

A Study of Improvement of Left Ventricle Ejection Fraction in Heart Failure Patients with Reduced Ejection Fraction with Coronary Artery Diseases after Revascularization by Percutaneous Coronary Intervention (PCI)

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Authors' contributions

This work was carried out in collaboration among all authors. All authors participated in the following-up of the patients in OPD and interpretation of data and all authors was the major contributor in writing the manuscript. All authors participated in the following-up of the patients during hospitalization and patients follow up data and prepared the collected clinical data to be ready for statistical analysis. All authors analyzed and interpreted the patient data and share in waiting the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background: Left ventricular dysfunction is the single strongest predictor of mortality and one of the most frequent and deadly complication following coronary artery diseases.

Aim: This work aims to study and explore the left ventricle ejection fraction improvement after revascularization with percutaneous coronary intervention (PCI) and the predictive factors for left ventricle ejection fraction improvement.

Methods: One hundred patients with ischemic (HFrEF) who had complete revascularization with percutaneous coronary intervention (PCI), had survived at least 90 days and had undergone echocardiography review. The study duration was 1 year from April 2019 to May 2020.

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Result: We focused on a group of the common possible predictive factors affecting left ventricular improvement. Gender (male), CKD, DM, number of affected vessel(single vessel disease), CTO lesion, heart rate, ECG findings, presence of anginal pain, presence of dyspnea , usage of medications (ACEI and Clopidogrel),hyper urecemia and the time between presentation of complaints and PCI were correlated with improvement of left ventricular function after revascularization by PCI.

Conclusion: Time between appearance of symptoms and PCI was found to be independent predictor of LV EF improvement after revascularization. Other predictors were Male gender, DM, CKD, normal ECG finding ,absence of hyper urecemia, slower heart rate ,presence of chest pain and dyspnea , absence of CTO lesion , single vessel affection and administration of ACEI and Clopidogrel.

Keywords: Heart failure; ischemia; ejection fraction; revascularization; PCI.

1. INTRODUCTION

Left ventricular (LV) dysfunction is the single strongest predictor of mortality and one of the most frequent and deadly complications following ischemic heart diseases [1].

Patients with heart failure with reduced ejection fraction (HFrEF) now have multiple therapeutic options, including oral medications and cardiac devices, that improve quality of life, reduce the risk of readmission, and/or improve mortality. In the span of only decades, the goals of treatment have moved dramatically upstream from supportive care towards heart failure (HF) stabilization, reversal, and prevention [2].

Those caring for HF patients now face new challenges of integrating sophisticated genetic, biomarker and imaging information in the pursuit of patient-centered care while delivering guideline-directed therapies across an increasingly fragmented health care landscape for HF patients who are likely to have multiple comorbidities and an expanded treatment time horizon [3].

Although coronary artery disease is the most common cause of heart failure with reduced ejection fraction (HFrEF), the role of revascularization as a treatment strategy to improve survival, reduce morbidity, and enhance the quality of life has only begun to be investigated in recent years [4].

Revascularization therapy such as percutaneous coronary intervention (PCI) should be considered for heart failure with reduced ejection fraction (HFrEF). However, revascularization therapy does not always improve left ventricular ejection fraction (LVEF) [5].

2. PATIENTS AND METHODS

2.1 Study Design and Population

This study was a prospective observational study including all consecutive patients with ischemic (HFrEF) who had complete revascularization with percutaneous coronary intervention (PCI), had survived at least 90 days and had undergone echocardiography review; those were admitted at cardiology department of Tanta university hospital. Written informed consent was obtained from all patients in this study.

2.2 Duration of the Study

The study had been run for 12 months from April 2019 to May 2020, during which data collection and follow up have been done.

2.3 Inclusion Criteria

1. Patients with ischemic heart failure with reduced ejection fraction (HFrEF) who had received complete revascularization with percutaneous coronary intervention (PCI).
2. Viable myocardium "positive viability test" (MPI).

2.4 Exclusion Criteria

1. Patients who previously underwent coronary artery bypass graft (CABG).
2. Patient underdone primary percutaneous coronary intervention (PCI).

2.5 Statistical Analysis

Normally distributed scale variables were expressed as mean + standard deviation. Non-normally distributed variables were expressed as median and range. Categorical variables were expressed in numbers and percentages.

Analyses of categorical variables were performed by chi-square test. Parametric scale variables were analyzed by independent sample t test, and nonparametric scale variables were analyzed by Mann-Whitney U test. Multivariate logistic regression analyses were performed to determine the independent predictors of remodeling.

3. RESULTS AND DISCUSSION

3.1 Gender Distribution

100 patients included in the study, 51 of the study population were males and 49 were females. Group I included 32 males (64%) and 18 females (36%). Group II included 19 males (38%) and 31 females (62%). Male gender was statistically significant being more prevalent in group I (P value =0.009) (Table 1).

