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Predictors of Myocardial Viability in Patients with Coronary Artery Chronic Total Occlusion by Myocardial Perfusion Imaging

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Abstract

Coronary artery disease (CAD) still remains one of the leading causes of mortality in many countries with more than 17 million deaths worldwide. This study aimed to assess the predictors of myocardial viability in patient with coronary artery chronic total occlusion (CTO) by Myocardial Perfusion Imaging. Methods: This study included 100 patients with previous coronary angiography (CA) in which they detected that they have one or more vessel with CTO. And patients were divided in to two groups: Group 1: Viable Myocardium, and Group 2: Non-Viable Myocardium. Patients were subjected to complete history taking, general and local physical Examination, 12 Lead ECG, Laboratory investigation of serum troponin, conventional Echocardiography, Diagnostic Coronary angiography, and Single photon emission computed tomography (SPECT). This study included 100 male with no females included. Their mean age was 56±8 years. 66% of patient showed myocardial viability, while 34% showed myocardial not viable. There was statistical difference between viable and not viable groups regarding the MPI; all patients in non-viable group shows scar with no reversable ischemia, while 68.2% of the viable group show reversible ischemia, and 31.8%had mixed scar with reversible ischemia, $p<0.001$. EF could predict the viability, AUC= 0.992, at cut off value above 46%, the sensitivity was 0.949 and specificity was 0.934. IVSD could predict the viability, AUC= 0.950, at cut off value above 6.1 mm, the sensitivity was 0.974 and specificity was 0.967.

Keywords: Myocardial, Viability, Coronary, Occlusion, Perfusion.

1. Introduction

Coronary artery disease (CAD) still remains one of theleading causes of mortality in many countries with morethan 17 million deaths worldwide. CAD is aresult of atherosclerosis, which has been interpreted to bedue to endothelial dysfunction and inflammatory reaction [1].

Coronary chronic total occlusion (CTO) is a common finding with a reported prevalence of 18.4% in patients undergoing non-urgent coronary angiography in the absence of previous coronary artery bypass or those presenting with acute myocardial infarction [2].

Chronic total occlusion (CTO) remains one of the most difficult subsets for the interventionists because of the perceived procedural complexity [3].

Revascularization of CTO is associated with the improvement of cardiac function and long-term clinical outcome. Although the success rate of percutaneous coronary intervention (PCI) for revascularizing CTOs was low (51–74%), recent technological advances and interventional strategies have improved the success rate of PCI of CTO [4].

Although revascularization of CTO is important for symptoms control like, Angina, congestive heart failure and fatigue,improve LV function and for survival in the form of improve tolerance to acute myocardial infarction [5].

Chronic total occlusion (CTO) is a complete or near complete occlusion of the vessel by a heavy atherosclerotic plaque burden. It is a relatively common finding in patients indicated for invasive coronary angiography (CAG), with a reported incidence of up to 15–52 % [6].

Vascular resistance decreases beyond the occlusion site as a response to decreased luminal pressure within the arteriolar bed primarily supplied by the occluded artery. It causes a pressure gradient across the native collateral bed and increases the flow velocity toward the occluded artery. Such hemodynamic changes induce maturation of the native collateral channels along with the formation of de novo collateral channels as a result of biochemical changes involving various endothelial and inflammatory cells and induced cytokines [7].

Collateral circulation protects the jeopardized myocardium beyond the stenotic or occlusive lesions and consequently improves the prognosis of patients with coronary heart diseases [8].

Myocardial perfusion single-photon emission computed tomography (MPS) is a widely used tool that provides relative information on perfusion at a myocardial dimension [9].

Myocardial viability or ischemia of the collateral-dependent myocardium can be provided by MPS, which is of extreme importance to the decision concerning percutaneous coronary intervention (PCI) or bypass surgery in patients with CTO [10].

