Predictive Value of Dobutamine Stress Echocardiography–Derived Myocardial Viability in Patients with Ischemic Cardiomyopathy

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Abstract

Background: The primary validation of myocardial viability testing lies in its capacity to anticipate functional myocardial recovery after revascularization. While contractile improvement in stunned myocardium may occur as early as a few hours and up to several days post-revascularizationfunctional recovery in myocardium with chronic hibernation may be delayed for few months.

Aim of Study: The aim of this study is toassess the predictive significance of Dobutamine Stress Echocardiography (DSE)–based determination of myocardial viabilityin relation to clinical outcomes in patients presenting with ischemic cardiomyopathy (ICM).

Patients and Methods: This prospective study enrolled 60 patients diagnosed with ischemic cardiomyopathy (ICM) and left ventricular systolic dysfunction, as evidenced by an ejection fraction (EF) ≤40%, each of whom underwent evaluation of myocardial viability using DSE before revascularization.

Results: A significant improvement in New York Heart Association (NYHA) functional class, as determined statistically was noted, in most of the patients transitioning from Class III at baseline to Class II or lower during follow-up. Similarly, Canadian Cardiovascular Society (CCS) angina classification showed significant improvement, with most patients achieving Class I status by six months. The six-minute walk test (6MWT) distance also demonstrated significant enhancement over time, increasing from a baseline mean of 351.5±35.65 meters to higher values at both 3- and 6-month follow-up assessments. Non-viable myocardial segments were predominantly identified in the left anterior descending (LAD) artery territory in

75% of cases, followed by combined involvement of the LAD and right coronary artery (RCA) in 6.7%. A robust inverse correlation was noted between the extent of non-viable myocardium and the magnitude of improvement in left ventricular ejection fraction (LVEF), with statistical significance (p<0.001).

Conclusion: The results underscore the outcome-predicting capacity of myocardial viability particularly as evaluated by DSE in forecasting improvements in clinical outcomes among patients with ICM.

Key Words: Myocardial viability – Ischemic cardiomyopathy (ICM) – Clinical outcome.

Abbreviations and Acronyms:

6MWT : Six-Minute Walk Test. ACS : Acute Coronary Syndrome.

BP : Blood Pressure.

CABG: Coronary Artery Bypass Grafting.

CAD : Coronary Artery Disease.

CCS : Canadian Cardiovascular Society.
CMR : Cardiac Magnetic Resonance.

DM : Diabetes Mellitus.

DSE : Dobutamine Stress Echocardiography.

EF: Ejection Fraction.

HF: Heart Failure.

HR: Heart Rate.

HTN: Hypertension.

ICM: Ischemic Cardiomyopathy.

LV : Left Ventricle.

LVEF: Left Ventricular Ejection Fraction.
NYHA: New York Heart Association.
OMT: Optimal Medical Therapy.

PCI : Percutaneous Coronary Intervention. PET : Positron Emission Tomography.

REVIVED-BCIS2: Revascularization for Ischemic

Ventricular Dysfunction–British Cardiovascular Intervention Society Trial 2.

SPECT : Single-Photon Emission Computed Tomography. STICH : Surgical Treatment for Ischemic Heart Failure.

WMSI: Wall Motion Score Index.

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Introduction

THE pathophysiology of LV systolic dysfunction in ICMpredominantly involves myocardial necrosis resulting from insufficient oxygen delivery [1]. During myocardial infarction (MI), the interruption of circulatory flow distal to the occluded coronary artery leads to ischemia and subsequent necrosis of myocardial tissue. Over time, the necrotic myocardium is replaced by fibroelastic scar tissue, resulting in infarction, loss of viable contractile tissue, and impaired wall motion [2]. This remodeling process progresses over several months, ultimately leading to reduced LV systolic function and diminished cardiac output [3]. Myocardial stunning, defined by ongoing contractile impairment despite of the reestablishment of coronary blood flow, may also occur [4]. Stunning can result from transient episodes of mild ischemia or stress, particularly in the context of coronary artery narrowing, and functional recovery is possible if recurrent ischemic insults are prevented [2]. During acute coronary syndrome (ACS), myocardial stunning may occur alongside infarction, with partial improvement in function often observed following successful revascularization [5].

The theory of myocardial hibernation originated from clinical and experimental observations. that significant LV systolic dysfunction could be reversed following myocardial revascularization [6]. Hibernation represents an adaptive response in which myocardial contractile function is downregulated to preserve cell viability under conditions of chronic ischemia [7]. Although the precise severity and duration of ischemia required to induce hibernation remain uncertain, the phenomenon is commonly encountered among patients exihibiting advanced coronary artery disease (CAD). Hibernating myocardium is marked by diminishedmyocardial contractile function despite the maintenance of sufficient perfusion [8]. Both myocardial hibernation and stunning reflect reversible forms of ischemic myocardial dysfunction [4]. However, unlike stunning, which typically resolves spontaneously with the restoration of blood flow, hibernation necessitates therapeutic intervention to re-establish adequate oxygen supply [3,9]. Restoration of myocardial perfusion through any modality capable of improving oxygen delivery can reverse the hibernating state.

Myocardial viability:

At the cellular level, myocardial viability is defined by the presence of myocytes that have not sustained irreversible injury. Within clinical and scientific contexts, although, the terminology typically refers to myocardial regions demonstrating resting contractile dysfunction with the potential for functional recovery following revascularization [10]. This concept is intrinsically linked to myocardial hibernation, wherein myocardial contractile function is adaptively down-regulated to preserve cellular integrity in response to recurrent ischemic episodes [11,12].