3.2 Chronic Kidney Disease: (Fig. 1)

20 patients of the study population had CKD. In group I, 5 patients had CKD (10%), while in group II, 15 patients had CKD (30 % CKD was statistically significant being more prevalent in group II (P value = 0.012) (Table 4) (Fig. 1).

3.3 Considering Chronic Total Occlusion Lesion

72 patients of the study population did not have CTO lesion. In group I, 44 patients did not have CTO lesion (88.0%), while in group II, 28 patients did not have CTO lesion (56%). Absence of CTO was statistically significant being more prevalent in group I (P value =0.001) (Table 2).

Table 1. Distribution of the studied cases according to gender

Gender	Group I (n=50)		Group II (n=50)		Sig. test	P.
Males	32	64.0%	19	38.0%	6.763	0.009*
Females	18	36.0%	31	62.0%		

2: Chi square test; t: independent sample t test; * Statistically significant (p ≤ 0.05)

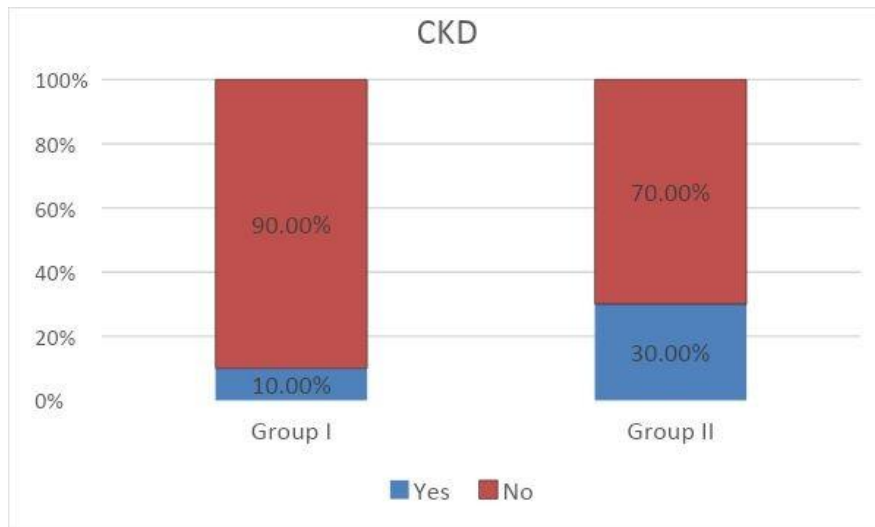


Fig. 1. Distribution of the studied cases according to chronic kidney disease

Table 2. Distribution of the studied cases according to presence of CTO lesion

Presence of CTO	Group I (n=50)		Group II (n=50)		Sig. test	P.
Yes	6	12.0%	22	44.0%	12.698	<0.001*
No	44	88.0%	28	56.0%		

2: Chi square test; * Statistically significant (p ≤ 0.05)

3.4 Data about Time between Presentation of Complaints and PCI in the Study

The time between presentation of complaints and PCI of the study population ranged from 1 to 16 months. In group I, the time ranged from 1.0 – 10.0 months with a mean time of 3.0 ± 2.0 months. In group II the time ranged from 8.0 – 16.0 months with a mean time of 12.0 ± 2.0 months. The time was statistically significant being shorter in group I (P value =0.035) (Table 3).

Univariate and multivariate analysis were performed to investigate the possible predictive factors affecting left ventricular improvement.

Gender (male), CKD, DM, number of affected vessel(single vessel disease), CTO lesion, heart rate, ECG findings, presence of anginal pain, presence of dyspnea , usage of medications (ACEI and Clopidogrel),hyper urecemia and the time between presentation of complaints and PCI

were correlated with improvement of left ventricular function after revascularization by PCI.

Regression analysis: Multivariate analysis logistic regression Variables with significant results in univariate analysis were included in the regression. Time between Presentation and PCI was a significant predictor for the outcome even after adjustment for other variables (P=0.001) (Table 4).

3.5 Discussion

3.5.1 Regarding the demographics in this study

3.5.1.1 Age

In this study Age showed no statistically significant difference between both groups (P value =0.136). Similar to our study, the study conducted by Ding Peng MD et al. [6] on 993 patients (P value =0.110).