SO, MPI in patients with CTO accurately predicted hard cardiac events (HCE), with extremely high sensitivity and negative predictive value, allowing for accurate triage of patients by MPI for consideration of revascularization if technically feasible [11].

This study aimed to assess the predictors of myocardial viability in patient with coronary artery chronic total occlusion (CTO) by Myocardial Perfusion Imaging.

2.Patients and methods

This study included 100 patients with previous coronary angiography (CA) in which they detected that they have one or more vessel with CTO. Patients were divided into 2 groups:

Group 1: Viable Myocardium.
Group 2: Non-Viable Myocardium.

2.1Inclusion criteria

- Previous CA.
- Patients with stable angina.

2.2Exclusion criteria

- Patient with unstable angina.
- Patient with congestive heart failure.
- Patient with cardiogenic shock**.**
- Any contraindication to MPIeg

This study was approved by the ethical committee of Benha Faculty of medicine. Informed consent was taken from all Patients for the study participation

2.3 All patients were subjected to:

1. Informed consent was taken from all Patients for the study participation.
2. Complete history taking: .including age, sex, risk factors for CAD as hypertension, diabetes mellitus, smoking, previous history for ACS, Myocardial infarction or Myocardial revascularization, family history of CAD.
3. Physical Examination:
4. General examination
5. Local examination of the heart
6. Electrocardiography: 12 Lead ECG.
7. Laboratory investigations of serum troponin
8. Conventional Echocardiography:
9. Diagnostic Coronary angiography
10. Single photon emission computed tomography (SPECT)

3. Statistical analysis

The data were coded, entered and processed on computer using SPSS (version 24). The results were represented in tabular and diagrammatic forms then interpreted. Mean, standard deviation, range, frequency, and percentage were use as descriptive statistics. The accepted level of significance was 0.05.

4. Results

This study included 100 patients with previous coronary angiography (CA) in which they detected that they have one or more vessel with CTO. 61% of patient was viable, 34% are non viable, while 5% was mixed viable. Table 1 shows the comparison between viable and non viable patients regarding sociodemographic data and risk factors; regarding age the non-viable group was older than the viable group (mean =59±8 and 55±8, respectively, p<0.001), regarding presence of hyperlipidemia; it was present in 97.1% of patients in non-viable group, compared to 78.8% in viable group (p=0.027), and regarding the history of coronary ischemia; all patients (100%) of the non-viable group had history of previous coronary ischemia, compared to 60.6% of the viable group (p<0.001), while there was no statistical difference between groups regarding, smoking, presence of hypertension or DM.

Table (1) Comparison between viable and non viable patients regarding sociodemographic data and risk factors.

		Viability				Test	p-value
		Non-viable		Viable & mixed viable			
		N=34	%	N=66	%		
Age	Mean±SD	59±8		55±8		t=2.57	P=0.013*
	Range	45-71		32-69			
Sex	Male	34	100%	66	100%	-	-
	Female	0	0%	0	0%		
Hyperlipidemia	No	1	2.9%	14	21.2%	X=4.88	P=0.027*
	Yes	33	97.1%	52	78.8%		
Hypertension	No	11	32.4%	28	42.4%	X=0.98	P=0.377
	Yes	23	67.6%	38	57.6%		
Smoking	No	1	2.9%	3	4.5%	X=3.2	P=0.19
	Yes	20	58.8%	49	74.2%		
	Ex-smoker	13	38.2%	14	21.2%		
DM	No	0	0.0%	4	6.1%	X=2.66	P=0.103
	Yes	34	100.0%	62	93.9%		
History of coronary ischemia	No	0	0.0%	26	39.4%	X=22.4	P<0.001*
	Yes	34	100.0%	40	60.6%		

Fig (1) shows statistical differences between groups regarding ECG; 100% of non-viable group shows abnormal Q wave, compared to 36.4% of the viable group (P<0.001) and serum troponin was positive in 2.9% of non-viable group, compared to 90.9% of the viable group (P<0.001).