Is myocardial viability a reliable predictor of recovery in left ventricular performance?

Myocardial viability testing has been primarily validated based on its capacity to anticipate the restoration of contractility following revascularization. Contractile recovery of stunned myocardium may occur within a timeframe of hours to days, whereas in myocardium affected by advanced hibernation, restoration may require several months [13]. Observational studies consistently demonstrate that viability assessment provide reliable prediction of improvements in global left ventricular function following revascularization [6,11].

A meta-analysis encompassing 158 studies concluded that all available modalities of cardiac imaging were comparably effective in assessing myocardial viability. Positron emission tomography (PET) achieved the highest levels of sensitivity and negative predictive value, while DSE outperformed in terms of specificity and positive predictive accuracy for segmental myocardial recovery [14]. Cardiac magnetic resonance imaging (CMR) with contrast enhancement allows for the appraisal of myocardial scarring, wherein late gadolinium enhancement (LGE) serves as a marker of necrosis and irreversible myocardial damage [15].

Early clinical studies have shown that low-dose DSE can support effective assessment of prognostic risk and predict clinical outcomes following revascularization [16]. While some studies demonstrated an association between inducible ischemia and improved outcomes post-revascularization, other investigations suggested that this relationship becomes less significant when factors such as scar burden are accounted for [17].

Aim of the study:

The aim of this study is toassess the predictive significance of DSE-based determination of myocardial viabilityin relation to clinical outcomes in patients presenting with ICM, including changes in NYHA functional class, CCS angina class, 6MWT performance, and LVEF.

Ethics Approval:

The data collected from patients remain strictly confidential. Patients were not identified by name in any reports or publications related to this study. Prior to enrollment in the study, patients were given a comprehensive explanation of its purpose, nature, and risk—benefit assessment. Informed consent was obtained from all participants, and the study protocol was approved by the Ethics Committee of the Faculty of Medicine, Alexandria University, under approval number 0107765.

Patients and Methods

Study population:

A cohort of 60 patients with a diagnosis of ICM and impaired LV systolic function was recruited in the study, defined by an estimated EF of 40% or less. All participants underwent myocardial viability assessment using DSE prior to revascularization. The study was carried out at Alexandria University Hospital, Smouha University Hospital, and the International Cardiac Center between April 2023 and April 2024, with clinical and echocardiographic follow-up at three and six months post-revascularization. The study excluded individuals with contraindications to DSE.

Study design:

The study included 60 patients diagnosed with ICM and LV dysfunction resulting from ischemic heart disease, all of whom had an estimated EF of 40% or lower, despite being maintained on optimal guideline-directed medical therapy (GDMT) based on the most recent heart failure (HF) guidelines [18]. All patients underwent myocardial viability assessment using DSE prior to revascularization. The study was carried out at Alexandria University Hospital, Smouha University Hospital, and the International Cardiac Center between April 2023 and April 2024, with clinical and echocardiographic follow-up at three and six months post-revascularization. Myocardial viability [19] was assessed using available imaging modalities, specifically DSE.

Assessment:

All patients underwent the following assessments: (1) Detailed history taking with an emphasis on the clinical manifestations of HF complaints, NYHA functional classification, [20] CCS angina class, [21] drug history, coexisting comorbid conditions and any contraindication to DSE; (2) The 6MWT [22] is a standardized submaximal exercise test utilized to measure functional capacity and tolerance to physical exertion. The primary outcome measure is the total distance ambulated within six

minutes, which serves as an indicator of functional exercise performance and is used to monitor changes over time, (3) Standard 12-lead electrocardiography (ECG) to identify arrhythmias, bundle branch block (BBB), QRS complex width, pathological Q waves or ST-segment and T-wave changes; (3) DSE [23].

Pharmacologic stress protocol with dobutamine:

An intravenous infusion of dobutamine was initiated using an automated syringe pump, beginning at a dose of $5\mu g/kg/min$ for 5 minutes, and incrementally increased to 7.5 and then $10\mu g/kg/min$ in staged intervals; Resting and post-stage blood pressure and 12-lead ECGs were recorded throughout the dobutamine stress echocardiography to assess cardiovascular response; The endpoint was defined as reaching 10% above baseline heart rate, with reassessment of EF and wall motion score index (WMSI) at each incremental stage; Four distinct patterns were examined in segments that were dysfunctional at baseline: (Fig. 1).

- 1- Biphasic response: Initial improvement in wall motion at low-dose dobutamine (5 or 10μg), followed by worsening with high-dose dobutamine.
- 2- Sustained improvement: Continuous improvement in wall motion at either low or high-dose dobutamine, with no subsequent deterioration.
- 3- Worsening: Deterioration in wall motion at either low or high-dose dobutamine.
- 4- No change: No improvement or worsening of wall motion throughout the test.

Dysfunctional segments were considered viable if they displayed any pattern except for the "no change" pattern.

(4) PCI was performed for revascularization. Follow-up assessments were performed at three and six months following revascularization to evaluate clinical outcomes, including changes in NYHA functional class, 6MWT performance, and CCS angina class, as well as echocardiographic evaluation of using the Modified Simpson's method.

