Original Article

Comparison between Revascularization and Optimal Medical Therapy in Patients with Stable Angina Pectoris

***Maryam Nabati**[1] Ehsan Vazirian[2] Ali Ghaemian[1] Jamshid Yazdani[3] Maryam Hosseinzadeh[4]

1- Department of Cardiology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
2- Department of Cardiology, School of Medicine, Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran
3- Department of Biostatics, School of Health, Mazandaran University of Medical Sciences, Sari, Iran
4- Department of Cardiology, Fatemeh Zahra Hospital, Mazandaran University of Medical Sciences, Sari, Iran

***dr.Mr.Nabati@gmail.com**

(Received: 9 Oct 2015; Revised: 21 Mar 2016; Accepted: 25 May 2016)

Abstract

Background and Purpose: Regarding usefulness of revascularization versus optimal medical therapy in patients with stable angina pectoris, data are challenging. The aim of this 12-month follow-up study was to compare the survival benefit associated with revascularization versus optimal medical therapy on the patients with stable angina pectoris.

Materials and Methods: A prospective clinical study was conducted on 181 patients with stable angina pectoris or an evidence of myocardial ischemia that underwent coronary arteriography. Patients with left main or left main equivalent were excluded from our study. Of these patients, 57 received full medical therapy alone, 79 were assigned to the percutaneous coronary intervention (PCI) and 45 to the coronary artery bypass graft (CABG) group. The patients were compared for primary outcomes including cardiac death and non-fatal myocardial infarction and secondary outcomes including disabling angina by chi-square and Fisher's exact test.

Results: After 12 months, cardiac death occurred in 8.8% of patients in the medical group and 0.0% of patients in the PCI and CABG group. This was statistically significant (P = 0.004). Disabling angina occurred in 23.1% of patients in the medical group, 17.7% of patients in the PCI group, and 15.5% of patients in CABG group (P = 0.349). Cerebrovascular accident occurred in 1.9% of patients in the medical group, 1.3% of patients in the PCI group, and 6.7% of patients in CABG group (P = 0.167). These were not statistically significant.

Conclusion: Revascularization compared with the optimal medical therapy may be a better strategy in reducing cardiovascular mortality in patients with stable angina pectoris and suitable coronary anatomy.

*[*Nabati M, Vazirian E, Ghaemian A, Yazdani J, Hosseinzadeh M.* **Comparison between Revascularization and Optimal Medical Therapy in Patients with Stable Angina Pectoris**. *Iran J Health Sci 2016; 4(2): 71-80] http://jhs.mazums.ac.ir*

Keywords: Coronary Disease, Prognosis, Revascularization, Everolimus, Stent

1. Introduction

Patients with coronary artery disease (CAD) represent an inhomogeneous group, both anatomically and clinically. Symptoms can encompass a broad range from sudden death to no symptom (1). However, untreated CAD eventually culminates in refractory angina, myocardial infarction (MI), heart failure, and death (2). The treatment of stable angina has two major concerns. The goals of the treatment include relief of symptoms, inhibition or slowing of disease progression, prevention of future cardiac events such as MI and improved survival. Treatment guidelines recommend an initial approach with intensive medical therapy, risk factor modification, and lifestyle modification (known as optimal medical therapy) (3, 4). Recommendations for the treatment of stable angina were largely based on previous clinical trials comparing percutaneous coronary artery intervention (PCI) to medical therapy and PCI to coronary artery bypass grafting (CABG). However, there are several important limitations regarding the applicability of the results of these trials to current practice:

In patients who received bare metal stents, current antithrombotic (e.g., clopidogrel), and anticoagulant (e.g., glycoprotein IIb/IIIa inhibitors) regimens were not used. Furthermore, in the most recent trials, drug-eluting stents (DES) that significantly decrease the rate of restenosis were used in the less percentage of patients. Furthermore, in patients who underwent CABG, saphenous vein graft use was more prevalent than internal mammary arteries that are associated with more long-term graft patency and patient survival (2). Therefore; the aim of our study was to determine whether revascularization with PCI or CABG reduces cardiovascular outcomes when compared with medical therapy in patients with stable CAD.

