

Role of Nitroglycerin Echocardiography in Detection of Viable Myocardium in Post Myocardial Infarction Patients in Comparison to the Standard Low Dose Dobutamine Stress Echocardiography.

Heidi A. Mohamed⁽¹⁾, Ahmed I. Nassar⁽¹⁾, Mazen T. Ibrahim⁽¹⁾, Sameh S.Raafat⁽¹⁾, Adham A. Abdeltawab⁽¹⁾.

Department of Cardiology

(1) Faculty of Medicine – Ain Shams University, Abbassia, Cairo, Egypt .

Abstract

Objectives: Dobutamine as an agent used in stress echocardiography is known to cause some side effects that can be severe and annoying to the patient during the study. Alternatively, Nitroglycerin (NTG) can give the same results without these side effects and relatively low cost. Therefore, we evaluated the role of using NTG echo in assessing viable myocardium in post Myocardial infarction patients in comparison to low dose dobutamine echocardiography (LDDE).

Methods: This prospective interventional study was performed on 45 adult patients who developed previous myocardial infarction and LV systolic dysfunction ($EF \leq 40\%$).

All the patients had echo findings showing akinetic segments related to the infarcted territory. 24 patients underwent viability test using LDDE while 21 patients underwent NTG echo.

Coronary angiography (CA) was performed only in patients with positive viability with LDDE or NTG echo intervening in the artery consistent with the results of the non invasive test. Patients who underwent CA based on the results of LDDE and NTG echo were followed up 3 months later by a “2D” echocardiographic examination to assess improvement in wall motion in segments showing positive viability.

Results: All the patients underwent a viability test using either LDDE or NTG echo and only patients with viable akinetic segments underwent coronary revascularization. 2D Echo was followed up 3 months after revascularization in those patients showing viable akinetic territories, concluding that ejection fraction was significantly improved in the follow up echo of the improved cases in the NTG group (55.57 ± 5.94), compared to LDDE group (45.00 ± 7.91) and this was statistically significant.

The wall motion score index (WMSI) in the NTG group decreased from (2.33 ± 0.31) to (0.97 ± 0.22), while for the LDDE group, the mean WMSI decreased to (1.91 ± 0.03) instead of (2.76 ± 0.22) and this was statistically highly significant. From this result, we found that WMSI showed a significant improvement in the NTG group compared to the LDDE group confirming myocardial viability in the group that underwent viability test using NTG.

Conclusion: Nitroglycerin echocardiography is a safe tool and may provide an interesting diagnostic alternative to dobutamine echo to detect myocardial viability in post-MI patients.

Keywords: trans-thoracic echocardiography, low dose dobutamine echocardiography, Nitroglycerin echocardiography, wall motion score index.

List of abbreviations:

LDDE:Low dose dobutamine echocardiography

NTG:Nitroglycerin

WMSI:Wall motion score index

EF:Ejection fraction.

MI:Myocardial infarction

CAD:Coronary artery disease

LVSD:Left ventricular systolic dysfunction

DCM:Dilated cardiomyopathy

HCM:Hypertrophic cardiomyopathy

HTN:Hypertension

DM:Diabetes mellitus.

IDDM:Insulin dependent diabetes mellitus

NIDDM: Non insulin dependent diabetes mellitus

NSTEMI:Non ST elevation myocardial infarction.

AF:Atrial fibrillation

RBBB:Right bundle branch block.

RWMAs:Resting wall motion abnormalities.

CA:Coronary angiography

MVD:Multi vessel disease

CABG:Coronary artery bybass graft surgery.

LM:Left main coronary artery

LAD:Left anterior descending artery

LCX:Left circumflex artery

OM1:Obtuse marginal branch.

RCA:Right coronary artery

CVR:Coronary vascular resistance

1.Introduction:

Detection of viable myocardium is an important issue and is sometimes crucial in the diagnostic work of ischemic patients. It has important clinical use in patients with coronary artery disease (CAD) and left ventricular systolic dysfunction (LVSD).

The goal of identifying a viable heart muscle is to identify and offer revascularization procedures only to patients who are best likely to achieve a better quality of life and prolonged survival. Such benefits can be attainable in patients with LVSD with viable myocardium. ⁽¹⁾

Accordingly, assessment of myocardial viability should be part of a diagnostic assessment of all patients who developed CAD and LVSD to determine future treatment plan including the need for revascularization and the prediction of long-term outcomes. ⁽²⁾

The anti-anginal effects of organic nitrates improve coronary blood flow through vasodilation of capacitve veins and leading arteries, mitigation in ventricular volumes, preload and afterload. ⁽³⁾

Nitroglycerin improves myocardial perfusion by reducing wall tension and myocardial oxygen demand. ⁽⁴⁾

These compounds can provide additional blood flow in the remaining viable zones of healed myocardial infarction through vasodilation of the collateral vessels. ⁽⁴⁾

Collaterals can maintain viability or provide minimal nutrition to the myocardial regions located distal to occluded coronary arteries. ⁽⁵⁾

Previous studies have shown that coronary collateral vessels are generally not visible until coronary occlusion exceeds 90%, however, recent publications have reported that people with angiographically normal coronary arteries have functional collateral blood vessels to a greater degree such that one-fifth to one-quarter of them show no signs of myocardial ischemia during transient vascular occlusions. ⁽⁶⁾

2.Methods:

This prospective interventional study was performed on 45 adult patients.