Statistical methods:

Data were entered into a computerized database and subsequently analyzed with IBM SPSS Statistics software, version 20.0 (Armonk, NY: IBM Corp). Qualitative data were expressed as frequencies and percentages. The normality of the data distribution was evaluated using the Shapiro-Wilk test. Quantitative data were presented as range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). A 5% significance level was used to assess the statistical

significance of the results. Categorical variables between groups were compared using the Chi-square test, with Fisher's Exact test applied when more than 20% of cells had an expected count of less than 5. The Student's *t*-test was applied to compare normally distributed quantitative variables between two groups, while the Mann-Whitney test was used for non-normally distributed quantitative variables.

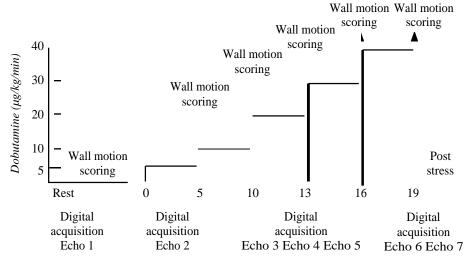


Fig. (1): Dobutamine stress echocardiography protocol.

Results

Demographic data:

Patients included in the study had a mean age of 58. 9±9.9 years. Male patients constituted 76.7% of the cohort, while female patients comprised 23.3%. A history of smoking was identified in 70.0% of the patients. Diabetes mellitus (DM) was present in 48.3% of the cohort, and hypertension (HTN) was reported in 48.3% of the patients. A history of ACS was present in 81.7% of the patients, and 35.0% had been revascularized previously, either via PCI or coronary artery bypass grafting (CABG). Chronic kidney disease (CKD) was diagnosed in 23.3% of the patients.

Clinical profile at baseline:

At baseline, assessment in accordance with NYHA functional class criteria revealed that no patients were classified as Class I or Class IV. A total of 51.7% of patients were categorized as Class II, while 48.3% were classified as Class III. Regarding the CCS angina classification, most patients were categorized as CCS Class 2 (55.0%) or CCS Class 3 (41.7%), with only 3.3% classified as CCS Class 1. The 6MWT distances ranged from 250 to 420 meters at baseline. Baseline heart rate (HR) ranged from 60 to 95 beats per minute (bpm). Systolic blood pressure (BP) at baseline ranged from 90 to 140 mmHg, with a mean of 112.83±14.15 mmHg. Diastolic BP ranged from 50 to 90 mmHg. (Table 1).

Table (1): Baseline clinical characteristics.

	Baseline (n=60)		
	No.	%	
NYHA Class:			_
Class I	0	0	
Class II	31	51.7	
Class III	29	48.3	
Class IV	0	0	
CCS Angina stage:			
Stage 1	2	3.3	
Stage 2	33	55.0	
Stage 3	25	41.7	
Stage 4	0	0	
6MWT:			
Range	250-420		
Mean \pm S.D.	351.50±35.645		
HR:			
Range	60-95		
Mean \pm S.D.	74.70±8.191		
Systolic BP:			
Range	90-140		
Mean \pm S.D.	112.83±14.153		
Diastolic BP:			
Range	50-90		
Mean \pm S.D.	69.50±9.284		

Myocardial viability assessment:

Among the 60 patients who underwent DSE, 75% demonstrated non-viable myocardial segments in the territory of the LAD artery, representing the most frequently affected region. A smaller proportion of patients exhibited non-viable segments in the RCA (6.7%) or in both the LAD and RCA territories (6.7%). Non-viable segments in the Left Circumflex (LCX) artery were identified in only one patient (1.7%). Overall, viable myocardial segments were present in 10% of the cohort.

Pertaining to the extent of myocardial non-viability, the range of number of the affected segments was from 0 to 9, with a mean of 5.17±2.60 segments. The median number of non-viable segments was 5.0, with an interquartile range (IQR) of 5.0 to 7.0, indicating a relatively broad distribution of myocardial scarring among the patients.

An improvement in EF by ≥ 5 percentage points was observed in 29 patients (48.3%) following the DSE study, whereas 31 patients (51.6%) showed either no improvement or an EF increase of less than 5 percentage points. (Table 2).

Table (2): DSE Findings.

	No.	%		
Non-viable segment territory:				
No	6	10.0		
LAD	45	75.0		
LCX	1	1.7		
RCA	4	6.7		
LAD & RCA	4	6.7		
No. of non-viable segments:				
Min. – Max.	0.0 - 9.0			
Mean \pm SD.	5.17	5.17 ± 2.60		
Median (IQR)	5.0 (5.	5.0 (5.0 – 7.0)		
<i>EF Increase</i> ≥5 <i>points:</i>				
Present	29	48.3		
Absent	31	51.6		

Follow-up evaluation of clinical data at 3 and 6 months:

All patients underwent revascularization via PCI, and clinical outcome parameters were evaluated three and six months after the procedure.

NYHA Functional class follow-up assessment at 3 and 6 months:

At three months post-revascularization, NYHA functional class showed marked improvement. Specifically, 16.7% of patients were classified as NYHA Class I, and the proportion in Class II in-

creased significantly to 71.7%. The percentage of patients in Class III declined markedly to 11.7%, with no patients categorized as Class IV.

