached (90'), test was prolonged to maximal stress. D: In 3 min. of 40 mcg/kg/min infusion there is a marked strain drop of whole antero-lateral LV wall and apex – moderate-to-severe ischemia (“two phased answer”) without sufficient coronary reserve in LAD territory. Patient successfully underwent LCA LAD PCI by DES.

STATISTICAL ANALYSIS

Data was analyzed using SPSS 20.0 software package for Windows (SPSS Inc., Chicago). Continuous variables are presented as mean \pm SD, categorical – as percentages. In all cases p-value <0.05 was considered statistically significant. Method accuracy was evaluated by calculating sensitivity, specificity, positive and negative predictive values, and index of method prognostic ability “area under curve” (AUC). Intra- and interobserver variability were evaluated by repeated strain quantification and visual estimation of same video records within 10 – 14 days intervals and by two different independent operators in 10 randomly selected pts.

RESULTS AND DISCUSSION

Mean pts age was 57.6 ± 11.3 years (84 men – 60,0%) with mean LV ejection fraction (EF) $54.4 \pm 15.8\%$. AH with sustained medical treatment in history was in 118 (84.3%) pts. 38 (27.1%) pts had diabetes mellitus (DM) type II. 56 (40.0%) pts were tobacco smokers. High CAD risk according to SCORE charts was found in 121 (86.4%) pts, while compromised CAD family history was registered in 127 (90.7%) пациентов. In 10 (7.1%) pts there were various corrected or uncorrected congenital or valvular heart disease: 2 (1.4%) pts. after mitral (MV) and aortic (AV) valve replacement (MVR & AVR) due to rheumatic disease, 2 (1.4%) pts after AVR due to congenital bicuspid AV degeneration, 2 (1.4%) pts after congenital interatrial and interventricular septum correction (hemodynamically insignificant), and 4 (2.8%) pts with insignificant

atherosclerotic AV disease. 22 (15.7%) pts had a history of different arrhythmia: 14 (10.0%) pts with paroxysmal AF, including 2 (1.4%) pts after radiofrequency ablation (RFA) without relapses, and 8 (5.7%) pts with various supraventricular (SVES) and ventricular (VES) low grade premature beats. Complete left hemiblock of unsure origin was diagnosed in 6 (4.3%) pts. 2 (1.4%) pts had DCM phenotype of unsure origin. All pts had normal BP and HR by the examination beginning (Table II).

There were no significant hemodynamics alterations during DSE. Maximal systolic (SBP) and diastolic (DBP) BP elevation at peak stress compared to rest values were 158.2 ± 9.4 vs. 129.8 ± 10.5 ($p < 0.0001$) and 88.4 ± 6.2 vs. 82.6 ± 11.7 ($p < 0.0001$) mm Hg, respectively. HR mean increase was $47.4 \pm 14.9'$ (113.8 ± 23.8 vs. $66.4 \pm 8,1$, $p < 0.0001$). Age-adjusted submaximal HR was reached only in 72 (51.4%) pts, which was explained by the facts that: 1) a significant proportion of pts received BB due to AH and/or HF; 2) ischemia criteria were reached much earlier than HR was reached; 3) maximal dobutamine dose was seldom reached. BP and HR restitution in all pts was reached spontaneously in 3 – 5 min after dobutamine was stopped and required no medication correction. There was no significant difference between SBP, DBP and HR growth in the patients with positive and negative test results.

Maximal dobutamine dose constituted 26.6 ± 10.3 mcg/kg/min., and majority of pts – 88 (62.9%) – reached maximal dose of 20 mcg/kg/min. In 2 (1.4%) pts test was stopped already at 10 mcg/kg/min stage due to marked ischemia signs by STE (severe strain decrease or inversion), while 50 (35.7%) pts made it to maximal stress of 40 mcg/kg/min,