They were classified into two groups:

- ❖ Low dose dobutamine echo group (LDDE): 24 patients accounted for 53.3%.
- ❖ Nitroglycerin echo group (NTG): 21 patients representing 46.7%.

All the patients had echocardiographic findings showing akinetic segments related to the infarcted territory.

2.1 Study period: two years

2.2 Study Population:

The current study included 45 adult patients who had a history of myocardial infarction with

LV systolic dysfunction (EF: $\leq 40\%$) and echocardiographic findings revealing akinetic segments related to the affected territory.

On the other hand, the exclusion criteria were as follows:

- a- Patients with MI lasting less than 4 weeks.
- b- Patients with functional class IV heart failure
- c- Left bundle branch block.
- d- Patients with other significant heart disease including severe valvular heart disease.
- e- Myocardial disease including DCM, restrictive cardiomyopathy, HCM and apical ballooning syndrome (Takotsubo cardiomyopathy).
- f- basal systolic blood pressure < 90 mmHg.
- g- Improper acoustic window

2.3 Ethical Considerations:

This work was done in compliance with ethical standards. Ethical approval and informed consent: Written informed consent was obtained from all study participants, implemented in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Ain Shams, Faculty of Medicine, Egypt (Federal Wide Assurance No:000017585).

2.4 Study procedures:

All the patients were subjected to the following:

1-Complete medical history including age, gender, risk factors such as smoking, hypertension, diabetes mellitus, dyslipidemia, positive family history of coronary heart disease, previous MI recorded by ECG changes in the form of abnormal Q waves⁽⁷⁾ and with an increase and / or decrease in cardiac troponin with at least one value at the 99th percentile of the upper reference limit⁽⁸⁾ and a history of chronic medical treatment such as acetylsalicylic acid, beta-blockers, statins, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, Ca-channel blockers or oral nitrates.

2-Clinical examination which includes a general examination with particular emphasis on blood pressure, pulse, peripheral pulsations and the presence or absence of elevated JVP.

A thorough local cardiac assessment was also performed with emphasis to rule out the murmurs for severe valvular affection.

3-laboratory tests including: CBC, kidney and liver profile, blood glucose and cardiac enzymes.

4-Resting 12-lead ECG focusing on:

- a-Localization of myocardial infarction.*
- b- Arrhythmias and conduction abnormalities.*

5- Stress echocardiography:

Low-dose dobutamine echo was performed in 24 patients, while nitroglycerin echo was performed in 21 patients to detect viable myocardium according to the following protocol.

A basic “2D” echocardiographic examination was first performed in all patients in a parasternal long-axis, mid ventricular parasternal short-axis, apical four-chamber and apical two-chamber views to detect akinetic segments.

Basal 2D echocardiography was used to assess segmental wall motion as assessed by the wall motion scoring index based on the 17-segments approach of the American Society of Echocardiography “ASE”^{(9), (10)}.

Low dose dobutamine echocardiography:

- Dobutamine echo was performed in 24 patients.
- A graded dobutamine infusion was typically given at an initial dose of 5 µg / kg / min with increments of 10 to 20 µg / kg / min every 3-5 minutes according to the protocol of the American Society of Echocardiography (ASE).guidelines in 2007.⁽¹¹⁾
- Echocardiographic images were recorded with each incremental increase in parasternal long-axis, mid ventricular parasternal short-axis, apical four-chamber, and apical two chamber views to evaluate the improvement in segmental wall motion based on the wall motion score index of 17 segments similarly to basal images.

Nitroglycerin Echocardiography:

- 21 patients underwent nitroglycerin echocardiography.
- Nitroglycerin echocardiography was performed at the peak of NTG infusion.
- The nitroglycerin infusion was started at a rate of 0.4µg / kg/ minute with 0.4µg/kg increment every five minutes up to 2 µg/ kg/ minute.
- Continuous ECG and blood pressure monitoring were recorded every five minutes.
- Echocardiographic images were obtained at the peak of NTG infusion in the same way as basal images.
- Regional wall motion assessment was done based on 17 segments model as mentioned before.

A conventional scoring system was applied as follows:

- 1 = normal (> 25% systolic thickening) 2 = hypokinesia (<25% systolic thickening) 3 = akinesia (lack of endocardial excursion and systolic thickening) 4 = dyskinesia (outward movement in the systole).
- The “WMSP” known as regional wall motion score index is calculated by dividing the sum of the

scores of all 17 segments by the number of segments evaluated⁽¹²⁾.

- Myocardial viability is determined by a decrease in the wall motion score in each segment by > 1 point, for example from 3 to 2 (or 1) or from 2 to 1, while improvement of wall motion score from grade 4 to 3 does not indicate viability.⁽¹³⁾
- Myocardial viability is defined as $\geq 20\%$ decrease in LV WMSI as previously suggested.⁽¹⁴⁾

6-Interventional coronary angiography:

- Coronary angiography was performed only in patients with positive viability with LDDE or NTG echo intervening in the artery consistent with the results of the non invasive test.