By the end of six months, further clinical improvement was documented. A total of 27.6% of patients achieved NYHA Class I status, and 62.1% remained in NYHA Class II. The proportion of NYHA Class III patients further declined to 8.6%, while 1.7% of patients were newly categorized as NYHA Class IV. Statistical analysis demonstrated significant differences across the assessed time points, with *p*-values <0.001 at both three and six months compared to baseline, indicating a statistically significant improvement in NYHA functional classification over time.

Follow-up assessment of angina severity according to CCS classification at 3 and 6 months:

The findings demonstrated significant changes in CCS angina classification across the evaluated time points.

At three months post-revascularization, a substantial improvement in anginal symptoms was observed, with 80.0% of patients categorized as CCS Class I, while the proportions of patients in CCS Class II and III decreased to 18.3% and 1.7%, respectively.

This positive trend persisted at six months, with 82.8% of patients classified as CCS Class I, and only 15.5% and 1.7% classified as Class II and III, respectively. Notably, no patients were classified as Class IV at any time point.

Statistical analysis revealed *p*-values of <0.001 at both three and six months, indicating ameaningful improvement in CCS classification with statistical significance and a marked reduction in symptom severity over time.

6MWT Performance over time:

The 6MWT distances demonstrated progressive improvement over the follow-up period. At baseline, the mean distance covered was 351.50 ± 35.65 meters. This increased to 368.17 ± 40.27 meters at 3 months and further to 399.20 ± 58.52 meters at 6 months. The range of distances spanned from 230 to 450 meters at 3 months and from 230 to 530 meters at 6 months. The mean improvement from baseline was 18.97 ± 34.78 meters at 3 months and 48.03 ± 49.64 meters at 6 months. These gains were statistically significant across both time intervals, with p-values of 0.001 and <0.001, respectively, indicating a meaningful enhancement in functional capacity.

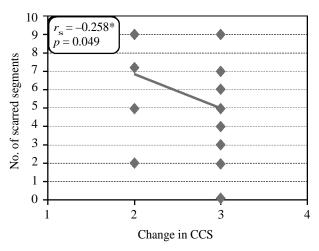
Predictive role of myocardial viability on clinical outcomes:

Correlation between non-viable myocardial segments and NYHA functional class at 3 and 6 months:

The analysis of the relationship between changes in NYHA functional class and the number of non-viable myocardial segments (qualitative data) yielded a p-value of 0.073, indicating that the number of non-viable myocardial segments did not differ significantlyacross groups based on NYHA class changes. However, the quantitative data trends indicate that patients who developed a betterment in the NYHA functional classgenerally had fewer non-viable segments on average: A Spearman correlation coefficient (ρ) of -0.280, with a p-value of 0.033, was noted, indicating amoderate negative correlation, with statistical significance, was observed between the change in NYHA class and the number of non-viable segments. This suggests that a greater number of non-viable segments is associated with less improvement in NYHA functional status.

Correlation between non-viable myocardial segments and CCS angina classification at 3 and 6 months:

A moderate negative correlation was noted between changes in CCS angina classification and the number of non-viable segments with Spearman correlation coefficient (ρ) of -0.258, with a *p*-value of 0.049. This suggests that as the number of non-viable segments increases, the extent of enhancement in CCS angina classification tends to decrease. In other words, patients with a greater extent of myocardial scarring generally exhibit less improvement in their clinical status, as reflected in the CCS angina classification. (Fig. 2).



1=Dis improved, 2=The same, 3=Improved

Fig. (2): Correlation between non-viable segments and CCS Classification at 3 and 6 Months (n=58).

Correlation between non-viable myocardial segments and 6MWT by 6 months:

A lack of statistically significant correlation was found between changes (improvement) in 6MWT performance and the number of non-viable segments. The Spearman correlation coefficient (ρ) was -0.233, and the p-value was 0.078, indicating statistically insignificant relationship. This result suggests that the improvement in physical functional status, as measured by the 6MWT, is not related to the extent of non-viable myocardium.

Correlation between non-viable myocardial segments and EF changes at 3 and 6 months:

A statistically significant correlation was identified between changes in EF and the number of non-viable segments over the follow-up duration. A greater number of non-viable segments was linked to a smaller improvement in EF.

There was a significant negative linear correlation between the number of non-viable segments and EF at both three months (r=-0.487, p<0.001) and six months (r=-0.493, p<0.001). These observations imply that a higher number of non-viable segments is significantly linked with a reduced EF at both the three-month and six-month evaluations. (Fig. 3).

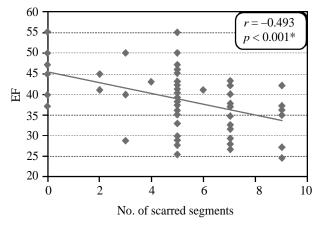


Fig. (3): Correlation between non-viable segment count and changes in Ejection Fraction (EF) at 6 Months (n=58).

Correlation between EF increase ≥ 5 points by DSE and EF change at 3 and 6 months:

A statistically significant correlation was found between an EF increase of >_5 points detected by DSE and changes in EF during the follow-up period. Patients who demonstrated an EF increase of >_5 points on DSE exhibited greater improvements in EF over time. There was a statistically significant and robust positive correlationbetween the EF increase by DSE and EF change at both three

months (r=0.80, p<0.001) and six months (r=0.85, p<0.001), supporting the prognostic value of myocardial viability in predicting EF recovery following revascularization.