2. Materials and Methods

From 2012 to 2013, a prospective 12-month follow-up study was conducted. 181 patients with Canadian Cardiovascular Society (CCS) Class II-IV stable angina or evidence of myocardial ischemia on the resting electrocardiogram (ECG) or during stress test who underwent coronary arteriography were included in our study. The study was performed according to the guidelines of the Helsinki Declaration and was approved by the Ethics Committee of the Hospital. Written informed consent was obtained from all patients. Demographic, clinical and echocardiographic data were collected from the study population. Transthoracic echocardiography was performed within 24 hours before coronary angiography for all patients by a Vivid S5 (GE Healthcare, Wauwatosa, WI, USA), 1-3 MHz transducer. Left ventricular (LV) ejection fraction (LVEF) was defined as end diastolic volume (EDV) minus end systolic volume divided by EDV from biplane apical two and four chamber views using modified Simpson' technique.

Entry criteria included stenosis of at least 70% in at least one epicardial coronary artery and objective evidence of myocardial ischemia (typical angina or significant ST-segment depression or T-wave inversion on the resting ECG or

inducible ischemia with exercise stress). The patients with fever, immune deficiency, autoimmune disorders, concomitant valvular or other heart disease, predominant congestive heart failure, LV systolic function of < 35%, unsuitable coronary anatomy, and significant left main stenosis or left main equivalent disease were excluded from this study. The follow-up period was 12-month.

Hypertension (HTN) was defined as a systolic blood pressure ≥ 140 mm Hg, a diastolic blood pressure ≥ 90 mm Hg, or requiring antihypertensive medication (5). Blood samples were obtained during fasting, and levels of plasma glucose and total cholesterol (T-chol) were measured. Hyperlipidemia (HLP) was defined as T-chol > 200 mg/dl or requiring cholesterol-lowering drugs. Diabetes mellitus (DM) was defined according to the criteria of the American Diabetes Association or requiring insulin or oral hypoglycemic drugs (6). All patients received antiplatelet therapy with aspirin at a dose of 80 mg/day, Medical anti-ischemic therapy included beta-blockers, calcium channel blockers (if beta blockers were contraindicated or not tolerated), and nitrates, along with aggressive cholesterol-lowering therapy, angiotensin converting enzyme inhibitors, and glycemic control. PCI was performed in patients with CCS Class II-IV angina and/or evidence of myocardial ischemia and at least 70% stenosis in at least one epicardial coronary artery with suitable anatomy for intervention and XIENCE stents (Everolimus Eluting Coronary Stent System, 3200 Lakeside Drive, Santa Clara, CA 95054, USA) were used.

Procedural success was defined as the successful deployment of the stent and residual stenosis < 30% (7). Clopidogrel for an average of 12 months was prescribed in patients who had undergone PCI. CABG was performed in patients with the diffuse three-vessel coronary disease or left anterior descending stenosis that had unfavorable anatomy for PCI. Other patients with suitable coronary anatomy for revascularization, who refused revascularization, received optimal medical therapy.

Follow-up was obtained by review of hospital databases and direct interviews. Thereafter, primary and secondary end points were determined. Primary endpoints were cardiac death and non-fatal MI. Cardiac death was described as death owing to acute MI, congestive heart failure, life-threatening arrhythmias, or cardiac arrest; also, unpredictable sudden death was recognized as cardiac death. MI was described as the exhibition of new symptoms of myocardial ischemia or ischemic ECG changes associated with augmentation in markers of myocardial necrosis. Secondary endpoints were persisting disabling angina (CCS Class III-IV angina) (2).

Continuous variables are expressed as the mean ± standard deviation. Categorical variables were compared with a chi-square test and Fisher's exact test and continuous variables were compared using the ANOVA test. A $P < 0.050$ was considered statistically significant. Confounder effects were determined by model selection log-linear analysis. All statistical calculations were performed using SPSS Software (version 18; SPSS Inc., Chicago, IL, USA).

Table 1. Baseline clinical and echocardiographic characteristics

Characteristics	Medical group (N = 57)	PCI group (N = 79)	CABG group (N = 45)	P value
Age (years)	63.96 ± 11.47	60.51 ± 9.40	60.38 ± 10.90	0.110
Sex N (%)				
Male	33 (58)	45 (57)	30 (67)	0.540
Female	24 (42)	34 (43)	15 (33)	
Diabetes	20 (35.1)	26 (32.9)	14 (31.1)	0.910
HTN	24 (42.1)	31 (39.2)	12 (26.7)	0.240
HLP	37 (64.9)	36 (45.6)	18 (40)	0.024
LVEF (%)	48.77 ± 8.72	52.15 ± 5.70	50.44 ± 6.90	0.430

CABG: Coronary artery bypass grafting, LVEF: Left ventricular ejection fraction, PCI: Percutaneous coronary intervention, HTN: Hypertension, HLP: Hyperlipidemia

3. Results

Our study included a total of 181 patients. A total of 73 women and 108 men were enrolled in the study population. The mean age was 61.56 ± 10.50 years. Within study population, 60 patients (33.1%) were diabetic; 67 patients (37%) were hypertensive; 91 patients (50.3%) had HLP. Mean LVEF was 50.66% ± 7.17%. Of these patients, 57 received full medical therapy alone, 79 were assigned to the PCI, and 45 to the CABG group. Clinical, echocardiographic and angiographic characteristics of the patients are summarized in tables 1 and 2.

