

# Color kinesis-dobutamine stress echocardiography pinpoints coronary artery disease

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## Ethics Committee Approval

The study has been approved by Istanbul Atlas University Clinical Research Ethics Committee on 21.12.2021 with protocol number E-22686390-050.01.04-10993.

All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

## Conflict of Interest

No conflict of interest was declared by the authors.

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## Abstract

**Background/Aim:** Dobutamine stress echocardiography (DSE) can identify significant coronary artery disease (CAD) and where it is localized. However, determining endocardial borders with poor echocardiographic views may create unsatisfactory results. Color kinesis (CK) shows endocardial movement with color, and allows easier and more objective evaluation of ventricular wall motion. In this study, our aim was to evaluate the role of CK in determining CAD localization during DSE.

**Methods:** The study group consists of patients whose CAD diagnosis was confirmed with coronary angiography (CA). Patients with atrial fibrillation (A-Fib), left bundle branch block, poor echocardiography image quality, left ventricular (LV) ejection fraction < 40%, and non-ischemic LV wall motion abnormality were excluded. CK-DSE and dobutamine stress-induced myocardial perfusion scintigraphy (MPS) was done in all patients and compared to CA.

**Results:** A total of twenty patients [16 males (80%) and 4 females (20%)] were included in the study. CK-DSE results were consistent with CA in determining CAD localization (kappa 0.66). Vessel-based kappa values for LAD, RCA, and Cx were 0.81, 0.70 and 0.61, respectively. Consistency between MPS and CK-DSE was evaluated by the area under curves (AUC) within a ROC curve analysis ( $P>0.05$ , 95% CI).

**Conclusion:** Our study showed that CK allows for rapid, objective, and automatic evaluation of segmental wall motion. In addition, CK-DSE is consistent with CA results.

**Keywords:** Color kinesis, Coronary artery disease, Stress echocardiography

## Introduction

Coronary artery disease (CAD) is the world's leading cause of morbidity and mortality. Due to improved primary prevention and healthcare services, mortality has decreased over the past three decades [1]. Its prevalence in Turkey is estimated to be around 2.8% [2]. CAD is approximately 40% and 50% of all mortality in men and women, respectively. Patients may have insignificant symptoms or be asymptomatic. Sudden cardiac death increases in all forms with silent ischemia. Early diagnosis is critical, so that all available data is considered and easy-to-apply, with reliable diagnostic methods. Invasive and noninvasive diagnostic methods are also widely used in this respect. Other techniques are resting electrocardiography (ECG), the exercise stress test, myocardial perfusion scintigraphy (MPS), echocardiography, and coronary computed tomography angiography (CCTA) [3].

Transthoracic echocardiography and dobutamine stress echocardiography (DSE) help in the detection of myocardial infarction (MI), visualization of proximal coronary arteries, examination of wall motion abnormalities, evaluation of systolic and diastolic functions of the ventricles, and risk stratification of CAD [4-9]. Difficulties in locating endocardial borders and poor echocardiographic windows may cause unsatisfactory results. With these limitations, color kinesis (CK) was developed with acoustic quantification (AQ). CK, based on coding the inward and outward movements of the endocardium with color cues, helps with objective evaluation of wall motion abnormalities [10,11].

Stress echocardiography is another frequently-used method, dobutamine being the most used pharmacological agent for this [12]. Objective wall motion analysis can be performed by stress echocardiography in association with CK [5]. In this study, we aimed to evaluate the role of dobutamine stress echocardiography in association with color kinesis (CK-DSE) to determine the localization of coronary artery disease (CAD).