7- Follow up:

- Patients who underwent coronary angiography based on the results of non invasive testing were followed up 3 months later by a“2D” echocardiographic examination to assess improvement in wall motion in segments showing positive viability.

2.5 Statistical analysis:

All Data were calculated and statistically analyzed using appropriate methods. Data were collected, revised, coded and entered to the Statistical Package for Social Science (SPSS) version 23.

The confidence interval was set to 95% and the margin of error accepted was set to 5%.So the p-value was considered significant as the following:

P > 0.05: Non significant

P < 0.05: Significant P < 0.01: Highly significant.

3.Results:

Baseline characteristics and clinical data:

There was no statistically significant difference between LDDE group and NTG group regarding age, sex.

On studying the distribution of the risk factors between the study groups,it was found that there was no statistically significant difference between the two groups regarding all risk factors except for positive family history of CAD which was higher in LDDE group.

Also,there was no significant difference between the two groups regarding all laboratory investigations.

ECG characteristics among the two groups:

There was no statistically significant difference between the two groups regarding ECG findings with (P value > 0.05) however,the only arrhythmia detected in both groups was AF and the only conduction abnormality was RBBB.

Echocardiographic findings:

- ❖ There was no significant difference between the two groups regarding Echo findings as

shown in table (1).

- ❖ Among LDDE group, 11 patients out of 24 had viable akinetic segments compared to 11 patients out of 21 in NTG group. The difference was non significant between the two groups as shown in table (2).
- ❖ Finally it was found that WMSI was (2.60 ± 0.33) in LDDE group versus (2.62 ± 0.33) in NTG group with no significant difference between both groups.
- ❖ Regarding coronary angiography, there was no significant difference between the two groups regarding the number of stented and affected vessels. (P value > 0.05).
- ❖ Regarding follow up Echo after 3 months, table (4) shows that in NTG group, the number of patients who showed actual improvement in the territories supposed to be viable by NTG were numerically higher than that of LDDE, (7 versus 5) but this did not reach statistical significance due to small sample size. (P value > 0.05).
- ❖ Also, false detection of viable myocardium was less in NTG group being 4 versus 6 in LDDE group however, this did not reach statistical significance.
- ❖ As shown in table (5): Regarding the improved cases of LDDE group (5 patients), the mean resting EF and WMSI were (31.60 ± 7.92) and (2.76 ± 0.22) respectively while in follow up echo, the mean EF was (45.00 ± 7.91) and the mean WMSI was (1.91 ± 0.03) and this was statistically highly significant. (P value < 0.01).
- ❖ As regards the improved cases of NTG group (7 patients), the mean resting EF and WMSI were (35.43 ± 5.13) and (2.33 ± 0.31) , while in follow up echo, the mean EF and WMSI were (55.57 ± 5.94) and (0.97 ± 0.22) and this was statistically highly significant as demonstrated in table (6).
- ❖ Regarding follow up Echo as shown in table (7), it was found that the EF in the follow up echo of the improved cases of NTG group (7) was significantly improved than that of the LDDE group (5) and this was statistically significant.
- ❖ Also, it was found that the mean WMSI decreased to (0.97 ± 0.22) instead of (2.33 ± 0.31) in NTG group in comparison to LDDE group in which the mean WMSI decreased to (1.91 ± 0.03) instead of (2.76 ± 0.22) and this was statistically highly significant. (P value < 0.01). We concluded from this result that also WMSI showed significant improvement in the NTG group compared to LDDE group.
- ❖ Finally table (8) demonstrates Comparison between LDDE group and NTG group regarding the difference between resting and follow-up echocardiography in total number of patients with viable myocardium, improved cases and non improved cases showing that

in improved cases, the difference in the mean value of EF in LDDE group was (13.40 ± 2.30) versus (20.14 ± 2.12) in NTG group and this was statistically highly significant indicating better improvement in NTG group. Also, the difference in mean WMSI was significantly lower in NTG group (-1.36 ± 0.46) indicating better results and justifying viability in that group.

- ❖ Finally while comparing non improved cases of LDDE group with those of NTG group, it was demonstrated that the follow up EF and WMSI were better as a numerical value in NTG group but without statistical significance because of small sampling.

4. Discussion:

Identification of viable myocardium is an important clinical issue in patients with

“CAD” and “LVSD”

The main aim of the study was to evaluate the role of using the new diagnostic tool Nitroglycerin echocardiography in the detection of viable myocardium in patients following myocardial infarction compared to low-dose dobutamine echocardiography.

In our study, all patients underwent basic echocardiography “45 patients”. 24 patients underwent LDDE compared to 21 patients who underwent NTG echocardiography for accurate detection of viable myocardium.

In this study, there was no significant difference between the two groups in relation to demographic data, risk factors and ECG abnormalities and this was in accordance with many studies. ^{(15), (16), (17)}.