There was no significant difference in average age and LVEF between the groups. Furthermore, there was no significant difference in DM and HTN prevalence between them. HLP was significantly more frequent among patients on medical therapy.

After 12 months, cardiac death occurred in 8.8% of patients in the medical group and 0.0% of patients in the PCI and CABG group. Fisher's exact test showed that it was statistically significant (Figure 1).

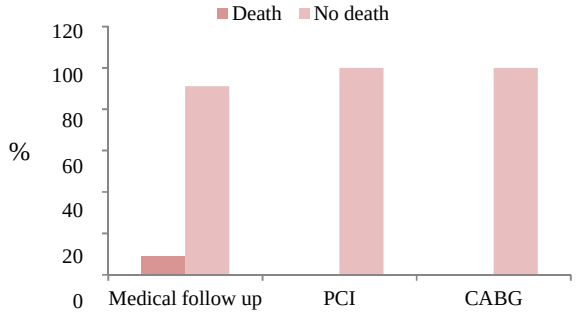

Figure 1. Correlation between cardiac death and treatment modality in patients with stable angina pectoris.
CABG: Coronary artery bypass grafting, PCI: Percutaneous coronary intervention

Primary outcome (including cardiac death and non-fatal MI) occurred in 22.3% of patients in the medical group, 16.5% of patients in the PCI group, and 15.6% of patients in CABG group. Disabling angina (Functional Class III and IV) occurred in

Table 2. Angiographic characteristics of subjects categorized by treatment modality

Angiographic characteristics	Treatment modality			P value
	Medical group N (%)	PCI group N (%)	CABG group N (%)	
Single vessel disease	13 (22.8)	31 (39.2)	2 (4.4)	< 0.001
Two vessel diseases	19 (33.3)	29 (36.7)	10 (22.2)	
Three vessel diseases	25 (43.9)	19 (24.1)	33 (73.4)	

CABG: Coronary artery bypass grafting, PCI: Percutaneous coronary intervention

Table 3. Primary and secondary outcome of subjects categorized by treatment strategy

Adverse cardiovascular outcomes	Medical group N = 57 (%)	PCI group N = 79 (%)	CABG group N = 45 (%)	P value
Clinical symptoms at 12 months				
FCI	21 (40.4)	35 (44.3)	27 (60.0)	0.397
FCII	19 (31.7)	30 (50.0)	11 (24.4)	
FCIII	11 (21.2)	12 (15.2)	5 (11.1)	
FCIV	1 (1.9)	2 (2.5)	2 (4.4)	
CVA at 12 months	1 (1.9)	1 (1.3)	3 (6.7)	0.167
MI at 12 months	7 (13.5)	13 (16.5)	7 (15.6)	0.896
Admission at 12 months	20 (38.5)	32 (40.5)	18 (40)	0.972
Death	5 (8.8)	0 (0.0)	0 (0.0)	0.004
Primary outcomes at 12 months	12 (22.3)	13 (16.5)	7 (15.6)	0.822
Disabling angina at 12 months	12 (23.1)	14 (17.7)	7 (15.5)	0.349

CABG: Coronary artery bypass grafting, CVA: Cerebrovascular accident, FC: Functional class, MI: Myocardial infarction, PCI: Percutaneous coronary intervention

23.1% of patients in the medical group, 17.7% of patients in the PCI group, and 15.5% of patients in CABG group (Table 3).

Cerebrovascular accident (CVA) occurred in 1.9% of patients in the medical group, 1.3% of patients in the PCI group and 6.7% of patients in CABG group (Figure 2).