## Materials and methods

### Study population

The minimum number of patients to test consistency between CK-DSE and CA was 20 patients, statistically. Patients with atrial fibrillation (A-Fib), left bundle branch block, poor echocardiographic image quality (< 30% visible endocardial border), left ventricular (LV) ejection fraction < 40%, and non-ischemic LV wall motion abnormality (Wolf-Parkinson-White syndrome, and a previous history of cardiac surgery, pacemaker rhythm issues, cardiomyopathies, and severe aortic and mitral valve insufficiency) were excluded. The background of all patients was recorded, resting ECGs taken, exercise ECGs, CK-DSE, and MPS examinations performed. Thirty-two patients who met the above criteria enrolled in the study. Ten patients for whom CA was not performed and 2 patients with poor echocardiographic image quality were later excluded. As per protocol, enrollment was ended after achieving the target patient number, with the study group consisting of 20 patients after all exclusions. Written informed consent was obtained from participants, and the study was conducted in accord with the

principles of the declaration of Helsinki (1964): its protocol was also approved by the institutional review board.

### Evaluation of CK-DSE

All evaluations were performed with Hewlett Packard (Palo Alto, CA, USA) Sonos 2500 echocardiography, using a 2.5-3.5 MHz transducer. Anti-ischemic and anti-hypertensive drugs were discontinued at least 2 days before the examination, after 4 hours of fasting. The parasternal long and short axes, and the apical two- and four-chamber echocardiographic windows were used for evaluation. AQ resting in two-dimensional echocardiographic views was used for CK recordings thereafter. Dobutamine infusion was started with a dose of 5 mcg/kg/min and increased every three minutes to 10, 20, 30, and 40 mcg/kg/min. ECG, blood pressure, and patient heart rate were recorded with each step. Age-adjusted target heart rate was calculated as follows:  $220 - \text{age (years)} \times 0.8$ , and 0.25 mg IV atropine injection was used as the last step for patients who could not reach a target heart rate. Two-dimensional and CK images were recorded for at least 3 cycles. Dobutamine infusion was terminated in patients who had angina pectoris, hemodynamically significant arrhythmia,  $\geq 2$  mm of ST depression on ECG recordings, and ischemia-induced echocardiographic findings.

Two-dimensional and CK dobutamine stress echocardiographic recordings were evaluated by an experienced cardiologist, unaware of the patients' history, MPS, and CA reports. Segments with color layers from red to blue in CK analysis were accepted as having inward endocardial movement and as normokinetic. Segments with thin color layers were interpreted as hypokinetic, but those with thin layers of color (red-orange) were interpreted as akinetic; segments with outward movement and thin layers of color (red-orange) were interpreted as dyskinetic. CK-DSE findings with the presence of ischemia are summarized in Table 1.

Table 1: Interpretation of CK-DSE

Resting wall motion	Wall motion at maximum stress	Interpretation
Normal	Hyperkinetic	Normal
Normal	Hypokinetic	Ischemia
Normal	Delayed contraction (tardokinesia)	Ischemia
Hypokinetic	Increased contractility	Normal
Hypokinetic	No change	Ischemia
Hypokinetic	Decreased contractility	Ischemia
Hypokinetic	Akinetic	Infarction
Akinetic	Not evaluated	Infarction

LV wall motion was evaluated at rest; however, for all steps of the stress test and then during the recovery period, this was done with CK. Broderick's classification system was used to define left ventricle wall segments [13]. Septum, anterior, anteroseptal wall, and apical segments were accepted as the left anterior descending artery (LAD), lateral and posterior wall segments were accepted as the circumflex artery (Cx) and inferior wall, while interventricular septum basal segments were accepted as right coronary artery (RCA) territory. Apical inferior and lateral segments were accepted as overlapping. If septal or anterior wall motion accompanied a lateral apical segment wall motion abnormality, it was considered LAD territory. Posterior or posterolateral wall motion abnormality with lateral apical segment wall motion abnormality was considered Cx territory. For inferior wall apical segment evaluation, accompanying inferior wall motion abnormality was considered RCA territory,

while anterior or anteroseptal wall motion abnormality was considered LAD territory [14, 15].