In our study, there was no significant difference between the two groups concerning the Echo findings including resting EF, number of akinetic segments and WMSI. This agreed with a study by *Afridi et al.* concluding no significant difference in resting WMSI in the group that underwent a viability test with dobutamine alone compared to the group in which dobutamine was used in combination with nitroglycerin however, no comparative data were available for resting EF. ⁽¹⁸⁾

A study done by *Afridi et al.* showed that the combination of low-dose dobutamine and nitroglycerin significantly increased wall thickness to a greater extent than either drug alone in

hibernating myocardium subtending severe coronary stenosis or viable (stunned/hibernating) myocardium around the infarcted (peri-infarcted) region supplied by a significant residual stenosis.⁽¹⁸⁾

In the previously mentioned study, Dobutamine and dobutamine in combination with nitroglycerin echocardiography were done to detect regional wall motion prior to coronary revascularization in 29 patients with MI. Regional wall motion was assessed again approximately 3 months following revascularization.⁽¹⁸⁾

In the present study, we clinically tested NTG solely as a drug for the detection of viable myocardium in ischemic patients post-myocardial infarction by echocardiography compared to LDDE.

In our study with regard to coronary revascularization, we found that there was no significant difference between the two groups considering the number of stented vessels and the vessels involved, so in conclusion, vessel affection did not influence the outcome of viable or non-viable condition and this was consistent with *Helfant et al. and Chesebro et al.*^{(15),(19)}

There was no statistically significant difference in resting echocardiography between patients with viable akinetic segments among both groups however, 3 months follow-up Echo following revascularization showed that the EF of improved cases in the NTG group was significantly better than in LDDE group.

It was also found that the mean WMSI in the NTG group was significantly lower compared to LDDE group confirming the viable areas allegedly present in the group that underwent a viability test using NTG.

Our results were concordant with *Afridi et al.* who found that in combining low-dose dobutamine with nitroglycerin echocardiography, WMSI was significantly reduced compared to low-dose dobutamine alone and documented no significant difference in WMSI on performing the standard low-dose dobutamine uptitration revealing no improvement with higher doses of dobutamine alone.

Depending on these results, it was found that WMSI is a better indicator of improvement

than the ejection fraction confirming a viable myocardium.

In addition, no ischemia was found in the combination of dobutamine with nitroglycerin echocardiography as induced by dobutamine only.⁽¹⁸⁾

Another study by *Helfant et al.* showed that 15 of the 18 asynergic segments that improved after sublingual nitroglycerin had similar improvements after revascularization, while the 3 segments that were persistently dysfunctional after nitroglycerin remained unchanged after revascularization confirming the accuracy of nitroglycerin to figure out myocardial viability.⁽¹⁵⁾

This study was supportive to the use of nitroglycerin in detection of viable myocardium which is in agreement with the concept of our thesis demonstrating that 7 patients out of 11 who had viable akinetic segments on performing viability test using NTG were actually improved in the follow up echo compared to LDDE group in which only 5 patients out of 11 showed actual improvement. (Decrease of WMSI > 20% from the resting value).

Similarly, *Chesebro et al.* observed a good correlation between nitroglycerin-induced changes in wall thickness and changes recorded few months after revascularization confirming nitroglycerin viability, and this was consistent with our study.⁽¹⁹⁾

Several authors have studied the effect of nitrate administration on myocardial perfusion and agreed that myocardial perfusion improves well with the use of nitrates.^{(16), (20)}

Maurea et al. and Bisi et al. found that the combination of isosorbide dinitrate infusion and rest ^{99m}Tc-sestamibi tomography increases tracer uptake in some chronically hypoperfused asynergic areas. Increased tracer uptake was associated with functional recovery after revascularization.

There is also evidence that nitroglycerin given prior to thallium redistribution may increase the number of reversible defects and thus the detection of residual viability in ischemic regions.^{(21), (22)}

Also, a study by Solimana et al. Concluded that NTG enhances regional blood flow during thallium 201 reinjection imaging and thus improved wall motion, as observed by SPECT sestamibi imaging in segments with perfusion defects.⁽²³⁾

Another study by *Tadamura et al.* provides important support for the use of nitrate-enhanced imaging to detect viable myocardium.

Tadamura et al. compared the effects of nitroglycerin spray on MBF and coronary resistance (CVR) in 23 CAD patients and eleven healthy volunteers. Nitroglycerin spray beneficially reduced the CVR of ischemic viable myocardium. After nitroglycerin spray, tracer uptake in ischemic myocardium was relatively increased comparable to non-viable and non-ischemic myocardium.⁽²⁴⁾

Our study is consistent with these studies as the follow-up echo showed a statistically significant improvement in myocardial function and wall motion abnormalities documented at resting echocardiography for the NTG group compared with the LDDE group after revascularization.

In 1995, Chen et al. showed that the failure of dobutamine in improving regional wall thickening may be the result of greatly reduced perfusion which does not improve adequately with low-dose dobutamine.⁽²⁵⁾

Sadeghian et al. included forty-six patients with coronary artery disease and left ventricular systolic dysfunction (ejection fraction <40%) using low-dose DSE and (99m) Tc-sestamibi MPS.⁽¹⁷⁾

In this study, it was concluded that the proportion of segments showing a positive response to dobutamine was significantly lower than with technetium uptake.