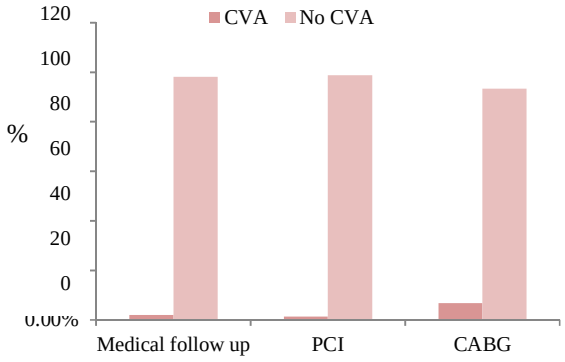

Figure 2. Correlation between cerebrovascular accident and treatment modality in patients with stable angina pectoris.
CABG: Coronary artery bypass grafting, CVA: Cerebrovascular accident, PCI: Percutaneous coronary intervention

Moreover, hospitalization for acute coronary syndrome or decompensated heart failure occurred in 38.5% of patients in the medical group, 40.5% of patients in the PCI group, and 40.0% of patients in CABG group. These were not statistically significant. Fisher's exact test did not show any significant difference between death and number of diseased vessels (Table 4).

Table 4. The relationship between death and number of diseased vessels

Death	Number of diseased vessels			P value
	One vessel (%)	Two vessels (%)	Three vessels (%)	0.727
Yes	2 (1.1)	1 (0.6)	2 (1.1)	
No	44 (24.3)	57 (31.5)	75 (41.4)	

Therefore, we did not enter vessel score as a confounder in the log-linear model. For determining the confounding effect of HLP on mortality, a model selection log-linear analysis was used. Mortality was not correlated with HLP state (P = 0.440) (Table 5).

Table 5. Log linear model for determining confounder effect of Hyperlipidemia (HLP) on death

Step[a]	Effects	Chi-square[c]	df	Significance	Number of iterations
0					
Generating Class[b]	Treatment*death*HLP	< 0.001	0		
Deleted effect					
1	Treatment*death*HLP	< 0.001	2	1.000	3
1					
Generating Class[b]	Treatment*death, treatment*HLP, death*HLP	< 0.001	2	1.000	
Deleted effect					
1	Treatment*death	10.518	2	0.005	2
2	Treatment*HLP	6.227	2	0.044	2
3	Death*HLP	0.595	1	0.440	2
2					
Generating Class[b]	Treatment*death, treatment*HLP	0.595	3	0.897	
Deleted effect					
1	Treatment*Death	11.867	2	0.003	2
2	Treatment*HLP	7.576	2	0.023	2
3					
Generating Class[b]	Treatment*Death, treatment*HLP	0.595	3	0.897	

a, b, c: P value less than 0.05 was considered significant.
HLP: Hyperlipidemia

4. Discussion

Appreciating the significant differences between an invasive and non-invasive approach, researchers have conducted large clinical trials to assess and compare medical therapy to revascularization and CABG to PCI. Despite limited applicability, these studies created the basis for clinical practice guidelines and evidence-based care.[1] Stents control two of three mechanisms of restenosis including initial elastic recoil and late remodeling. However, they cannot reduce intimal hyperplasia. Indeed, stents may increase it (8). The introduction of stents that release drugs with inhibition on intimal hyperplasia may reduce or eliminate the main limitation of angioplasty (9). Polymer-based paclitaxel-eluting stents and sirolimus-eluting stents have been shown to significantly reduce angiographic restenosis in comparison with bare metal stents. However, the rates of primary stent thrombosis are increased. With the goal of further augmenting the security and effect of DES, an everolimus-eluting stent (EES) has been designed (10). In our study, an EES was used in all patients who underwent PCI. Gimelli et al. evaluated the effects of coronary revascularization in 180 patients with LV dysfunction with and without angina symptoms for 3 years. They concluded that patients with LV dysfunction, maintained viability and without angina symptoms may benefit from coronary revascularizationv (11).

In BARI 2D trial from 2001 to 2005, 2368 patients with Type 2 diabetes and heart disease were randomly assigned to

undergo either revascularization with intensive medical therapy or intensive medical therapy alone. At 5 years, there was no significant difference in the rates of death and major cardiovascular events between the two groups (12). Otherwise, in patients who received bare metal stents, the current antithrombotic (e.g., clopidogrel) and anticoagulant (e.g., glycoprotein IIb/IIIa inhibitors) regimens were less commonly used. Furthermore, drug-eluting stents that significantly decrease the rate of restenosis were used in a smaller percentage of patients. In addition, in patients who underwent CABG, saphenous vein graft use was more prevalent than internal mammary arteries, which are associated with more long-term graft patency and patient survival (2).

