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A Survey of LV Ejection Fraction at One Year Follow up after Successful Percutaneous Coronary Intervention for Left Coronary Chronic Total Occlusions in Imam Ali Hospital of Kermanshah in 2010-2013

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Abstract: The objective of the present study was to determine the Left Ventricular (LV) function at 1 year follow-up of patients with chronic total occlusion of the left main coronary artery who underwent successful treatment at Imam Ali Hospital of Kermanshah, Iran from 2010-2013. This cross-sectional analytical study included 128 patients who were diagnosed by chronic total occlusion of the left main coronary artery and underwent coronary angiography and successful PCI (Percutaneous Coronary Intervention) from 2010-2013. The sampling method was convenient method. The required data were gathered using a questionnaire and included demographic data such as age, gender, family history of cardiac diseases, diabetes mellitus, hypertension, hyperlipidemia, cigarette smoking, opioid abuse as well as LV ejection fraction based on echocardiography examination. The data were analyzed using the SPSS Software (Ver. 20.0) using descriptive indices and the Kolmogorov-Smirnov and Wilcoxon tests. The results showed that PCI in chronic total occlusion was effective on LVEF. Gender, family history of cardiac diseases, cigarette smoking, opioid abuse, hyperlipidemia and hypertension had no effect on this outcome. It is recommended to perform PCI in chronic total occlusion in suitable patients.

Key words: Percutaneous coronary intervention, chronic total occlusion, ejection fraction, left ventricle, diabetes mellitus, hyperlipidemia, cigarette smoking, opioid

INTRODUCTION

Chronic Total Occlusion (CTO) is defined as sudden ending in the coronary epicardialarteries. Retrograde and anterograde collaterals are important in determining the length of the segment with CTO. Successful crossing of a guide-wire through a CTO is dependent on the lesion length and morphological factors such as bridging collaterals and lesion length of >15 mm. Newer generations of guide-wires and more experienced cardiologists has yield higher rate of succesful management of such patients. However, CTO is still a major reason to refer the patients for doing Coronary Artery Bypass Grafting (CABG) (Mann *et al*., 2014).

CTO diagnosis plays a major role among patients who present repeatedly for CABG or medical treatment. The advantages of doing Percutaneous Coronary Intervention (PCI) in CTO include improvement of symptoms, patient's health, improvement in the Left Ventricular (LV) function, decreased need for CABG and better survival rate (Grantham *et al*., 2009). The main value of revascularizations in PCI is to improve the symptoms of patients with chronic Coronary Artery Disease (CAD). PCI decreases mortality rate and Myocardial Infarction (MI) rate in acute coronary events compared to pharmacological therapy. However, these two treatments have comparable effects on stable angina (Mann *et al*., 2014). PCI has become more popular in management of CAD in the recent decades. Regardless of involved coronary arteries there are >1 million PVI prcedures annually performed in the US. It is estimated that PCI be used 1-5 times more commonly in the following decades owing to the increasing rate of obesity and diabetes in the communityas well as the fact that population is aging. Performing PCI in CTO is less common than other forms of coronary artery involvement due to less successful rate of this procedure (Sohrabi *et al*., 2013). Other reasons for not using CTO-PCI include increased risk of coronary

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artery occlusion and the need to perform PCI for the second time as well as increased rate of complications of this procedure (Mann *et al*., 2014). The exact mechanisms responsible for improved survival in CTO-PCI are not known but possible mechanisms includefewer rate of arrhythmias in the future, better LV function,, reduction in the extent of ischemia, better toleration of possible future MIs in other coronary arteries without CTO, decreased need for doing CABG and fewer rate of Acute Coronary Syndrome (ACS) rate in the future (Grantham *et al*., 2009).

Several studies have shown that the average cardiac output has increased after PCI (Salehi *et al*., 2016; Hoebers *et al*., 2015; Buszman *et al*., 2007). But in a 3 month follow-up study it was shown that cardiac output decreased. LV Ejection Fraction (LVEF) increased from 56.9-49.3% after 3 month after performing PCI. However, at 3 year follow-up, LVEF reached 46.8%.

It seems that opening of CTO can have effect on cardiac output. However, this is a matter of controversy and not enough studies have been performed. Here we intended to determine the role of PCI in management of TCO at 1 year follow-up in patients who were treated successfully with this method.