Table 3. Time between presentation of complaints and PCI

	Group I (n=50)				Group II (n=50)				Sig. test	P.		
	Mean	±	SD	.Min	.Max	Mean	±	SD			.Min	.Max
Time between Presentation and PCI (months)	3.0	±	2.0	1.0	10.0	12.0	±	2.0	8.0	16.0	4.577	0.035

(t: independent sample t test; * Statistically significant (p ≤ 0.05))

Table 4. Multivariate analysis logistic regression for Response

	B	SE	Sig.	95% CI	
				LL	UL
Gender	0.042	0.035	0.240	-0.028	0.112
CKD	-0.053	0.044	0.232	0.035	0.015
Time between Presentation and PCI	0.088	0.004	0.001*	0.096	0.828
Presence of CTO	0.022	0.042	0.532	-0.060	0.105

B: UN standardized Coefficients; SE: Standard Error; CI: Confidence interval; LL: Lower limit; UL: Upper Limit; *: Statistically significant at p ≤0.05

3.5.1.2 Gender

In our study male patients were found to be more prone to improve of LV function (P value =0.009). In contrast to our study, the study conducted by Jane E Wilcox et al. [7] on 3994 where female gender had statistically significant impact on LVEF improvement (P <0.01).

3.5.2 Regarding clinical risk factors

3.5.2.1 Diabetes mellitus

In our study DM was shown to have statistically significant impact on improvement of LV function (P =0.001). In contrast to our study, the study conducted by Ding Peng MD et al [6] on 993 patients where DM did not have statistically significant difference between both groups (P value =0.059).

3.5.2.2 Hypertension

In our study, hypertension did not have statistically significant impact on LVEF improvement.

Similar to our study, the study conducted by Ding Peng MD et al [6] 150] on 993 patients where HTN did not have statistically significant impact on LVEF improvement (P value =0.056).

In contrast our study ,the study conducted by Pravesh Kumar Bundhun et al. [8] who studied 100 articles in this meta-analysis with a total number of 844,190 patients to be analyzed; Results from this meta-analysis showed that the hypertensive patients were significantly higher with RR 1.43; 95% CI: (1.05–1.94); (P=0.02).

3.5.2.3 Dyslipidemia

Our study showed no statistically significance of dyslipidemia on LVEF improvement (P = 0.687). Similar our study ,the study conducted by Pravesh Kumar Bundhun et al. [8] who studied 100 articles from randomized controlled trials and observational studies in this meta-analysis .The patients with dyslipidemia did not reach statistical significance (P=0.66).

3.5.2.4 Chronic kidney disease

In our study CKD was statistically significant on improvement of LV function (P value =0.012).

Similar to our study ,the study conducted by Aasim Afzal et al. [9] in that study patients with CKD had increased post PCI complications and mortality(P value =0.01).

3.5.3 Regarding time between presentation and PCI in the study

Early revascularization was statistically significant in our study (P value =0.035).

Similar to our study, the study conducted by Bax, J et al. [10] on 85 patients (P >0.05) that showed early revascularization was very important factor in improvement of LVEF.

3.5.4 Regarding medications

3.5.4.1 Angiotensin converting enzyme inhibitors

Administration of ACE Inhibitors was shown to have statistically significant impact on LV function improvement (P =0.006). In contrast to our study , the study by Ding Peng MD et al. [6] on 993 patients show that usage of ACE Inhibitors had no statistically significant an impact on improvement LV function (P=0.846).

3.5.4.2 Clopidogrel

Administration of Clopidogrel was shown to have statistically significant impact on LV function improvement in our study (P =0.012). Similar to the study that was conducted by Ding Peng MD et al. [6] on 993 patients show that usage of Clopidogrel had statistically significant an impact on improvement LV function (P=0.002).

3.5.5 Regarding lab investigations

As regarding hemoglobin level, serum creatinine and urea level, there was no statistically significant difference between both groups.

Similar to our study, the study conducted by Ding Peng MD et al. [6] and study that was conducted by Joyce et al. [11] on 964 patients.

Hyperuricemia in our study had statistically significant impact on improvement LV function (P value <0.001). In contrast to our study ,the study that was conducted by Ding Peng MD et al. [6] on 993 patients showed that hyperurecemia had no statistically significant impact on improvement LV function (P value <0.101).

3.5.6 Regarding angiographic results: Vessels affected

In our study Single vessel disease had statistically significant impact on improvement LV function (P value<0.001).

In contrast to our study the study that was conducted by Ding Peng MD et al. [6] on 993

patients, showed that single vessel disease had no statistically significant impact on improvement LV function ($P=0.030$).

3.5.7 Presence of CTO lesion

In our study absence of CTO was shown to have statistically significant impact on improve LV function (P value =0.00). Similar to our study, the study that was conducted by Mashayekhi et al. [12] showed no significance improvement of LVEF after revascularization CTO lesion; The CTO PCI group comprised 101 patients and the no CTO PCI group 104 patients. No benefit was seen for CTO PCI in terms of the primary endpoint ($p=0.57$).

In contrast to our study, the study that was conducted by Alfredo R Galassi et al. [13] on 839 patients (mean 64.6 ± 10.5 years of age, 87.7% men) underwent CTO PCI attempts. Baseline LVEF $\leq 35\%$ was present in 72 (8.6%) patients. In patients with LVEF $\leq 35\%$, LVEF improved significantly in the presence of a successful CTO PCI from $29.1 \pm 3.4\%$ to $41.6 \pm 7.9\%$ ($p < 0.001$).