Discussion

This prospective cohort study investigates the myocardial viability as an independent predictor of favorable clinical outcomes in patients diagnosed with ICM treated with PCI, with particular emphasis on changes in NYHA functional classification, CCS classification of angina severity, and functional exercise tolerance. The results of this study were evaluated in comparison with key clinical trials such as STICH [24], REVIVED-BCIS2 [25], ISCHEMIA [26], and others, to position the findings within the broader scope of current evidence and to better elucidate their clinical implications.

In terms of NYHA functional status, our cohort closely resembled the STICH trial population, with the most patients categorized as NYHA class II or class III at baseline, in contrast to the RE-VIVED-BCIS2 trial, where most participants were grouped under NYHA class I or class II.Notably, none of the patients in our study were designated as NYHA functional class IV. Follow-up evaluation revealed a notable enhancement in NYHA functional status, marked by a substantial decline in the number of patients in class III (48.3% at baseline) as most transitioned to class II or lower (p<0.001).

Unlike our study, neither the STICH nor the REVIVED trials reported changes in NYHA class as a specific outcome. While NYHA classification remains a subjective parameter, the improvement observed in our cohort may reflect not only the effect of revascularization but also the optimization of GDMT during follow-up. These findings underscore the potential role of PCI in enhancing symptomatic status in patients with ICM. However, further well-designed randomized controlled trials are warrantedto validate the relationship between PCI and improvements in patient-reported dyspnea.

Bax et al. [27] reported comparable improvements in NYHA functional classification after coronary revascularization procedures in patients presenting with ischemic LV dysfunction and evidence of myocardial viabilityassessed by DSE. The study included 68 patients and evaluated outcomes at three months post-revascularization. Patients exhibiting four or moreviable myocardial segments on DSE (Group A, n=22) demonstrated a statistically significant increase in LVEF, which increased from 27%±6% to 33%±7% (p<0.01), along

with notable improvements in NYHA functional classification (from 3.2 ± 0.7 to 1.6 ± 0.5 ; p<0.01) and CCS angina class (from 2.9 ± 0.3 to 1.2 ± 0.4 ; p<0.01). Conversely, patients having fewer than four viable myocardial segments (Group B, n=40) showed no significant changes in LVEF or NYHA functional class. Nevertheless, there was a marked improvement in CCS angina class, decreasing from 3.0 ± 0.8 to 1.3 ± 0.5 (p<0.01). Furthermore, Group B experienced a significantly higher long-term event rate in comparison to Group A (47% vs. 17%, p<0.05), highlighting the predictive significance of myocardial viability in guiding revascularization decisions.

In our cohort, most patients presented at baseline with CCS angina class II (55%) or class III (48%), with no patients classified as CCS class IV. In comparison, the REVIVED and STICH trials reported lower baseline angina burden, with a significant proportion of patients being asymptomatic (66% in REVIVED and 36% in STICH) or classified as CCS class I or II (32% and 56%, respectively). In our study, angina severity improved significantly, with the majority of patients transitioning to CCS class I status by six months post-intervention (p<0.001). Notably, both REVIVED and STICH trials did not explicitly evaluate or report angina class improvement as a clinical endpoint following revascularization.

In our study, the 6MWT distance demonstrated a significant improvement over time, increasing from a baseline mean of 351.5±35.65 meters to notably higher values at both 3 and 6 months. This enhancement was particularly evident in patients with a lower number of non-viable myocardial segments.

Myocardial viability assessment:

In our study, myocardial viability was assessed using DSE. Non-viable myocardial segments were most commonly localized to the LAD artery territory (75%), followed by combined LAD and RCA involvement (6.7%). An inverse correlation was found between the number of non-viable myocardial segments and the degree of recovered LVEF during follow-up (r=-0.493, p<0.001), implying that a higher burden of non-viable myocardium adversely impacts post-revascularization LV functional improvement.

These findings are consistent with previously reported findings by Bax et al., [27] who established a significant correlation between the number of viable myocardial segments identified by DSE and the degree of enhancement in LVEF following revas-

cularization ($y = 1.37 \times -2.04$; p < 0.001, r = 0.70, n = 62). Their study found no significant association between the number of non-viable segments and LVEF changes. A threshold of >-4 myocardial segments exhibiting dysfunction but retaining viability was associated with optimal accuracy of diagnostic methods for forecasting LVEF improvement, with a sensitivity of 86%, specificity of 90%, negative predictive value of 93%, and positive predictive value of 82%.

Viability assessment has long been regarded as a pivotal element in the clinical evaluation of ICM patients, serving as a predictive marker for functional improvement following revascularization [28]. In our analysis, a robust negative correlation was shown between the number of non-viable myocardial segments and LVEFincrease, only moderate negative correlations were noted for changes in NYHA class (r=-0.280, p=0.033) and CCS angina class (r=-0.258, p=0.049),on the other hand, no meaningful correlation was found for changes in 6MWT distance (r=-0.233, p=0.078). Conversely, a notable positive association was demonstrated between a DSE-predicted LVEF increase of >-5% and the actual change in LVEF during follow-up (r=0.85, p<0.001).

The present results are supported by the meta-analysis conducted by Allman et al., [13] which included 24 limited-scale, single-institution studies totaling 573 patients having CAD and reduced LVEF (mean 33%, range 27%–46%). The analysis confirmed that the existence of viable myocardial tissue was a strong prognostic indicator of improved outcomes following coronary revascularization. However, the conclusions were limited by the retrospective design of the included studies, heterogeneous viability assessment methods, lack of standardized treatment protocols, and absence of randomization, all of which introduced potential for systematic bias.