### Myocardial perfusion scintigraphy (MPS)

When the maximum heart rate was reached during CK-DSE, 10 mCi Tc 99m MIBI was injected for scintigraphy evaluation. After 45 minutes, stress images were taken. Rest images were taken three hours later, 45 minutes after the MIBI injection. All images were taken with single-photon-emission computed tomography (SPECT).

Perfusion defects in the anterior, lateral, and apical wall segments were considered LAD territory, lateral and posterior wall segments were considered Cx territory, inferior wall, and posterior and interventricular septum basal segments were accepted as RCA territory. MPS findings were evaluated by an experienced nuclear medicine specialist who was unaware of the patients' history, CA, and CK-DSE results.

### Coronary angiographic evaluation

Coronary angiographies and left ventriculography evaluations were performed with a Toshiba CC-i angiography device (Minato, Tokyo) by interventional cardiologists with standard methods. A coronary artery with > 70% percent stenosis was seen as an ischemia-related artery.

### Statistical analysis

Variables are expressed as numbers and percentages. CK-DSE and dobutamine MPS's compatibility with angiography was generally and individually evaluated for all coronary arteries. Cohen's kappa coefficient was used for CK-DSE and MPS to test the consistency of CA. A kappa value  $\geq 0.7$  was considered high, and between 0.4 and 0.7 was considered moderate consistency. Kappa values for MPS and CK-DSE were analyzed with receiver-operating characteristic (ROC) curve analysis, while consistency between tests was evaluated by comparison of area under curves (AUC) with 95% confidence interval (CI) as previously described by DeLong et al. [16]. All statistical procedures were performed with SPSS v.16.0 (IBM-SPSS, Inc., Armonk, NY, USA). A *P*-value < 0.05 was seen as statistically significant.

## Results

In 13 (65%) patients, DSE was completed, but was ended early in 5 patients due to angina pectoris, and in 2 patients due to  $\geq 2$  mm ST segment depression. There were no significant side effects during DSE; 11 patients had no side effects, while others experienced dizziness, palpitations, headaches, and burning sensations, which was eliminated by terminating the test.

Resting wall motions were normal in 8 (40%) patients. During the dobutamine challenge, segmental wall motion abnormality developed in all patients, despite normal resting wall motion. Four developed wall motion abnormality in Cx territory, 3 developed it in LAD territory, and 1 developed it in RCA territory.

Twelve (60%) patients had abnormal resting wall motion of various degrees. Wall motion abnormalities remained unchanged or deteriorated in 10 patients. One had resting hypokinesia in Cx territory, which was resolved during the dobutamine challenge and accepted as normal. Three patients had akinetic or dyskinetic segments of LAD territory, 4 had akinetic segments of RCA territory, having had previous MIs. In

5 patients, resting hypokinesia of LAD territory was increased during the dobutamine challenge and considered to be ischemia. In one patient, resting hypokinetic segments in RCA territory became akinetic during a dobutamine challenge and the patient was found to have had a previous MI.

According to the CK-DSE results, 1 patient was considered normal, 11 (55%) as having single-vessel disease, 2 (35%) as having two-vessel disease, and 1 (5%) as having three-vessel disease. As per the MPS results, 1 patient was considered normal, 8 (40%) had single-vessel disease, 9 (45%) had two-vessel disease, and 2 (10%) had three-vessel disease.

More than 70% percent with stenosis of the coronary arteries were related to inducible ischemia, yet accepted as significant CAD. CA had shown single-vessel disease in 10 (50%), two-vessel disease in 9 (45%), and three-vessel disease in 1(5%). Nine LAD, 11 RCA, and 11 significant Cx lesions could detect CA. Left ventriculography had shown segmental wall motion abnormality in 9 (45%) patients, and apical aneurysm in 3 (15%).

The kappa coefficient of CK-DES was 0.66 in determining CAD localization. Vessel-based kappa values for LAD, RCA, and Cx were found at 0.81, 0.70, and 0.61, respectively.