3.5.8 Presence of collaterals

In our study presence of collaterals had no statistically significant impact on improvement of LV function ($P = 0.564$).

In contrast to our study, the study conducted by Traupe et al. [14]. And the study conducted by Van Dongen et al. [15], a sub analysis of the explore randomized controlled trial. Well-developed collaterals were present in 162(54%) patients; these patients had a significantly higher LVEF at 4 months ($46.2 \pm 11.4\%$ vs. $42.1 \pm 12.7\%$, $p=0.004$) when compared with patients with poorly developed collaterals.

3.5.9 Regarding ECG findings

Normal ECG finding was shown to have statistically significant impact on improvement of LV function in our study ($P =0.001$). Similar to our study, the study conducted by Ralf Surber et al. [16] which studied angiographic follow-up after 5 ± 1.4 months documented reocclusion in eight patients.

3.5.10 Regarding ECHO findings

3.5.10.1 Before PCI:

Ejection fraction: In our study LVEF before PCI was shown to have no statistically significant impact on improve LV function (P value <0.110).

In contrast to our study, the study by Ding Peng MD et al. [6] that was conducted on 993 patients showed that severely impaired LVEF had statistically significant an impact on improvement LV function ($P <0.001$). Also the study by Arend F L Schinkel et al [17] that was conducted on 258 patients showed that severely impaired LVEF had statistically significant an impact on improvement LV function ($P <0.0001$). And the study conducted by Mohamed Samy et al [18] on 75 patients.

S' wave and E/e' ratio: In our study s' wave by TDI and E/e' ratio findings before PCI were shown to have no statistically significant impact on improve LV function (P value <0.100) (P value <0.246).

3.5.10.2 3 months after PCI

Ejection Fraction: In our study LVEF was shown to have statistically significant impact on improve LV function after revascularization ($P =0.001$). Similar to our study, the study conducted by Holper et al. [19] in the Dynamic Registry, compared with patients without CHF, patients with CHF had a higher-risk clinical and angiographic profile, and a higher mortality rate both in hospital (2.6% vs. 0.4%, $P \leq .001$) and at 1 year (13.1% vs. 3.0%, $P < .001$).

S'-wave velocity by tissue Doppler: In our study S'-wave velocity by tissue Doppler findings were shown to have statistically significant prediction on improve LV function after revascularization ($P =0.001$).

Similar to our study, the study that was conducted by Mohamed Samy et al. [18]. This prospective study included 75 patients. Our study showed significant improvement of S-wave velocity by tissue Doppler 6 months post PCI in low LVEF group and mid-range LVEF group ($P < .05$). The delta change in LVEF was significantly more in low LVEF group, compared to the other two groups ($F = 4.739$, $P < .05$).

E/e' ratio: In our study E/e' ratio findings were shown to have statistically significant impact on improve LV diastolic function after revascularization ($P =0.001$).

Similar to our study, the study conducted by Hashemi et al. [20] on In a quasi-experimental clinical trial study (before and after), 51 patients with CAD scheduled for elective PCI were investigated provided that their Ejection Fraction

(EF) was > 30%. Before and three months after PCI, echocardiography was carried out to evaluate left ventricular indices including the E/e' (P =0.05).

And similar to the study conducted by Mandal et al. [21] on 100 patients. This study included 100 patients presented with ischemic cardiac chest pain, ejection fraction (EF) less than 55%, significant coronary occlusion (>70%) in a recent angiography, and were candidates for PCI. Echo study was done before and 3 months after PCI including conventional echo and TDI of both LV functions.

Significant improvement in the global LV systolic and diastolic functions occurs after PCI in patients with baseline impaired LV systolic function owing to coronary artery disease as assessed using conventional echo, TDI (P >0.001).

4. CONCLUSION

This work had studied and explored the predictive factors for left ventricle ejection fraction improvement. Those factors were: Male gender, DM, CKD, time between presentation and PCI, normal ECG finding, hyper urecemia, presence of angina pain, decrease heart rate, presence of chest pain and dyspnea, absence of CTO lesion, single vessel affection and administration of ACEI and Clopidogrel.

5. LIMITATION

1. The small sample size is a limitation, due to short study duration and the fact that study population represent only the subset of patients that had survived after revascularization.
2. The short duration of follow up.
3. Difficult tracking of the patients.

CONSENT

Written informed consent was obtained from all patients in this study.

ETHICAL APPROVAL

Ethics approval and consent to participate: this study was approved by the local ethics committee of Faculty of Medicine, Tanta University, Egypt.

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COMPETING INTERESTS

The authors declare that they have no conflicts of interest concerning this paper.

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