This suggests that the cellular mechanisms responsible for the positive inotropic response to adrenergic stimulation required a higher degree of myocyte functional integrity than those responsible for 99mTc-sestamibi uptake, so that stress echo using dobutamine agent sometimes underestimates the detection of myocardial viability.⁽¹⁷⁾

Nuclear imaging techniques appear to be more sensitive in predicting functional recovery, while stress echocardiography appears more specific.⁽²⁶⁾

Panza et al. Performed a head-to-head comparison between thallium-201 imaging and dobutamine stress echocardiography in patients with chronic ischemic LV dysfunction. A total of 311 segments were analyzed using both techniques. He found that thallium-201 imaging was more sensitive than dobutamine echo to detect viable tissue.⁽²⁷⁾

Similar results were analysed by *Cornel et al.* who evaluated 40 patients with chronic ischemic LV dysfunction by FDG imaging and dobutamine echocardiography. Again, nuclear imaging was more sensitive to detect viable tissue, as evidenced by 27% of dysfunctional segments with FDG uptake but without showing contractile reserve.⁽²⁸⁾

We hypothesized that agents that improve coronary blood flow and oxygen supply/demand balance as nitrates may increase the sensitivity of dobutamine stress echocardiography to detect hibernating myocardium.

In contrast to our study, *Fallen et al.* showed that NTG altered MBF, preferentially increasing blood flow to areas with decreased perfusion with little impact on global MBF by PET scan.⁽²⁹⁾

Recently, several studies have suggested the efficacy of NTG to assess myocardial viability and prognosis.⁽³⁰⁾

Another study by *Galli et al.* showed a significant reduction in mean perfusion defects in 54% of patients after receiving intravenous nitroglycerin. Thus, the addition of nitrates to the Tc-99m MIBI perfusion imaging is important for the detection of viable myocardium.⁽³¹⁾

Considering the unique pharmacological properties of NTG, our study attempted to rediscover this agent as an ideal stimulus for the evaluation of viable myocardium in ischemic patients.

Pontillo et al. In 1996, selected 20 patients with previously documented myocardial infarction. All patients underwent NTG echocardiography and thallium perfusion scintigraphy.

In this study, it was concluded that neither NTG echocardiography nor thallium perfusion scintigraphy showed a significant difference in the number of patients expressing positive myocardial viability testing. Analysis of NTG echocardiography / thallium data showed that the sensitivity and specificity of NTG echocardiography were 90% and 80%, respectively.⁽³²⁾

La Canna et al. stated that although dobutamine echo is useful in assessing myocardial hibernation, it may underestimate viability in some cases. In response to dobutamine, 13 percent of the segments showing no change in wall motion recovered after angioplasty.

Most of these segments were akinetic at rest and no change in wall motion occurred during dobutamine infusion.⁽³³⁾

NTG echocardiography is completely safe, where none of our patients developed hypotension, arrhythmia, or chest pain during the nitroglycerin infusion and this is supported by *Pontillo et al. in 1996*, who mentioned that they were never forced to stop the test for adverse effects and might be due to careful stepwise NTG infusion and titration.⁽³²⁾

The same authors concluded that NTG echocardiography may be an interesting alternative to dobutamine echocardiography, but further experience is needed to extend the results of their study to the general group of CAD patients.⁽³²⁾

Thus, NTG echocardiography may be a reliable method to detect myocardial viability. Our results cannot be extended to the general group of CAD patients, given the small selected patient population and the selection bias that usually occurs when testing a new diagnostic method.

5. Conclusion:

NTG echocardiography is a reliable method to detect viable myocardium in patients following myocardial infarction and a safe tool that can be compared to dobutamine echocardiography.

6. Disclosure of Funding:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

7. Disclosure of any conflict of interest:*none declared.***Table (1): Comparison between the two groups regarding Echo findings.**

ECHO findings		LDDE		NTG		Test value	P-value	Sig.	
		No. = 24		No. = 21					
Resting Ejection fraction	Mean ± SD	31.17 ± 8.26		27.33 ± 9.04		1.486*	0.145	NS	
	Range	20 – 40		15 – 40					
RWMA's in the form of akinetic territories.		Positive	24 (100.0%)		21 (100.0%)		NA	NA	NA
No. of akinetic segments	Mean±SD	10.79 ± 2.48		11.90 ± 2.79		1.416	0.164	NS	
	Range	6 – 16		8 – 16					
WMSI	Mean±SD	2.60 ± 0.33		2.62 ± 0.33		0.198	0.844	NS	
	Range	2 – 3		2 – 3					

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)*:Chi-square test; •: Independent t-test.

Table (2): Comparison between the two groups regarding the number of patients showing positive viability in each group.

Viability	LDDE (24)		NTG (21)		Test value*	P-value	Sig.
	No.	%	No.	%			
Negative	13	54.2%	10	47.6%	0.192	0.661	NS
Positive	11	45.8%	11	52.4%			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)*:Chi-square test; •: Independent t-test.

Table (3): Comparison between the two groups regarding Coronary angiography findings for viable akinetic segments.