In contrast to our results, the findings of the STICH trial yielded different outcomes.

The STICH trial was the first prospective study to study the association between viability of myocardial segments and clinical outcomes in ICM patients. While the main results of the trial affirmed the benefit of surgical revascularization, the pre-specified viability sub-study did not provide evidence for statistically significant interplay between the degree of myocardial viability and the administered treatment. Despite the association of myocardial viability with a modest increase in LVEF ($\pm 2.29 \pm 0.56\%$) Throughout the follow-up period, this

effect was independent of the assigned treatment strategy and had no impact on survival outcomes. These findings were reinforced by subsequent retrospective studies that similarly showed no clear survival benefit from surgical revascularization based on viability status or postoperative changes in LVEF [29,30]. However, the STICH sub-study faced limitations, including its non-randomized viability assessment, use of multiple non-uniform SPECT protocols, and lenient thresholds for defining viability, [31] which may have limited its ability to detect clinically meaningful associations.

Earlier retrospective studies have indicated that significant hibernating myocardium, defined as greater than 15%–20% of left ventricular mass on PET imaging, may serve as a marker for guiding patient selection for coronary revascularization based on predicted benefit. The present findings were corroborated by the small Ottawa sub-study of the PARR-2 trial, which comprised 111 patients. This sub-study revealed a significantly reduced incidence of cardiovascular events among patients who underwent PET-guided myocardial revascularization relative to those managed with standard therapy (p=0.005). However, since mortality endpoints, including overall and cardiac-specific mortality, were not within the study's objectives, its broader clinical applicability remains limited [32].

A meta-analysis performed by Liga et al. (2023), [33] which contained all available evidence from major randomized controlled trials (RCTs) in ICM, found no significant additional efficacy of a viability-based therapeutic approach comprising coronary revascularization in patients demonstrating substantial viability alongside optimal medical therapy (OMT) was assessed in comparison to OMT alone with respect to survival. Data regarding patient management guided by viability imaging were available for 1,623 subjects. The predominant portion of these patientswere recruited in the REVIVED-BCIS2 (N = 700; 43%) and STICH (N= 601; 37%) trials, with smaller numbers from the PARR-2 (11%) and HEART (9%) trials. Of these, 858 patients (53%) had management decisions guided by viability imaging results, while 765 patients' management was independent of imaging results. No significant heterogeneity was observed between studies.

Conclusion:

This study underscores the predictive value of myocardial viability in improving clinical outcomes for patients with ICM, particularly in those with fewer non-viable myocardial segments.

Recommendation:

Advanced myocardial viability assessment such as DSE or CMR should be systematically integrated into clinical decision-making to determine which ICM patients are most suitable candidates for PCI based on expected therapeutic benefit, particularly those with a lower burden of non-viable myocardial segments. Functional recovery should be evaluated through structured follow-up using validated tools, including the NYHA and CCS angina classifications, along with the 6MWT, to objectively assess improvements in symptoms and exercise capacity. Additionally, the establishment of comprehensive patient education initiatives, combined with routine follow-up at dedicated heart failure clinics, is essential to ensure adherence to GDMT, thereby optimizing sustained clinical outcomes and quality of life indicators as reported by patients.

Study Limitation:

In this study, myocardial viability was assessed using DSE, which, while widely accessible and practical, may have reduced sensitivity in patients exhibiting marked baseline regional wall motion abnormalities. Moreover, DSE accuracy is subject to operator expertise, introducing potential variability in interpretation. Additional limitations comprise the limited sample size and brief follow-up period and this could restrict the generalizability and long-term applicability of the findings.

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Disclosure of Interests:

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Authors declare no acknowledgments.

References

- 1- PASTENA P., FRYE J.T., HO C., GOLDSCHMIDT M.E. and KALOGEROPOULOS A.P.: Ischemic cardiomyopathy: Epidemiology, pathophysiology, outcomes, and therapeutic options. Heart Fail Rev., 29 (1): 287-99, 2024.
- 2- FISHBEIN G.A., FISHBEIN M.C., WANG J. and BUJA L.M.: Myocardial ischemia and its complications. In: Buja L.M., Butany J. (eds). Cardiovascular pathology. New York: Elsevier, 407-45, 2022.
- 3- DEL BUONO M.G., MORONI F., MONTONE R.A., AZ-ZALINI L., SANNA T. and ABBATE A.: Ischemic Cardiomyopathy and Heart Failure After Acute Myocardial Infarction. Curr. Cardiol. Rep., 24 (10): 1505-15, 2022.

4- HEUSCH G.: Myocardial stunning and hibernation revisited. Nat. Rev. Cardiol., 18 (7): 522-36, 2021.