Boden et al. in Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation trial compared an initial management strategy of PCI combined with intensive optimal medical therapy with a strategy of deferred PCI and optimal medical therapy on 2287 patients at the follow-up period of 2.5-7 years. Nearly, one-third of patients had single-vessel disease. At 5 years, there was no difference in rates of death, MI, stroke or hospitalization between the two treatment groups. However, PCI was associated with more relief of angina. DES was used in only 15% of patients (13).

Hueb et al. in Medicine, Angioplasty, or Surgery Study-II trial evaluated a randomization on 611 patients who were assigned to CABG (n = 203), PCI (n = 205), or MT (n = 203) at 9-15 years. Lowest rate of primary endpoints (total mortality, Q-wave MI and refractory angina requiring revascularization) was seen in the CABG group, and the highest rate was seen in a medical therapy group. Stroke was relatively infrequent but appeared highest among CABG group (14). In this trial, none of the patients had single-vessel disease. Furthermore, patients with left main or left main equivalent were included in our study.

Pretorian et al. compared these three therapeutic options for stable angina pectoris on 98 patients, 36 patients to undergo PCI, 28 patients to undergo CABG, and 34 patients with optimal medical therapy alone during the follow-up period of 3-year. There was no significant difference in primary and secondary endpoints between these subgroups. However, there was no statistically significant difference in favor of revascularization compared with optimal medical therapy (2).

de Bruyne et al., in Fame 2 trial measured FFR in all patients with significant coronary artery stenosis. Patients in whom at least one stenosis was functionally significant (FFR $\leq$ 0.80) were randomly assigned to FFR-guided PCI and the optimal available medical therapy (PCI group) or the optimal medical therapy alone (medical-therapy group). Recruitment was stopped prematurely due to a significant inter-group difference in the percentage of patients who had a primary endpoint event: 4.3% in the PCI group and 12.7% in the medical-therapy group ($P < 0.001$). The difference was produced by a lower rate of urgent revascularization in the PCI group than in the medical-therapy group (1.6% vs. 11.1%; $P < 0.001$); notably, in the PCI

group, lesser urgent revascularizations were elicited by a MI or evidence of ischemia on electrocardiography (P < 0.001). Due to premature termination of the study (mean follow-up period was 7 months), differences in the rates of death and MI between the strategies of PCI and medical therapy alone could not be confirmed (15).

Hannan et al. evaluated 933 patients with stable CAD undergoing cardiac catheterization between 2003 and 2008. Patients receiving routine medical treatment (RMT) or PCI with RMT. Patients who received PCI experienced significantly lower mortality, MI and revascularization rates (16).

Wijeysundera et al. compared routine medical therapy with PCI or CABG in 39,131 patients with stable ischemic heart disease. Mean follow-up was 2.5 years. Revascularization was associated with fewer deaths [hazard ratio (HR): 0.76; 95% confidence interval (CI): 0.68-0.84; P < 0.001], MI (HR: 0.78; 95% CI: 0.72-0.85; P < 0.001) and repeat PCI/CABG (HR: 0.59; 95% CI: 0.50-0.70; P < 0.001) than medical therapy (17).

Again in another study, de Bruyne et al. compared FFR-guided PCI with medical therapy alone in 1220 patients with stable CAD. The primary end point was a composite of death from any cause, non-fatal MI, or urgent revascularization within 2 years. The rate of death or MI from 8 days to 2 years was lower in the PCI group than in the medical-therapy group (4.6% vs. 8.0%, P = 0.040) (18). In our study, CABG and PCI were associated with significant mortality benefits compared with medical therapy alone. MI, disabling angina and admission rate were lowest and CVA rate was highest in CABG group. Lowest rate of CVA was seen in PCI group. Disabling angina was less prevalent in PCI group compared with medical therapy group. These findings were not statistically significant. It may be due to smaller sample size and short follow-up period.

Limitations

The study is single-center design which can certainly overlook patient and center specific characteristics related to the wide spectrum of stable angina. Another limitation of our study was the small sample size. Furthermore, our follow-up period was 1-year.

Conclusion

Revascularization compared with optimal medical therapy may be a better strategy in reducing cardiovascular mortality in patients with stable angina pectoris and suitable coronary anatomy. Larger sample size and longer follow-up period in future studies is recommended.

Conflict of Interests

The Authors have no conflict of interest.