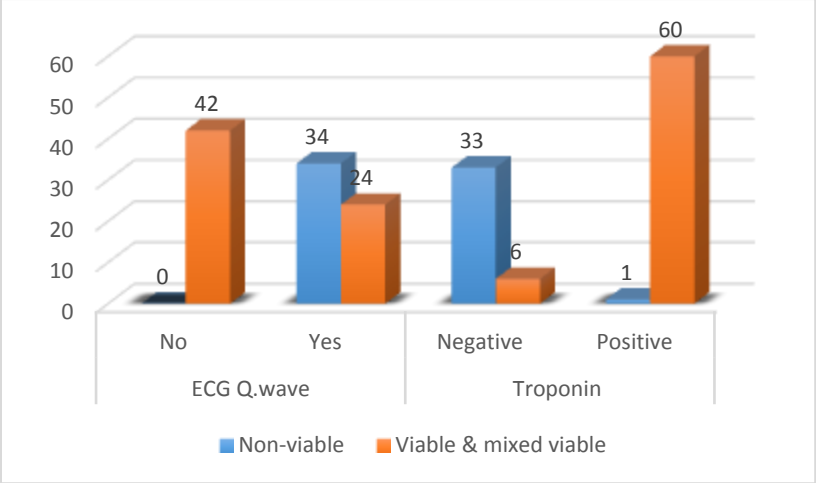

Fig (1) Comparison between viable and non viable patients regarding ECG, and serum troponin.

Table (2) shows statistical differences between viable and not viable groupss regarding Echocardiography;

Table (2) Comparison between viable and non viable patients regarding echocardiography.

			Viability		Test	p-value
			Non-viable	Viable & mixed viable		
			N=34	N=66		
EF %	Mean±SD		38.6±4.2	54.9±5.7	t=15.3	P<0.001**
	Range		29 - 48	42 - 61		
IVSD (mm)	Mean±SD		5.87±0.23	8.5±1.2	t=13.39	P<0.001**
	Range		5-6	6-11		
LVISd (cm)	Mean±SD		5±0.58	3.91±0.36	t=12.3	P<0.001**
	Range		4-6	3-5		
LvIDd (cm)	Mean±SD		6.7±0.48	5.6±0.4	t=12.7	P<0.001**
	Range		6 - 7	5 - 6		
ESV (ml)	Mean±SD		110.8±8.3	57.1±14.9	t=20.5	P<0.001**
	Range		90 - 127	40 - 115		
Relative wall motion	Akinesia	N	34	0	X^2=38.3	P<0.001**
		%	100%	0%		
	Akinesia-hypokinesia	N	0	6		
		%	0%	9.1%		
	Hypokinesia	N	0	60		
		%	0%	90.9%		

EF: ejection fraction; IVSD: interventricular septum thickness; LVISd: Left Ventricular Internal-Systolic Dimension; LvIDd: Left Ventricular Internal-Diastolic; ESV: End-systolic volume.

Table (3) shows statistical difference between viable and non-viable groups regarding the MPI; all patients in non-viable group shows scar with no reversable ischemia, while 68.2% of the viable group show reversible ischemia, and 31.8%had mixed scar with reversible ischemia, p<0.001.

Table (3) Comparison between viable and non viable patients regarding the myocardial perfusion imaging.

		Viability				Test	p-value
		Non viable		Viable & mixed viable			
		N=34	%	N=66	%		
MPI	**Mixed scar with reversable ischemia**	0	0.0%	21	31.8%	X^2=81.6	P<0.001**
	Reversible ischemia	0	0.0%	45	68.2%		
	SCAR with no reversable ischemia	34	100.0%	0	0.0%		

MPI: Myocardial perfusion imaging

ROC curve was done to assess the performance of Echo. Parameters in prediction of myocardial viability: EF could predict the viability, AUC= 0.992, at cut off value above 46%, the sensitivity was 0.949 and specificity was 0.934. IVSD could predict the viability, AUC= 0.950, at cut off value above 6.1 mm, the sensitivity was 0.974 and specificity was 0.967. LVIsd could predict the viability, AUC= 0.950, at cut off value below 4.3 cm, the sensitivity was 0.869 and specificity was 0.897. LvIDd could predict the viability, AUC= 0.966, at cut off value below 6.05 cm, the sensitivity was 0.902 and specificity was 0.872. ESV could predict the viability, AUC= 0.989, at cut off value below 93.5 ml, the sensitivity was 0.984 and specificity was 0.974 Table (4).