MATERIALS AND METHODS

This study was performed from 2010-13 at our university hospital. The study population consisted of all patients for whom coronary angiography was done and CTO of the left main coronary artery was diagnosed. They underwent successful PCI. Sampling method was of convenience method. Exclusion criteria were those medical records with defective data, the patients who were not able to be followed up, involvement of the right coronary artery or those who dies of any reason. The sample size was calculated using the reference number 8 and variables of quality of life and the maximum number was calculated as 128 subjects.

The data were gathered using a checklist. These included demographic data including gender, age, family history of CAD, diabetes mellitus, hypertension, hypercholesterolemia, cigarette smoking and opium usage. The LVEF was also reviewed using the echocardiographic data. All patients underwent echocardiography after PCI. The patients were followed over one year.

The written informed consent was obtained from all patients. The data were analyzed using the SPSS Software (Ver. 20). Descriptive indices including mean and its standard deviation were used to express the data. Also, the normal distribution of the data was determined by the Kolmogorov-Smirnov test. For analytical purposes, the Mann-Whitney U test and Wilcoxon test were used. The significance level was set at 0.05.

RESULTS AND DISCUSSION

There were 128 patients which included 87 males (68%) and 41 females (32%). Cigarette smoking was positive in 41 cases (32%), opium use in 28 cases (21.9%), hypertension in 61 cases (47.7%), hyperlipidemia in 56 cases (43.8%), diabetes in 35 cases (27.3%) and family history of CAD in 40 cases (31.2%). Table 1 presents the Wilcoxon test result of cardiac output before and afterPCI. As seen, mean LVEF increased significantly from 45.07 (7.55)-53.12(7.88%) after PCI which shows increased cardiac output Table 1.

Table 2 presents difference of LVEF before and after PCI based on baseline variables. Mean LVEF in hypertensive patients was 45.56 (7.71%) before PCI which increased to 53.68 (8.05%) after PCI. In those without hyperlipidemia, mean LVEF was 44.55 (7.42%) which increased to 52.61 (7.73%) after PCI. The changes seen in patients with and without hypertension were not significant. It can be stated that hypertension did not have effect on PCI outcome.

Mean LVEF was 46.09 (6.56%) in females before PCI which increased to 54.14 (7.06) after PCI. In males, this figure was 44.59 (7.96) before PCI and increased to 52.64 (8.24) after PCI. The change was higher in females but this was not statistically significant and the difference observed was relatively comparable between the genders. It can be stated that the effect of PCI on LVEF is independent of gender. The results showed that the increase observed in LVEF in patients with positive family history of CAD was more significant than those without this history. Although, LVEF was higher before PCI in those with this history, it was not statistically different (Table 2).

The results obtained here demonstrated that PCI increased LVEF significantly from a mean value of 45-53%. This is compatible with former studies (Salehi *et al*., 2015; Hoebers *et al*., 2015; Buszman *et al*., 2007; Mehran *et al*., 2011). But in study of Bitnz who evaluated LVEF of PCI patients in several time points concluded that mean LVEF before PCI was 46.9%

Table 1: The Wilcoxon test result to determine the difference of cardiac output before and after PCI

Variable	Cardiac output before PCI	Cardiac output after PCI	Z-value	Sig.
Mean	45.07 (7.55)	53.12 (7.88)	-9.17	<0.001

Table 2: The Mann-Whitney U test results to compare left ventricular ejection fraction before and after PCI based on demographic variables

Variables	Categories	Pre-PCI LVEF	Post-PCI LVEF	Difference
Hypertension	Yes	45.65 (±7.71)	53.68 (±8.05)	8.03 (±5.02)
	No	44.55 (±7.42)	52.61 (±7.73)	8.05 (±5.14)
	p-value	0.4	0.17	0.96
Diabetes	Yes	45.42 (±8.85)	52.28 (±1.05)	6.85 (±5.56)
	No	44.94 (±7.05)	53.44 (±6.67)	8.49 (±4.82)
	p-value	0.34	0.81	0.17
Hyperlipidemia	Yes	46.51 (±6.31)	54.28 (±7.16)	7.76 (±5.03)
	No	43.95 (±8.26)	52.22 (±8.34)	8.27 (±5.11)
	P-value	0.16	0.09	0.7
Gender	Male	44.59 (±7.96)	52.64 (±8.24)	8.04 (±5.19)
	Female	46.09 (±6.56)	54.14 (±7.06)	8.04 (±4.85)
	p-value	0.24	0.31	0.75
Smoking	Yes	44.14 (±8.05)	52.68 (±8.81)	8.53 (±4.90)
	No	45.51 (±7.31)	53.33 (±7.45)	7.81 (±5.15)
	p-value	0.228	0.786	0.35
Opium use	Yes	44.01 (±9.23)	51.07 (±9.84)	6.96 (±5.32)
	No	46.96 (±5.32)	45.35 (±7.04)	53.7 (±7.19)
	P-value	0.89	0.25	0.23
Family history of CAD	Yes	46 (±6.62)	55.12 (±5.82)	9.12 (±5.41)
	No	44.65 (±7.94)	52.21 (±8.53)	7.55 (±4.85)
	p-value	0.39	0.04	0.2