Acknowledgement

This study was Dr. Ehsan Vazirian post-graduate's thesis. The authors would like to thank all of the patients who enrolled in this study and the staff at the Fatemeh Zahra hospital, Sari, Iran. Financial support was obtained from the Research Council of the Mazandaran University of Medical Sciences to Dr. Maryam Nabati, Assistant Professor, and Fellowship of Echocardiography.

References

1. Williams DO, Vasaiwala SC, Boden WE. Is optimal medical therapy "optimal therapy" for multivessel coronary artery disease? Optimal management of multivessel coronary artery disease. Circulation 2010; 122(10): 943-5.
2. Pretorian A, Borda A, Suciu C, Pretorian AM. Medical versus revascularization therapy in the management of stable angina pectoris. Acta Medica Marisiensis 2011; 57(2): 98-101.
3. Fraker TD, Fihn SD, Gibbons RJ, Abrams J, Chatterjee K, Daley J, et al. 2007 chronic angina focused update of the ACC/AHA 2002 guidelines for the management of patients with chronic stable angina: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Writing Group to develop the focused update of the 2002 guidelines for the management of patients with chronic stable angina. J Am Coll Cardiol 2007; 50(23): 2264-74.
4. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, Jacobs AK, Kern MJ, King SB 3rd, et al. ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention--summary article: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). Circulation 2006; 113(1): 156-75.
5. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003; 42(6): 1206-52.
6. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010; 33(Suppl 1): S62-S69.
7. Sasao H, Endo A, Hasegawa T, Oimatsu H, Takada T. Comparison of three-year clinical outcome of the multi-link stent with the Palmaz-Schatz stent in Japanese patients with coronary artery disease: a case control study. J Invasive Cardiol 2003; 15(8): 433-6.
8. Alonso JJ, Duran JM, Gimeno F, Ramos B, Serrador A, Fernandez-Aviles F. Coronary angioplasty in diabetic patients. Current and future perspectives. Rev Esp Cardiol 2002; 55(11): 1185-200. [In Spanish]
9. Regar E, Serruys PW. The Ravel trial. Zero percent restenosis: A cardiologists dream comes true! Rev Esp Cardiol 2002; 55(5): 459-62. [In Spanish]
10. Stone GW, Midei M, Newman W, Sanz M, Hermiller JB, Williams J, et al. Randomized comparison of everolimus-eluting and paclitaxel-eluting stents: Two-year clinical follow-up from the Clinical Evaluation of the Xience V Everolimus Eluting Coronary Stent System in the Treatment of Patients with de novo Native Coronary Artery Lesions (SPIRIT) III trial. Circulation 2009; 119(5): 680-6.
11. Gimelli A, Neto JA, Marcassa C, Ferrazzi P, Glauber M, Marzullo P. Beneficial effects of coronary revascularization in patients with ischaemic left ventricular dysfunction with and without anginal symptoms. Interact Cardiovasc Thorac Surg 2002; 1(1): 9-15.
12. Frye RL, August P, Brooks MM, Hardison RM, Kelsey SF, MacGregor JM, et al. A randomized trial of therapies for type 2 diabetes and coronary artery disease. N Engl J Med 2009; 360(24): 2503-15.
13. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, et al. Optimal medical therapy with or without PCI for stable coronary disease. N Engl J Med 2007; 356(15): 1503-16.

14. Hueb W, Lopes N, Gersh BJ, Soares PR, Ribeiro EE, Pereira AC, et al. Ten-year follow-up survival of the Medicine, Angioplasty, or Surgery Study (MASS II): A randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease. Circulation 2010; 122(10): 949-57.
15. de Bruyne B, Pijls NH, Kalesan B, Barbato E, Tonino PA, Piroth Z, et al. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. N Engl J Med 2012; 367(11): 991-1001.
16. Hannan EL, Samadashvili Z, Cozzens K, Walford G, Jacobs AK, Holmes DR, et al. Comparative outcomes for patients who do and do not undergo percutaneous coronary intervention for stable coronary artery disease in New York. Circulation 2012; 125(15): 1870-9.
17. Wijeysundera HC, Bennell MC, Qiu F, Ko DT, Tu JV, Wijeysundera DN, et al. Comparative-effectiveness of revascularization versus routine medical therapy for stable ischemic heart disease: A population-based study. J Gen Intern Med 2014; 29(7): 1031-9.
18. de Bruyne B, Fearon WF, Pijls NH, Barbato E, Tonino P, Piroth Z, et al. Fractional flow reserve-guided PCI for stable coronary artery disease. N Engl J Med 2014; 371(13): 1208-17.