Table II. Pts demographics in the study group

Patients demographics	Total (n = 140)
Men, n (%)	84 (60.0%)
Age, yeas	57.6±11.3
Arterial hypertension, n (%)	118 (84.3%)
DM, type II, n (%)	38 (27.1%)
Smoking, n (%)	56 (40.0%)
LV EF, %	54.4±15.8
SBP, mm Hg	129.8±10.5
DBP, mm Hg	82.6±11.7
HR, beats/min.	66.4±8.1
High CAD risk, n (%)	121 (86.4%)
CAD family history, n (%)	127 (90.7%)
Valvular and congenital heart defects, including valvular replacement history, n (%)	10 (7.1%)
Arrhythmia history, n (%)	22 (15.7%)
Complete left hemiblock, n (%)	6 (4.3%)

mainly due to high coronary reserve (32 (22.9%) pts) or (18 (12.9%) pts) due to negative test result.

Pts with negative DSE result had no complications during or after procedure at all.

In the patients with positive DSE results, overall frequency of any complications during the study was only 15 (12.9%) cases. We had no cases of manifested angina pain, BP drop or VT paroxysms. In 4 (3.5%) pts AF paroxysm developed at submaximal or maximal dobutamine stress – in 2 (1.72%) cases cardioversion was used, while in 2 (1.72%) cases spontaneous sinus rhythm restoration took place in 10 – 15 min after dobutamine infusion stopped. In 6 (5.2%) pts there were solitary and group VES. 2 (1.72%)

pts had frequent SVES, all hemodynamically insignificant and having stopped spontaneously in 5 – 10 min after infusion stop. 1 (0.86%) patient had relative HR decrease without manifested bradycardia. In 2 (1.72%) pts with history of AH and LV hypertrophy at the dose of 20 mcg/kg/min we found previously undiagnosed obstructive hypertrophic cardiomyopathy (HCM) with severe dynamic LV outflow tract obstruction (ΔP peak 127 and 135 mm Hg) (Table III and IV).

In 116 (82.9%) pts DSE result was positive, in 24 (17.1%) – negative. In the pts with positive DSE in 68 (58.6%) pts ischemia markers were present already at rest, and the following test was performed for myocardial viability and

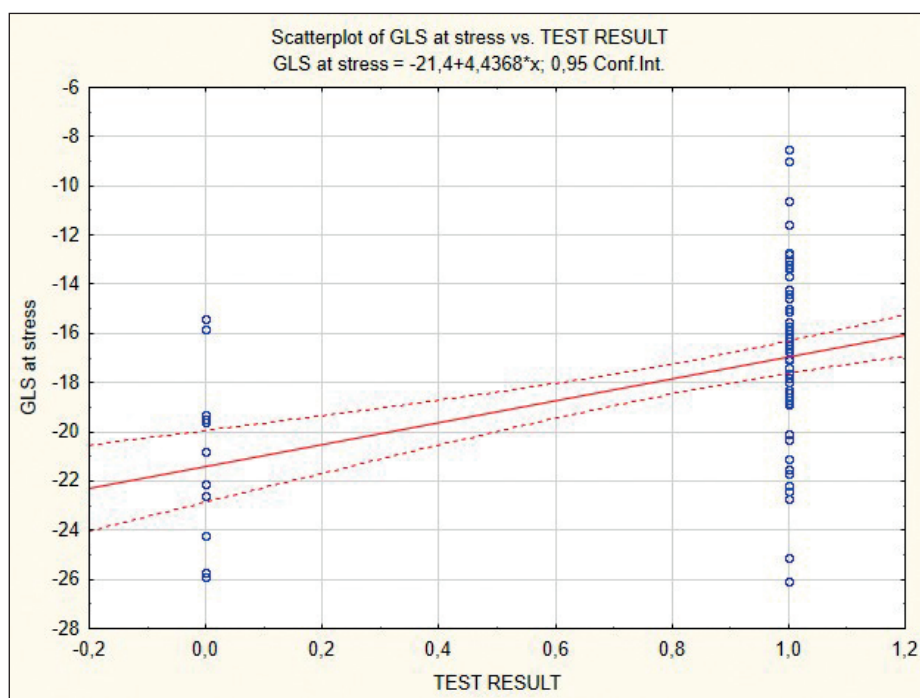


Fig. 5. Correlation between peak stress GLS value and general DSE test result ($r = 0.43, p < 0.0001$).