- 5- ALGOET M., JANSSENS S., HIMMELREICH U., GSELL W., PUSOVNIK M., VAN DEN EYNDE J., et al.: Myocardial ischemia-reperfusion injury and the influence of inflammation. Trends Cardiovasc. Med., 33 (6): 357-66, 2023.
- 6- RAHIMTOOLA S.H.: The hibernating myocardium. Am. Heart J., 117 (1): 211-21, 1989.
- 7- MANINTVELD O.: Protection against myocardial ischemia and reperfusion:Preconditioning, postconditioning and hibernation. PhD Thesis. Rotterdam, Netherlands: Erasmus University Rotterdam, 2008.
- 8- BABES E.E., TIT D.M., BUNGAU A.F., BUSTEA C., RUS M., BUNGAU S.G., et al.: Myocardial Viability Testing in the Management of Ischemic Heart Failure. Life (Basel), 12 (11): 1760, 2022.
- 9- BRADFORD J.: Prospects for human hibernation. In: Johnson L., Roy K. (eds). Interstellar Travel. New York: Elsevier, 191-208, 2024.
- 10- ARJOMANDI RAD A., TSERIOTI E., MAGOULIOTIS D.E., VARDANYAN R., SAMIOTIS I.V., SKOULARI-GIS J., et al.: Assessment of Myocardial Viability in Ischemic Cardiomyopathy with Reduced Left Ventricular Function Undergoing Coronary Artery Bypass Grafting. Clin. Cardiol., 47 (7): e24307, 2024.
- 11- RYAN M., MORGAN H., CHIRIBIRI A., NAGEL E., CLELAND J. and PERERA D.: Myocardial viability testing: All STICHed up, or about to be REVIVED? Eur. Heart J., 43 (2): 118-26, 2022.
- 12- ZHAO Y., XIONG W., LI C., ZHAO R., LU H., SONG S., et al.: Hypoxia-induced signaling in the cardiovascular system: Pathogenesis and therapeutic targets. Signal Transduct Target Ther., 8 (1): 431, 2023.
- 13- ALLMAN K.C., SHAW L.J., HACHAMOVITCH R. and UDELSON J.E.: Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: A meta-analysis. J. Am. Coll. Cardiol., 39 (7): 1151-8, 2002.
- 14- LI D.L. and KRONENBERG M.W.: Myocardial Perfusion and Viability Imaging in Coronary Artery Disease: Clinical Value in Diagnosis, Prognosis, and Therapeutic Guidance. Am. J. Med., 134 (8): 968-75, 2021.
- 15- WA M.E.L.K., ASSAR S.Z., KIRTANE A.J. and PERERA D.: Revascularisation for Ischaemic Cardiomyopathy. Interv Cardiol., 18: e24, 2023.
- 16- ANNABI M.S., TOUBOUL E., DAHOU A., BURWASH I.G., BERGLER-KLEIN J., ENRIQUEZ-SARANO M., et al.: Dobutamine Stress Echocardiography for Management of Low-Flow, Low-Gradient Aortic Stenosis. J. Am. Coll. Cardiol., 71 (5): 475-85, 2018.

- 17- GUPTA A., HARRINGTON M., ALBERT C.M., BA-JAJ N.S., HAINER J., MORGAN V., et al.: Myocardial Scar But Not Ischemia Is Associated With Defibrillator Shocks and Sudden Cardiac Death in Stable Patients With Reduced Left Ventricular Ejection Fraction. JACC Clin. Electrophysiol., 4 (9): 1200-10, 2018.
- 18- YANCY C.W., JESSUP M. and BUTLER J.: 2022 Update to the 2017 ACC/AHA/HFSA Heart Failure Guidelines: Focused Update on New Pharmacologic Therapies. J. Am. Coll. Cardiol., 79 (7): 849-70, 2022.
- 19- DAI H., WANG C. and LI L.: Wall motion score index as an indicator of left ventricular function in patients with ischemic heart disease. J. Echocardiogr., 19 (1): 1-6, 2021.
- 20- PONIKOWSKI P., VOORS A.A., ANKER S.D., BUENO H., CLELAND J.G.F., COATS A.J.S., et al.: 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur. Heart J., 37 (27): 2129-200, 2016.
- 21- ISHIBASHI Y., OHMORI T. and NAKAGAWA K.: A simple classification of angina based on the Canadian Cardiovascular Society classification. J. Am. Coll. Cardiol., 77 (14): 1756-67, 2021.
- 22- COTE A.T., GOSSELINK R. and LANGER D.: The six-minute walk test: A useful tool for assessing functional status in chronic respiratory disease. Respir Med., 178: 106289, 2021.
- 23- CHOI J.O., KIM Y.J. and KIM Y.H.: Myocardial viability assessment using dobutamine stress echocardiography in patients with coronary artery disease and left ventricular dysfunction. J. Am. Soc. Echocardiogr., 34 (7): 722-9, 2021.
- 24- VELAZQUEZ E.J., LEE K.L., DEJA M.A., JAIN A., SOPKO G., MARCHENKO A., et al.: Coronary-artery bypass surgery in patients with left ventricular dysfunction. N. Engl. J. Med., 364 (17): 1607-16, 2011.
- 25- PERERA D., CLAYTON T., O'KANE P.D., GREEN-WOOD J.P., WEERACKODY R., RYAN M., et al.: Per-