Table (4) ROC curve of Echo parameters performance in prediction of viability.

Variables	AUC	CI	p-value	Cut-off value	Sensitivity	Specificity
EF (%)	0.992	0.982-1	<0.001**	46%	0.949	0.934
IVSD (mm)	0.991	0.977-1	<0.001**	6.1	0.974	0.967
LVISd (cm)	0.950	0.908-0.991	<0.001**	4.3	0.869	0.897
LvIDd (cm)	0.966	0.937-0.994	<0.001**	6.05	0.902	0.872
ESV (ml)	0.989	0.968-1	<0.001**	93.5	0.984	0.974

EF: ejection fraction; IVSD: interventricular septum thickness; LVISd: Left Ventricular Internal-Systolic Dimension; LvIDd: Left Ventricular Internal-Diastolic; ESV: End-systolic volume.

5. Discussion

In this study, 66% of patient showed myocardial viability, while 34% showed myocardial not viable. this was in agreement with [12] study, 135 patients had myocardial viability, and 85 patients had non-viable myocardium. and in [13] study, Percentage of viable and non-viable segments by MPI: A Total of 241 segments in the 40 patients were assigned as abnormal segments (viable or nonviable) by MPI with nitrate potentiation, 114 out of 241 segments revealed viability while 127 segments were assigned as non-viable.

In this study, there was a statistical difference between groups regarding ECG; 100% of non-viable group shows abnormal Q wave, compared to 36.4% of the viable group (P<0.001).

H. Siha et al.,[14] study, 46% of 4341 patients with CTO, had baseline Q waves. Compared to those without Q waves, those with baseline Q waves were older, more frequently male, had higher heart rates, more advanced Killip class and had a longer time between the onset of symptoms and percutaneous coronary intervention. They also had higher one-year all-cause mortality than patients without baseline Q waves (baseline Q waves: 4.9%; no baseline Q waves: 2.8%; hazard ratio [HR] 1.78, 95% confidence interval [CI] 1.29–2.45, p < 0.001).

In this study, there was a statistical difference between groups regarding serum troponin; it was positive in 2.9% of non-viable group, compared to 90.9% of the viable group (P<0.001).

Recently, R. Wereski [15] conducted a study to assess cardiac troponin concentrations at presentation in patients with ST-segment elevation myocardial infarction (MI); At presentation, the median troponin concentration was 196 ng/L (interquartile range [IQR], 46-21 611 ng/L), Just 73.2% of patients (n = 677 of 925) had troponin concentrations greater than the rule-in threshold of 52 ng/L. Patients presenting within 2 hours of symptom onset (23.4%; 216 of 809) had lower troponin concentrations (96 ng/L; IQR,26-494 ng/L vs 294 ng/L; IQR, 59-3042 ng/L; P < .001), compared with those presenting later.

According to R. Wereski [15]**;** Patients presenting within 2 hours were more likely to have a troponin concentration at less than the 99th percentile; however, even in those who presented later, 1 in 6 had troponin concentrations at less than the diagnostic threshold. During myocardial infarction, abrupt coronary occlusion may prevent the release of troponin into the circulation until reperfusion has occurred. Observations are an important reminder of the limited role of troponin testing in the early assessment of patients with ST-segment elevation. Where clinical suspicion is high, troponin concentrations within the reference range should not delay the initiation of therapeutic agents or urgent coronary angiography.