		LDDE		NTG		Test value*	P-value	Sig.
		No.	%	No.	%			
CA for	No stenting	3	27.3%	3	27.3%	0.000	1.000	NS

+ve cases	Normal	1	9.1%	1	9.1%			
	MVD	2	18.2%	2	18.2%			
	Stenting of one vessel	2	18.2%	2	18.2%			
	Stenting of 2 vessels	6	54.5%	6	54.5%			
Vessels affected	LM	0	0.0%	1	9.1%	1.048	0.306	NS
	LAD	7	63.6%	8	72.7%	0.210	0.647	NS
	Diagonal	1	9.1%	0	0.0%	1.048	0.306	NS
	LCX	4	36.4%	3	27.3%	0.210	0.647	NS
	OM1	1	9.1%	1	9.1%	0.000	1.000	NS
	RCA	1	9.1%	1	9.1%	0.000	1.000	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS).*:Chi-square test.

Follow up echo 3months following revascularization procedure:

Table (4): Comparison between the two groups regarding Follow up Echo after 3 months.

Follow up echo after 3 months	LDDE		NTG		Test value*	P-value	Sig.
	No.	%	No.	%			
No improvement in territories supposed to be viable.	6	54.5%	4	36.4%	0.733	0.392	NS
Improvement in territories supposed to be viable.	5	45.5%	7	63.6%			

Table (5): Comparison between Resting and follow up Echo as regards viable akinetic segments in LDDE group.(11 patients).

LDDE		Resting	Follow up	Test value	P-value	Sig.
Total no. = 11	EF	34.55 ± 6.25	41.64 ± 6.42	8.444	0.000	HS
	WMSI	2.57 ± 0.38	2.08 ± 0.35	4.142	0.0002	HS
Improved cases (no. = 5)	EF	31.60 ± 7.92	45.00 ± 7.91	4.740	0.009	HS
	WMSI	2.76 ± 0.22	1.91 ± 0.03	9.184	0.001	HS

Not improved cases (no. = 6)	EF	37.00 ± 3.46	38.83 ± 3.43	21.164	0.000	HS
	WMSI	2.42 ± 0.44	2.23 ± 0.43	12.587	0.000	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant

(HS)*:Chi-square test; •: Independent t-test.

Table (6): Comparison between resting and follow up Echo as regard viable akinetic segments in NTG group.(11 patients).

NTG		Resting	Follow up	Test value	P-value	Sig.
Total no. = 11	EF	33.45 ± 5.32	47.73 ± 11.83	8.121	0.000	HS
	WMSI	2.38 ± 0.26	1.42 ± 0.65	4.826	0.001	HS
Improved cases (no. = 7)	EF	35.43 ± 5.13	55.57 ± 5.94	7.895	0.000	HS
	WMSI	2.33 ± 0.31	0.97 ± 0.22	7.783	0.000	HS
Non improved cases (no. = 4)	EF	30.00 ± 4.08	34.00 ± 1.15	7.033	0.006	HS
	WMSI	2.48 ± 0.13	2.20 ± 0.14	17.690	0.000	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)*:Chi-square test; •: Independent t-test.

Table (7): Comparison between the two groups regarding follow up Echocardiography.

Follow up		LDDE	NTG	Test value	P-value	Sig.
Total cases (11)	EF	41.64 ± 6.42	47.73 ± 11.83	-1.500	0.149	NS
	WMSI	2.08 ± 0.35	1.42 ± 0.65	3.006	0.007	HS
Improved cases	EF	45.00 ± 7.91	55.57 ± 5.94	-2.657	0.024	S
	WMSI	1.91 ± 0.03	0.97 ± 0.22	9.252	0.000	HS
Non improved cases	EF	38.83 ± 3.43	34.00 ± 1.15	2.672	0.028	S
	WMSI	2.23 ± 0.43	2.20 ± 0.14	0.148	0.886	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)*:Chi-square test; •: Independent t-test.

Table (8): Comparison between LDDE group and NTG group regarding the difference between resting and follow-up echocardiography in total number of patients with viable myocardium, improved cases and non improved cases.

Difference		LDDE	NTG	Test value	P-value	Sig.
Total cases (11)	EF	7.09 ± 6.30	14.27 ± 8.51	-2.246	0.025	S
	WMSI	-0.49 ± 0.39	-0.96 ± 0.66	-1.745	0.081	NS
Improved cases	EF	13.40 ± 2.30	20.14 ± 2.12	-2.877	0.004	HS
	WMSI	-0.85 ± 0.21	-1.36 ± 0.46	2.257	0.048	S
Non improved cases	EF	1.83 ± 1.47	4.00 ± 3.37	-1.226	0.220	NS
	WMSI	-0.18 ± 0.16	-0.28 ± 0.21	-0.877	0.380	NS

REFERENCES :