- cutaneous Revascularization for Ischemic Left Ventricular Dysfunction. N. Engl. J. Med., 387 (15): 1351-60, 2022.
- 26- MARON D.J., HOCHMAN J.S., REYNOLDS H.R., BANGALORE S., O'BRIEN S.M., BODEN W.E., et al.: Initial Invasive or Conservative Strategy for Stable Coronary Disease. N. Engl. J. Med., 382 (15): 1395-407, 2020.
- 27- BAX J.J., POLDERMANS D., ELHENDY A., CORNEL J.H., BOERSMA E., RAMBALDI R., et al.: Improvement of left ventricular ejection fraction, heart failure symptoms and prognosis after revascularization in patients with chronic coronary artery disease and viable myocardium detected by dobutamine stress echocardiography. J. Am. Coll. Cardiol., 34 (1): 163-9, 1999.
- 28- PARIKH K., CHOY-SHAN A., GHESANI M. and DON-NINO R.: Multimodality Imaging of Myocardial Viability. Curr. Cardiol. Rep., 23 (1): 5, 2021.
- 29- PANZA J.A., ELLIS A.M., AL-KHALIDI H.R., HOLLY T.A., BERMAN D.S., OH J.K., et al.: Myocardial viability and long-term outcomes in ischemic cardiomyopathy. N. Engl. J. Med., 381 (8): 739-48, 2019.
- 30- BONOW R.O., MAURER G., LEE K.L., HOLLY T.A., BINKLEY P.F., DESVIGNE-NICKENS P., et al.: Myocardial viability and survival in ischemic left ventricular dysfunction. N. Engl. J. Med., 364 (17): 1617-25, 2011.
- 31- ANAVEKAR N.S., CHAREONTHAITAWEE P., NARU-LA J. and GERSH B.J. Revascularization in Patients With Severe Left Ventricular Dysfunction: Is the Assessment of Viability Still Viable? J. Am. Coll. Cardiol., 67 (24): 2874-87, 2016.
- 32- ABRAHAM A., NICHOL G., WILLIAMS K.A., GUO A., DEKEMP R.A., GARRARD L., et al.: 18F-FDG PET imaging of myocardial viability in an experienced center with access to 18F-FDG and integration with clinical management teams: The Ottawa-FIVE substudy of the PARR 2 trial. J. Nucl. Med., 51 (4): 567-74, 2010.
- 33- LIGA R., COLLI A., TAGGART D.P., BODEN W.E. and DE CATERINA R.: Myocardial Revascularization in Patients With Ischemic Cardiomyopathy: For Whom and How. J. Am. Heart Assoc., 12 (6): e026943, 2023.

القيمة التنبؤية لقابلية عضلة القلب للبقاء على قيد الحياة باستخدام تخطيط صدى القلب الإجهادى باستخدام الدوبامين لدى المرضى المصابين باعتلال عضلة القلب الإقفارى

يكمن التحقق الأساسى من صحة اختبار قابلية عضلة القلب للحياة فى قدرته على توقع تعافيها الوظيفى بعد إعادة التروية. فى حين أن التحسن الانقباضى فى عضلة القلب المصابة بالذهول قد يحدث فى غضون بضع ساعات وحتى عدة أيام بعد إعادة التروية، إلا أن التعافى الوظيفى فى عضلة القلب المصابة بسبات مزمن قد يتأخر لبضعة أشهر.

تهدف هذه الدراسة إلى تقييم الأهمية التنبؤية لتحديد قابلية عضلة القلب للبقاء على قيد الحياة باستخدام تخطيط صدى القلب الإجهادي بالدوبامين فيما يتعلق بالنتائج السريرية لدى المرضى الذين يعانون من اعتلال عضلة القلب الإقفاري.

شملت هذه الدراسة الاستشرافية ٦٠ مريضًا تم تشخيصهم باعتلال عضلة القلب الإقفاري واختلال وظيفة البطين الأيسر الانقباضية، كما يتضح من كسر القذف ≤٤٠٪، وخضع كل منهم لتقييم قابلية عضلة القلب للحياة باستخدام تخطيط صدى القلب الإجهادى بالدوبامين قبل إعادة التروية.

لوحظ تحسن ملحوظ في التصنيف الوظيفي لجمعية نيويورك للقلب (NYHA)، كما هو محدد إحصائيًا، لدى معظم المرضى الذين انتقلوا من الفئة الثالثة عند بداية الدراسة إلى الفئة الثانية أو أقل أثناء المتابعة. وبالمثل، أظهر تصنيف الذبحة الصدرية للجمعية الكندية لأمراض القلب والأوعية الدموية (CCS) تحسنًا ملحوظًا، حيث وصل معظم المرضى إلى الفئة الأولى بعد سنة أشهر. كما أظهرت مسافة اختبار المشى لمدة ست دقائق (6MWT) تحسنًا ملحوظًا بمرور الوقت، حيث ارتفعت من متوسط أساسي بلغ ٥,١٥٣ ل متراً إلى قيم أعلى في تقييمات المتابعة بعد ٣ و٦ أشهر. وُجدت أجزاء عضلة القلب غير القابلة للحياة بشكل رئيسى في منطقة الشريان الأمامى النازل الأيسر (LAD) في ٧٥٪ من الحالات، تليها إصابة مشتركة للشريان الأمامى النازل الأيسر والشريان التاجي الأيمن (RCA) في ٧٠٪. «وتم ملاحظة وجود علاقة عكسية قوية بين مدى عضلة القلب غير القابلة للحياة وحجم التحسن في كسر القذف البطيني الأيسر (LVEF)، مع دلالة إحصائية (ح ٢٠٠٠).

وتؤكد النتائج على قدرة التنبؤ بنتائج قابلية عضلة القلب للبقاء - وخاصة كما تم تقييمها بواسطة اختبار تخطيط صدى القلب الإجهادي بالدوبامين - في التنبؤ بالتحسينات في النتائج السريرية بين المرضى الذين يعانون من اعتلال عضلة القلب الإقفاري.