In this study, there were statistical differences between viable and not viable groups regarding Echocardiography; the mean EF was statistically lower in non-viable group (38.6±4.2%) than the viable group (54.9±5.7%), p<0.001. The mean IVSD was statistically lower in non-viable group (5.87±0.23mm) than the viable group (8.5±1.2mm), p<0.001. The mean LVISd was statistically higher in non-viable group (5±0.58 cm) than the viable group (3.91±0.36), p<0.001. The mean LvIDd was statistically higher in non-viable group (6.7±0.48 cm) than the viable group (5.6±0.4 cm), p<0.001. The mean ESV was statistically higher in non-viable group (110.8±8.3 ml) than the viable group (57.1±14.9), p<0.001. regarding the relative wall motion; all patients in the non-viable group show akinesia, while 90.1% of the viable group shows hypokinesia, and 9.1% showed akinesia-hypokinesia, p<0.001.

In J. S. Woo, [16]**,** there were statistical differences between viable and non-viable groups regarding LVEDV

(p<0.01), LVEF (p<0.01), and Wall motion score (p<0.01), while there was no statistical difference between groups regarding LVEDV. Also in K. Padrón [17] study, there were statistical difference between viable and non-viable groups regarding EF, end diastolic volume, end systolic volume during rest and after nitroglycerine (NTG).

In H. Ran [18] study, The motion of all myocardium segments was analyzed visually on routine echocardiography. Among 720 segments derived from the 45 patients, 62 segments were found to be hyperkinetic, 290 normokinetic, 92 hypokinetic, 114 akinetic, and 162 dyskinetic. of 368 segments observed to have abnormal motion (hypokinetic, akinetic, and dyskinetic) on 2D echocardiography, 204 were defined as viable by SPECT/PET, and the remainder were nonviable. Of the other 352 segments without abnormal motion on 2D echocardiography, 300 were proven normal by SPECT/PET and were categorized as the control group.

In this study, there was a statistical difference between viable and not viable groups regarding the MPI; all patients in non-viable group shows scar with no reversable ischemia, while 68.2% of the viable group show reversible ischemia, and 31.8%had mixed scar with reversible ischemia, p<0.001.

ROC curve was done to assess the performance of Echo. Parameters in prediction of myocardial viability: EF could predict the viability, AUC= 0.992, at cut off value above 46%, the sensitivity was 0.949 and specificity was 0.934. IVSD could predict the viability, AUC= 0.950, at cut off value above 6.1 mm, the sensitivity was 0.974 and specificity was 0.967. LVIsd could predict the viability, AUC= 0.950, at cut off value below 4.3 cm, the sensitivity was 0.869 and specificity was 0.897. LvIDd could predict the viability, AUC= 0.966, at cut off value below 6.05 cm, the sensitivity was 0.902 and specificity was 0.872. ESV could predict the viability, AUC= 0.989, at cut off value below 93.5 ml, the sensitivity was 0.984 and specificity was 0.974.

Diagnostic markers of myocardial viability are: the preservation of wall thickness, the presence of contractility reserve, the presence of blood perfusion reserve, integrity of the wall cells, and preservation of cellular metabolism. Echocardiography and thallium or technetium imaging are methods currently used to assess myocardial viability because of their availability and relatively low cost [19]**.**

T. R. Porter [20] concluded that Assessment of left ventricular size and function with echocardiography is an essential tool for evaluation of myocardial viability. While wall thinning is not reliable to estimate reversible myocardial function, increased left ventricular size is associated with poor prognosis after revascularization.