- 1-Kasliwal RR, Paul B, Mustaqueem A, Bansal M, Trehan N. Low dose dobutamine echocardiography predicts recovery of left ventricular systolic function following revascularization even in presence of low contractile reserve. *Indian Heart J.* 2006;58(2):120-5, PMID: 18989055.
- 2-Dicarli MF, Asgarzadie F, Schlberr HR, Brunken RC, Laks H, Phelps ME, Maddahi J, et al. Quantitative relation between myocardial viability and improvement in heart failure symptoms after revascularization in patients with ischaemic cardiomyopathy. *Circulation.* 2005; 92:3436-3444, <https://doi.org/10.1161/01.CIR.92.12.3436>.
- 3-França-Silva MS, Balarini MC, Cruz JC, Khan BA, Rampelotto PH, Braga VA. Organic nitrates: past, present and future. *Molecules.* 2014;19(9):15314-23, <https://doi.org/10.3390/molecules190915314>.
- 4-Böttcher M, Madsen MM, Randsbaek F, Refsgaard J, Dørup I, Sørensen K. Effect of oral nitroglycerin on myocardial perfusion in areas subtended by stenosed and non stenosed coronary arteries. *Am J Cardiol.* 2002; 89:1019–24, [https://doi.org/10.1016/S0002-9149\(02\)02268-3](https://doi.org/10.1016/S0002-9149(02)02268-3).
- 5-Miwa K, Fujita M, Kameyama T, Nakagawa K, Hirai T, Inoue H. Absence of myocardial ischemia during sudden controlled occlusion of coronary arteries in patients with well-developed collateral vessels. *Coron Artery Dis.* 1999; 10:459- 63, DOI: 10.1097/00019501-199910000-00005.
- 6-Wustmann K, Zbinden S, Windecker S, Meier B, Seiler C. Is there Functional collateral flow during vascular occlusion in angiographically normal coronary arteries? *Circulation.* 2003; 107: 2213–20, <https://doi.org/10.1161/01.CIR.0000066321.03474.DA>.
- 7-Moon JC, De Arenaza DP, Elkington AG. The pathologic basis of Q- wave and non-Q- wave myocardial infarction: a cardiovascular magnetic resonance study. *J Am Coll*

- 8-Thygesen K, Alpert JS, White HD.** Universal definition of myocardial infarction. *Eur Heart J* 2007; 28:2525–2538, doi:10.1016/j.jacc.2007.09.011.
- 9-Feigenbaum H.** *Echocardiography 4 th ed* Lea and Febiger, Philadelphia. 1996.
- 10-Scognamiglio R, Marco M, Manuela M.** Post extra systolic presentation echocardiography in predicting reversible myocardial diffusion by surgical coronary revascularization *AM J. Cardiol.* 1998; 81: 36-40, DOI: 10.1016/s0735-1097(98)00593-2 .
- 11-Pellikka PA, Nagueh SF, Elhendy AA.** American Society of Echocardiography recommendations for performance, interpretation, and application of stress echocardiography. *J Am Soc Echocardiogr.* 2007; 20:1021–1041, DOI: 10.1016/j.echo.2007.07.003.
- 12-Moller JE, Hillis GS, Oh JK.** Wall motion score index and ejection fraction for Risk stratification after acute myocardial infarction. *Am Heart J.* 2006; 151: 419-425, <https://doi.org/10.1016/j.ahj.2005.03.042>.
- 13-Schiller, P.M Shah, M Crawford, et al. (1989).** Recommendations for quantitation of the left ventricle by two-dimensional echocardiography *J Am Soc Echocardiogr.* 1989; 2, pp. 358-367, [https://doi.org/10.1016/S0894-7317\(89\)80014-8](https://doi.org/10.1016/S0894-7317(89)80014-8).
- 14-C.G Cigarroa, C.R DeFilippi, E Brickner, L. Glvarez, M.A Wait, P.A, et al. (1993).** Grayburn Dobutamine stress echocardiography identifies hibernating myocardium and predicts recovery of left ventricular function after coronary revascularization. *Circulation.* 1993, 88, 430-436, <https://doi.org/10.1161/01.CIR.88.2.430>.
- 15-Helfant RH, Pine R, Meister SG, Feldman MS, Trout RG, Banka VS.** Nitroglycerin to unmask reversible asynergy: correlation with post coronary bypass ventriculography. *Circulation.* 1974; 50:108–113, <https://doi.org/10.1161/01.CIR.50.1.108>.
- 16-Cannizzaro, C, Calsamiglia C, Aprile C, Zoccarato O and Tavazzi L.** Detection of myocardial viability. *J. Nucl. Cardiol.* 1995; 2: S95, DOI 10.1016/S1071-3581(05)80463-5.
- 17-Sadeghian H, Majd-Ardakani J, Lotfi-Tokaldany M, Jahangiri C, Fathollahi MS.** Comparison between dobutamine stress echocardiography and myocardial perfusion scan to detect viable myocardium in patients with coronary artery disease and low ejection fraction. *Hellenic J Cardiol.* 2009; 50(1):45-51, PMID: 19196620.
- 18-Afridi I, Kleinman NS, Raizner AE, Zoghbi WA.** Dobutamine echocardiography in myocardial hibernation: optimal dose and accuracy in predicting recovery of ventricular function after coronary angioplasty. *Circulation.* 1995; 91:663–670, <https://doi.org/10.1161/01.CIR.91.3.663>.
- 19-Chesebro JH, Ritman EL, Frye RL.** Regional myocardial wall thickening response to nitroglycerin: a predictor of myocardial response to aorto coronary bypass surgery. *Circulation.* 1978; 57:952–957, <https://doi.org/10.1161/01.CIR.57.5.952>.
- 20-Zerbib E, Chauvel C, Cohen A, Carrat F, Askienazy S and Valty J.** Thallium-201 reinjection after sublingual nitroglycerin administration could improve sensitivity of rest-redistribution TI²⁰¹ imaging to detect myocardial viability. *J. Nucl. Cardiol.* 1995; 2: S98, DOI 10.1016/S1071-3581(05)80477-5.
- 21-Maurea S, Cuocolo A, Soricelli A, Castelli L, Nappi A, Squame F.** Enhanced detection of viable myocardium by technetium-99m-MIBI imaging after nitrate administration in chronic coronary artery disease. *J Nucl Med.* 1995; 36:1945–1952, PMID: 7472580