and increased to 49.3% after 3 month. However, after 3 year follow-up this decreased to 46.8%. This demonstrates the important role of time after PCI.

The researchers admit that the main reason for effectiveness of PCI on cardiac output is due to re-opening of occluded vessel and re-angiogenesis. This re-angiogenesis initiates 12 h-14 days after PCI and improves the cardiac output. Also, the contractility of the left ventricle improves in long-term. This has an important role in increase seen in cardiac output. It should be mentioned that these effects can be adjusted by factors such as angioplasty technique, using low-profile stents and anti-platelets such as glycoprotein receptor antagonists (Hoebers *et al*., 2015; Silva *et al*., 205). Considering the above mentioned facts, it seems that LVEF in PCI patients can be affected by demographic factors and clinical indicators (Cho *et al*., 2014). Also, there is evidence that if PCI is done late in patients with MI has no effect on improvement of LVEF (Nozari *et al*., 2012) which needs more studies to be elaborated.

Since, LVEF changes in hypertension group (the difference before and after PCI was 8.03%) did not have statistical difference compared to the group without hypertension (the difference of 8.11%), it can be concluded that hypertension has no effect on PCI outcomes. There was not enough evidence in the literature about the role of hypertension in cardiac output. However, regarding the fact that about half of CAD cases are associated with hypertension and it is a major factor of heart failure in such patients, hypertension should be assessed in these patients (Ali *et al*., 2011). This finding is compatible with former studies (Lee *et al*., 2012; Cecchi *et al*., 2014).Cecchi *et al.* (2014) showed that there was no significant difference between patients with hypertension who underwent PCI and those without hypertension regarding cardiac output and clinical outcomes. Other researchers reported that hypertension can have adverse effects on LV function and structure through LV hypertrophy (Bisognano *et al*., 2011). Also, in the study of Koo mean LVEF of patients with hypertension (53.5%) was higher than those without hypertension (51.8%) (Cho *et al*., 2014) which are in contrast to our results. Some studies report that in patients with CAD with hypertension, decreasing blood pressure can decrease myocardial perfusion and probably result in cardiac attack (Wallentin *et al*., 2009). Since, there are controversies regarding this issue and lack of enough information, it seems that further studies are required.

The results showed that diabetes did not have significant effect on cardiac output before and after PCI. There was no significant difference before and after PCI in diabetic patients vs. those without diabetes. This is compatible with some previous reports (Mathew *et al*., 2004; Harjai *et al*., 2003). Diabetes has no significant effect in short-term outcomes of angioplasty (after 1 month) in patients without MI. However, mortality and complications were more frequent in long-term in diabetics (Norhammar *et al*., 2010; Hasdai *et al*., 2000). Researchers advocate that diabetic patients suffer complications such as chronic inflammation and exudative stress which have major role in atherosclerosis and despite angiogenesis techniques and pharmacological therapies, these complications still occur (Mathew *et al*., 2004). Therefore, considering these complications and other basic structural disorders in such patients, Lee *et al*. (2010) in a meta-analysis showed that since diabetic patients have high mortality rate when undergoing CABG and cerebral vascular disorders, it has been suggested that PCI be substituted to CABG as a safer method.

Although, hyperlipidemia and high Low-density Lipoprotein (LDL) have been recognized as important factors leading to high mortality in MI patients and in fact are recognized as major cardiovascular diseases risk factors (Miura *et al*., 2016), we did not find any significant effect of hyperlipidemia on clinical outcome of PCI. This contradicts some previous studies (Makaya *et al*., 2009; Cho *et al*., 2010). It should be mentioned that LDL-C/HDL-C is an important predictive factor for CAD and values lower than 2 are desirable for prevention of cardiac diseases. In order to prevent complications in patients with established CAD, this rate should be lower than 1.5 (Nakamura *et al*., 2008; Nicholls *et al*., 2007). The detrimental effects of hyperlipidemia on CAD have been documented in several studies (Raal *et al*., 2012; Mihaylova *et al*., 2012). Therefore, for better illustration of the relationship between hyperlipidemia and cardiac output, further studies are required.