In G. LaCanna [21] study, Twenty-eight consecutive patients aged 58±9 years were studied. Of the 448 left ventricular segments, 263 were akinetic at rest; 230/263 (87%) had wall thickness ≥5mm, 135 (51%) had a positive response and 175 (66·5%) were graded viable on thallium. Of akinetic segments 61% improved after surgery. Left ventricular score decreased from 2·3±0·4 to 1·8±0·4 (*P*<0·01) and ejection fraction increased from 27±10 to 37±14% (*P*<0·01). For predicting results at 1 year, diastolic wall thickness had a sensitivity and a predictive accuracy of a negative test of 100% but a specificity of 28% and predictive accuracy of a positive test of 61%. The addition of dobutamine echocardiography or thallium-201 improved the predictive accuracy of a positive test to 76% and 69%, respectively; the addition of both tests was not of greater benefit than that of a single test.

In w. E. Juselius [22] **s**tudy, Diagnostic imaging rates were comparable for stress echocardiography (n=113) and MPI (n= 116): 97.4% vs. 94.8%, (p= 0.50) respectively. Study duration was lower with stress echocardiography (2.4 vs. 4.9 hours, p<0.0001), however, overall length of stay did not differ. Mean total hospitalization charges were reduced with stress echocardiography; this difference was driven entirely by lower stress-testing charges ($2,512 vs. $3,603 p< 0.0001). The majority of studies (94.1% and 89.1%, p=0.20) were negative for inducible ischemia. Overall, only 7 patients had coronary angiography performed and just one individual underwent revascularization. Provider satisfaction with timeliness and perceived safety of the testing strategy was higher with stress echocardiography (both p< 0.05).

The classic methodological gold standard for detecting myocardial viability has been positron emission tomography (PET). Since this technique is costly and not widely available, another most widely applied nuclear technique which is single-photon emission computed tomography (SPECT) utilizing the tracers 201Thallium, 99mTechnetium sestamibi, or 99mTechnetium tetrofosmin has long been used to evaluate viability. Besides these nuclear studies, the most widespread technique to assess regional myocardial viability and the potential for functional recovery has been dobutamine echocardiography [23]**.**

Wang et al., [24] evaluate myocardial infarction size with three-dimensional speckle tracking echocardiography in comparison with single photon emission computed tomography and they find correlation between global 3D strain detected by 3DSTE and infarction size detected by MPI

H. Ran [18] who compare viable myocardial segments detected by MPI as a gold standard with strain of the segments detected by 2DSTE and 3DSTE to compare between the results of viable and non-viable segments.

Newer studies have also demonstrated the comparable sensitivities and specificities of MCE to single photon-emission computed tomography (SPECT), cardiac myocardial resonance imaging and PET for the detection of myocardial viability [13]**.**

This study provided a new evidence that echocardiography, a quick and accessible method, for prediction of myocardial viability. However, his study had several limitations; Our findings was observational and represent a single-center experience. We could not

assess myocardial viability by cardiac MRI which was currently accepted as standard method, we did not assess the long term clinical outcomes. Finally, the small sample size didn't allow for a better analysis.

6. Conclusion

Assessment of myocardial viability is one of the most challenging areas of modern cardiology. Echocardiography is a quick and accessible method, for prediction of myocardial viability with high sensitivity and specificity . We found that patients with non viable myocardial are older , hyperlipidemic , has history of previous coronary ischemia , less chest pain , more dyspnea , additional heart sounds , abnormal Q wave and negative troponin. Echocardiography; the mean EF was statistically lower in non-viable group (38.6±4.2%) than the viable group (54.9±5.7%). The mean IVSD was statistically lower in non-viable group (5.87±0.23mm) than the viable group (8.5±1.2mm). The mean LVISd was statistically higher in non-viable group (5±0.58 cm) than the viable group (3.91±0.36), $p<0.001$. The mean LvIDd was statistically higher in non-viable group (6.7±0.48 cm) than the viable group (5.6±0.4 cm). The mean ESV was statistically higher in non-viable group (110.8±8.3 ml) than the viable group (57.1±14.9). regarding the relative wall motion; all patients in the non-viable group show akinesia, while 90.1% of the viable group shows hypokinesia, and 9.1% showed akinesia-hypokinesia .

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