Table III. Hemodynamics during DSE with STE and dobutamine stress dose in the study group

Indices	Rest	Stress
SBP, mm Hg	129.8±10.5	158.2±9.4, p<0.0001
DBP, mm Hg	82.6±11.7	88.4±6.2, p<0.0001
HR, beats/min.	66.4±8.1	113.8±23.8, p<0.0001
Maximal dobutamine dose, mcg/kg/min.		26.6±10.3
10 mcg/kg/min, n (%)		2 (1.4%)
20 mcg/kg/min, n (%)		88 (62.9%)
40 mcg/kg/min, n (%)		50 (35.7%)

Table IV. DSE with STE features and immediate results in the studied group

DSE with STE results	
Positive, n (%)	116 (82.9%)
Negative, n (%)	24 (17.1%)
CAD diagnosis dobutamine dose, mcg/kg/min	
At rest	68 (58.6%)
10 mcg/kg/min.	16 (13.8%)
20 mcg/kg/min.	26 (22.4%)
40 mcg/kg/min.	6 (5.2%)
Complications, n (%)	15 (12.9%)
Angina pain, n (%)	0 (%)
AF, n (%)	4 (3.5%)
VT "runs", n (%)	0 (%)
Frequent or multiform, n (%)	6 (5.2%)
Frequent SVES, n (%)	2 (1.72%)
Bradycardia or relative HR drop, n (%)	1 (0.86%)
Previously undiagnosed HCM, n (%)	2 (1.72%)

coronary reserve evaluation in the territories of interest. In 16 (13.8%) pts ischemia markers were diagnosed at minimal dose of 10 mcg/kg/min, in 26 (22.4%) pts – at 20 mcg/kg/min, in 6 (5.2%) pts with high coronary reserve – only at 40 mcg/kg/min. As stated above, hemodynamically insignificant transitory complications were present only in the positive DSE group, of which only 2 (1.72%) cases required intervention (AF paroxysms cardioversion) (Table IV).

GLS dynamics in general studied group of insignificant with minor GLS -0.3% drop (p=0.51). In the pts with positive DSE result there was insignificant general -0.9% GLS drop 0.9% (p=0.055), while in the pts with negative DSE result GLS significantly grew – Δ GLS = +2.7 (p=0.015). However, we also found that regardless of general test result GLS dynamics could be either positive or negative in both groups. In positive DSE group on third of pts (n=38, 32.8%, p<0.0001) showed significant GLS growth (Δ GLS = +2.7, p=0.0032), while in two thirds GLS significantly dropped (Δ GLS = -2.7, p<0.0001). In negative DSE group majority of pts (n=22, 91.7%, p<0.0001) showed significant GLS growth (Δ GLS = +3.1, p=0.011), while its decrease in the minority of pts (n=2, 8.3%, p<0.0001) was insignificant (Δ GLS = -0.8, p=0.09) (Table V). With this, correlation

between peak stress GLS and general test result was significant but weak (r = 0.43, p<0.0001) (Fig. 5).

All pts underwent CAG. In the pts with negative DSE result (24 (17.1%) pts) 2 (8.3%) cases of 1-vessel disease were diagnosed – 1 (4.15%) case of insignificant (50-60%) LAD lesion (patient with earlier undiagnosed HCM) and 1 (4.15%) case of insignificant (50 – 70%) RCA lesion with well-developed collaterals in both cases (false negative test result). Both cases were not stented. In the rest of cases, CAG showed intact coronary arteries (CA).

In the pts with positive DSE result (116 (82.9%) pts) there were 2 (1.7%) false-positive results with intact CA – both in the pts with long AH history and marked hypertensive "bull's eye" pattern at STE complicating results interpretation along with marked congenital CA tortuosity. Rest of cases showed different severity and prevalence of significant CA atherosclerotic lesions (Table VI).