The kappa coefficient of dobutamine MPS was found to be 0.67 for all coronary vessels. Vessel-based kappa values for LAD, RCA, and Cx were 0.79, 0.70, and 0.59, respectively. According to the ROC curve analysis, comparison of AUC for kappa values of MPS and CK-DSE in determining CAD was found to be statistically insignificant ( $P>0.05$ , 95% CI).

## Discussion

The following factors were considered while preparing our study protocol: 1- Reflecting routine daily cardiology practice, 2- Performing necessary and non-time-consuming procedures for patients, 3- Objective interpretation of the tests. The combination of these factors was obvious in patient selection, evaluation of data, and determination of diagnostic methods.

In this study, our aim was to determine the presence and localization of significant CAD. The population consists of a mixed group of patients, some of whom had a previous diagnosis of CAD, while others did not. Clinical, resting ECG, and echocardiography findings were evaluated and CK-DSE examination was only performed in suitable patients: MPS or CA was also recommended in them. Unnecessary CA was avoided in patients with a low probability of significant CAD in noninvasive tests. Two of 32 patients were excluded, as they were not eligible for CK-DSE, with 10 excluded from the study, not having an indication of CA. This approach increased the likelihood that CK-DSE and dobutamine MPS would yield similar results with CA. CK-DSE and MPS were performed for the same dobutamine challenge, so repeated dobutamine administration was avoided. Although it was not mentioned in the study protocol, the exercise stress test was performed in all patients to preclude unnecessary CA.

Mor-Avi et al. [17] performed CK-DSE in 20 patients, suggesting that CK allows for objective and rapid evaluation of CAD. Our impression was similar. Although we did not evaluate

patients with poor echocardiographic image quality, endocardial borders could be seen clearly with CK. A previous study had evaluated the role of DSE in determining ischemia-related coronary artery, but Segar et al. had shown that sensitivity was similar for each coronary artery [10]. Our study found that CK-DSE was consistent with CA results in determining CAD localization ( $\kappa=0.66$ ); however, predictive probability was different among all coronary arteries. This difference was mainly due to a lower predictive value in Cx lesions; it simulated a previous DSE study in which Geleijnse et al. [18] reported the sensitivity of DSE in determining LAD, RCA, and Cx lesions as 72%, 75%, and 55%, respectively. We explained the lower resolution of the lateral wall and differences in the Cx coronary artery.

DSE is a valuable diagnostic tool in determining CAD: in a recent study, its sensitivity and accuracy was reported as 85% and 90%, respectively [6, 19]. Studies comparing MPS and DSE to determine CAD localization found similar diagnostic performance [20]. The optimal test changes according to patient characteristics, laboratory conditions, and availability. The main advantage of DSE is that it allows for detection of additional information about cardiac disorders. It is also less expensive, radiation-free, and can be done at the bedside.

### Limitations

The main limitation of our study was that it was conducted with a relatively small number of patients. Given ethical considerations, 10 patients without a CA indication were not included, although we had already performed CK-DSE. Further studies conducted with a large patient population, comparing CK-DSE and CA in all patients, were needed. In our research, patients with an ejection fraction of  $< 40\%$  and A-Fib were not included in the study, such that these findings should not be extrapolated to this patient population. Although CK allows for more objective evaluation of wall motion abnormalities, there is a group of patients in whom healthy evaluation cannot be done due to poor image quality ( $n=2$  in our study). New techniques and improved CK may transcend image quality issues in this population.

### Conclusion

In determining CAD localization, CK-DSE led to results close to CA. Compared to MPS, no significant difference was found between methods. While their compatibility with CA was higher in determining ischemia in LAD and RCA territories, consistency was found as moderate for Cx territory. Although both CK-DSE and MPS produce similar results, CK-DSE has some advantages: it is easy to apply, less expensive, and detects accompanying cardiac disorders. The CK method allows for rapid, objective, and automatic evaluation of segmental wall motion. In our study, CK was used with DSE, with high diagnostic accuracy achieved.

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