According to the obtained results, although the changes in LVEF detected were greater in females, the difference was not statistically significant. Hence, it could be concluded that gender has no effective role on PCI outcome. In contrast to our study, a former report showed that gender is a significant factor in cardiac output (Guo *et al*., 2014). The authors of the mentioned study showed that mean LVEF was significantly lower in females before PCI and one day and six months after PCI. However, in another study which evaluated clinical characteristics and heart failure outcomes of patients, it was reported that cardiac output was higher in females. In this study, the background characteristics were different between two genders. For example, females had higher rate of obesity and renal failure but lower rate of Ischemic Heart Disease (IHD), arrhythmias and obstructive lung diseases. Subsequent to these differences, the risk of mortality because of heart failure was lower in women (Lam *et al*., 2015). However, there are studies which reported higher likelihood of heart failure following MI and primary and secondary complications in females than in males (Lam *et al*., 2015; Reynolds *et al*., 2012).

Regarding the challenging topic of the effect of gender on cardiac output, the reason of these differences should be investigated regarding background factors such as age, residential place, the time of presentation to doctor after becoming symptomatic, follow-up adherence after PCI and even the dominant culture of the region. In Iran, due to various causes, health indicators are better in females than in males (Bakhshi *et al*., 2015). The rate of metabolic syndromes is higher in Iranian females compared to males and females of other countries (Nezhad *et al*., 2012). Iranian men with cardiac conditions have better quality of life than Iranian women. This is attributed to physical characteristics, better spirit, cultural issues, more prominent role of men in social activities and higher rate of physical activities in men (Yaghoubi *et al*., 2012). The reason that we did not find any differences between the two genders regarding cardiac output can be adjusted by background variables.

According to our findings, cardiac output before and after PCI was generally lower in smokers than in non-smokers but this was not statistically significant. Also, in both groups LVEF improved which shows effectiveness of PCI in both groups. A former study showed that smoking is one of the predictive factors for heart failure and has less prominent role in decreasing cardiac output than older age, valvular diseases and diabetes mellitus (Ho *et al*., 2013). The rate of heart failure is estimated to be 21 times higher in smokers than in non-smokers (Gopal *et al*., 2012). Another study evaluated the effect of smoking on PCI outcome and reported that cardiac output was significantly lower in smokers than in non-smokers after 1 year of follow-up (52 vs. 55%) which are in contrast to our findings (Jang *et al*., 2015).

Opium use had no effect on cardiac output before and after PCI. This is in compatible with some studies (Sharafi *et al*., 2014; Davoodi *et al*., 2006).

Patients who had positive family history of CAD had significantly higher LVEF after 1 month post-PCI than those who did not such history. Reviewing the literature, we did not find any study that evaluated the influence of family history on cardiac output independently. However, a study which assessed cardiac output after PCI showed that no difference existed between two group with and without family history of CAD regarding successful rate of PCI ($p = 0.0662$) and both groups have similar risk for unsuccessful PCI (Rathore *et al*., 2009). Dimayer also evaluated the effect of family history of CAD on function and structure of the LV by echocardiography which showed family history of CAD had significant effect on LV volume and interventricular wall thickness but no effect on cardiac output (Meyer *et al*., 2013). Jin *et al*. (2011) also documented the insignificant role of family history of CAD on LV function and structure. Regarding the importance of LV structure in myocardial contraction and effective cardiac output (Szelenyi *et al*., 2015), despite what we observed here, the effect of family history on cardiac output is established. This effect can be due to other confounding factors such as family history of obesity, opium use and diet. This issue needs more studies for better clarification.

CONCLUSION

According to our findings, PCI improved cardiac output which is thought to be due to better myocardial perfusion and angiogenesis in coronary arteries. Of basic characteristics, only family history of CAD had effect on higher LVEF after PCI. However, this finding should be interpreted with caution as other factors may have role. More studies are required in this regard. Cardiac output improvement was independent of diabetes, hypertension, hyperlipidemia, smoking and opium use.

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