Therefore, DSE with STE results sensitivity and specificity regarding primary CAD diagnosis compared to CAG results, as the "golden standard", were 98.3% and 91.7%, respectively, with identical positive and negative predictive values and very high general method accuracy (AUC = 0.98) and relative risk (OR = 627.0, p<0.0001).

Table V. GLS dynamics during DSE with STE

	Rest	Peak stress
GLS in general group (n=140), %	-18.0±3.5	-17.7±4.0
ΔGLS, %	- 0.3, p=0.51	
GLS in positive DSE group (n=140), %	-17.9±3.5	-17.0±3.6
ΔGLS, %	- 0.9, p=0.055	
GLS in negative DSE group (n=140), %	-18.7±3.8	-21.4±3.6
ΔGLS, %	2.7, p=0.015	
Positive DSE group (n=116)		
Growth, n=38 (32.8%)		
GLS, %	-16.1±3.5	-18.8±4.2
ΔGLS, %	2.7, p=0.0032	
Drop, n=78 (67.2%), p<0.0001		
GLS, %	-18.7±3.1	-16.0±2.9
ΔGLS, %	-2.7, p<0.0001	
Negative DSE group (n=24)		
Growth, n=22 (91.7%)		
GLS, %	-18.5±4.0	-21.6±3.7
ΔGLS, %	3.1, p=0.011	
Drop, n=2 (8.3%), p<0.0001		
GLS, %	-20.3±0.3	-19.5±0.2
ΔGLS, %	-0.8, p=0.09	

Table VI. CAG results in the studied group

CA lesions features	Negative DSE group (n=24 (17.1%))	Positive DSE group (n=116 (82.9%))
1-vessel disease, n (%)	2 (8.3%)	56 (48.3%)
2-vessels disease, n (%)	0 (0%)	38 (32.7%)
3- vessels disease, n (%)	0 (0%)	22 (19.0%)
LCA main lesion, n (%)	0 (0%)	8 (6.9%)
LAD lesions, n (%)	1 (4.15%)	84 (72.4%)
Cx lesions, n (%)	0 (0%)	38 (32.8%)
RCA lesions, n (%)	1 (4.15%)	55 (47.4%)

Combined ΔGLS and ΔWMSI for ischemia diagnosis showed significantly lower sensitivity 86.2% (p=0.0002) and specificity 80.4% (p=0.0064) compared to integral evaluation of ischemia markers, myocardial viability and coronary reserve with significantly lower general method accuracy (AUC 0.83, p<0.0001).

Given lower ΔGLS and ΔWMSI accuracy according to existing publications compared to general DSE with STE test result with myocardial viability and coronary reserve evaluation [3], as well as demonstrated ability of GLS to significantly grow during stress in substantial proportion of pts (32.8%, p=0.0032) with definitely positive test result, in our routine practice we decided to no longer concentrate on GLS or WMSI dynamics. Today we prefer to evaluate GLS in each individual patient, concentrating rather on general test result taking into account myocardial viability and coronary reserve in each coronary territory. Such

decision is also confirmed by weak correlation between peak stress GLS and general DSE with STE test result (r = 0.43, p<0.0001) and significantly lower sensitivity and specificity of combined ΔGLS and ΔWMSI quantification with significantly lower method accuracy (AUC 0.83 vs. 0.98, p<0.0001).

According to DSE with STE the majority of positive result pts (114 (98.3%) pts) had viable myocardium, of which 94 (81.0%) had insufficient coronary reserve. The rest (22 (19.0%) pts) had significant coronary lesions with sufficient coronary reserve or well developed collaterals according to CAG. According to DSE and CAG results 96 (82.3%) pts underwent different revascularization procedures: 86 (89.6%) PCI's (54 (56.3%) pts – 1-vessel stenting; 32 (33.3%) pts – 2- vessels stenting). 10 (10.4%) pts with multi-vessel disease underwent CABG with good close results (Table VII).