- 22-Bisi G, Sciagra R, Pedenovi P, Briganti V, Santoro G and Fazzini P.** Improved detection of viable myocardium in infarcted patients with Tc-99m-sestamibi imaging in combination with nitrate infusion. *First International Congress of Nuclear Cardiology, France; 1993:25-28, [https://doi.org/10.1016/S1071-3581\(05\)80081-9](https://doi.org/10.1016/S1071-3581(05)80081-9).*
- 23-Solimana Mahmoud A, Shalaby Awny G, Esawy Ahmed S.** Assessment of myocardial viability with gated SPECT Tc-99m sestamibi imaging during administration of sublingual nitroglycerin. *Menoufia Medical Journal. 2019;32: 177-180, DOI 10.1016/S1071-3581(05)80471-4.*
- 24-Tadamura E, Mamede M, Kubo S.** The effect of nitroglycerin on myocardial blood flow in various segments characterized by rest-redistribution thallium SPECT. *J Nucl Med. 2003 ;44:745–751, PMID: 12732676.*
- 25-Chen C, Li L, Chen L, V. Prada J, Chen MH, Fallon JT, Weyman AE, Waters D, Gillam L, et al.** Incremental doses of dobutamine induce a biphasic response in dysfunctional subtending coronary stenosis. *Circulation. 1995; 92:756–766, <https://doi.org/10.1161/01.CIR.92.4.756>.*
- 26-Bax JJ, Poldermans D, Elhendy A.** Sensitivity, specificity, and predictive accuracies of various non-invasive techniques for detecting hibernating myocardium. *Curr Probl Cardiol. 2001;26:141–186, DOI: 10.1067/mcd.2001.109973.*
- 27-Panza JA, Dilsizian V, Laurienzo JM.** Relation between thallium uptake and contractile response to dobutamine. Implications regarding myocardial viability in patients with chronic coronary artery disease and left ventricular dysfunction. *Circulation 1995;91:990–998, <https://doi.org/10.1161/01.CIR.91.4.990>.*
- 28-Cornel JH, Bax JJ, Elhendy A.** Agreement and disagreement between metabolic viability and contractile reserve in akinetic myocardium. *J Nucl Cardiol. 1999;6:383–388, [https://doi.org/10.1016/S1071-3581\(99\)90003-X](https://doi.org/10.1016/S1071-3581(99)90003-X).*
- 29-Fallen EL, Nahmias C, Scheffel A, Coates G, Beanlands R, Garnett ES.** Redistribution of myocardial blood flow with topical nitroglycerin in patients with coronary artery disease. *Circulation. 1995; 91(5):1381-8, <https://doi.org/10.1161/01.CIR.91.5.1381>.*
- 30-Sciagra R, Leoncini M, Marcucci G, Dabizzi RP, Pupi A.** Technetium-99m sestamibi imaging to predict left ventricular ejection fraction outcome after revascularisation in patients with chronic coronary artery disease and left ventricular dysfunction: comparison between baseline and nitrate-enhanced imaging. *Eur J Nucl Med. 2001;28:680–687, <https://doi.org/10.1007/s002590100543>*
- 31-Galli M, Marcassa C, Imperato A, Campini R, Orrego PS, Giannuzzi P.** Effects of nitroglycerine technetium 99m Sestamibi tomoscintigraphy on resting global myocardial hypoperfusion in stable patients with healed myocardial infarction. *Am J Cardiol. 1994;74:843–848, [https://doi.org/10.1016/0002-9149\(94\)90573-8](https://doi.org/10.1016/0002-9149(94)90573-8).*
- 32-Pontillo D, Carboni GP, Capezuto A, Alessi C, Achilli A, Piccini F, et al.** Identification of viable myocardium by Nitrate echocardiography after myocardial infarction: comparison with planar thallium reinjection scintigraphy. *Angiology. 1996;47(5):437-46, <https://doi.org/10.1177/000331979604700502>.*
- 33-La Canna G, Alfieri O, Giubbini R, Gargano M, Ferrari R, Visioli O.** Echocardiography during infusion of dobutamine for identification of reversible dysfunction in patients with chronic coronary artery disease. *J Am Coll Cardiol. 1994;23:617-626, DOI: 10.1016/0735-1097(94)90745-5.*