Table VII. DSE with STE and CAG results regarding myocardial revascularization in the studied group

Results	Total (n = 58)
Positive DSE results, n (%)	116 (82.9%)
Viable myocardium, n (%)	114 (98.3%)
Insufficient coronary reserve, n (%)	94 (81.0%)
Sufficient or high coronary reserve, n (%)	22 (19.0%)
Interventions as per DSE results, n (%)	96 (82.3%)
PCI's as per DSE results, n (%)	86 (89.6%)
1-vessel stenting, n (%)	54 (56.3%)
2- vessels stenting, n (%)	32 (33.3%)
CABG as per DSE results, n (%)	10 (10.4%)

Thus, general result of DSE with STE results evaluation regarding positive or negative test criteria, myocardial viability and coronary reserve evaluation and defining indications for intervention and revascularization (according to CAG – the “golden standard” of verification) showed that DSE with STE has sensitivity 97.9% and specificity 91.7% (AUC 0,95) with identical respective positive and negative predictive value with high relative risk (OR = 564.0, $p < 0.0001$).

It is known that quantitative and semiquantitative 2D-strain assessment allows much better LV and RV regional wall motion abnormalities detection at rest [2,4-6,9,12,14,15]. Also, there is strong evidence that STE is a perfect visualization tool for DSE [2,10,13], especially taking into account the fact that rather often conventional EchoCG parameters in primary pts with CAD suspicion do not really differ.

B-mode strain may be quantified at any pharmacological stress stage during DSE, making it valuable instrument for ischemia diagnosis and myocardial viability and coronary reserve evaluation at rest and stress [2,10,16]. It has been shown that severe ischemia markers, namely longitudinal strain abrupt drop may take place at earliest DSE stages long before visual regional contractility impairment [2,8], which is fully supported by our study results.

Some studies show that longitudinal strain has higher diagnostic accuracy compared to circular and radial strain, and is at least as accurate as visual regional wall motion abnormalities evaluation in case of CAD diagnosis expertise [2]. Taking into account the fact that subendocardial myocardial layer is the most sensitive to ischemia in combination with simplicity and speed of strain quantification during DSE, in our clinical center we chose to use only 2D-longitudinal peak strain as an optimal ischemia diagnosis parameter, which our study results clearly demonstrate.

Our data confirm high safety of DSE in the pts with CAD suspicion, since we saw very rare clinically significant complications requiring additional medication treatment or intervention (2 (1.72%) cases of AF paroxysm cardioversion). Most cases of relatively rare arrhythmia ischemia equivalents were transitory, stopped spontaneously after dobutamine infusion stop and were hemodynamically

insignificant. Thus, we consider DSE the safest stress test in the pts with CAD suspicion.

The described cases of severe dynamic LVOT obstruction during DSE in the pts with previously undiagnosed HCM are of particular interest and should be a matter for separate studies.

LIMITATIONS

We did not limit pts inclusion by body mass index, including obese pts to avoid possible bias and DSE feasibility overestimation due to only optimal visualization analysis. Since the aim of our study was mainly the assessment of myocardial viability and coronary reserve, we did not limit pts inclusion by any LV EF value. Certain limitation might be in technical issues during STE due to suboptimal visualization, especially in high HR cases.

CLINICAL PERSPECTIVE

Myocardial deformation parameters, namely global and regional peak systolic strain, allow ischemia detection in early stages, which lead STE to take a significant niche in our center routine management of CAD pts requiring better risks stratification. Appropriate software algorithms development in the future might allow more effective implementation of DSE with STE into routine management of pts after ACS.

CONCLUSIONS

The present study allows considering DSE with semiquantitative 2D-longitudinal STE a safe optimal method for ischemia diagnosis and myocardial viability and coronary reserve evaluation in the pts with CAD suspicion. Given significantly lower Δ GLS and Δ WMSI quantification accuracy along with demonstrated GLS increase ability during DSE in a substantial proportion of pts, authors recommend integral general test interpretation (ischemia markers, myocardial viability and coronary reserve evaluation) rather than concentrating on GLS dynamics by itself.

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The Authors declare no conflict of interest

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