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ORIGINAL ARTICLE

Effectiveness of Medical and Revascularization Procedures as the Initial Strategy in Stable Coronary Artery Disease: A Cohort Study

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Abstract

Background: Coronary artery bypass grafting surgery (CABG) and percutaneous coronary intervention (PCI) are widely-used strategies in the management of stable coronary artery disease (CAD).

Objective: To evaluate the prognosis of patients with stable CAD initially treated by medical therapy (MT), compared to the patients who were submitted to revascularization procedures.

Methods: We conducted a prospective cohort study of 560 patients from an outpatient clinic in a tertiary hospital, with a mean follow-up of 5 years. Patients were classified into MT (n = 288), PCI (n = 159) and CABG (n=113) groups according to their initial treatment strategy. Primary endpoints were overall mortality and combined events of death, acute coronary syndrome, and stroke.

Results: During follow-up, death rates were 11.1% in MT, 11.9% in PCI and 15.9% in CABG patients, with no statistical difference (hazard ratio [HR] for PCI, 1.05; 95% confidence interval [95%CI], 0.59 to 1.84; and HR for CABG, 1.20; 95% CI: 0.68 to 2.15). Combined outcomes occurred more often among patients initially submitted to PCI compared to MT (HR 1.50, 95% CI 1.05 to 2.14), and did not differ between MT and CABG patients (HR 1.24, 95% CI 0.84 to 1.83). Among patients with diabetes (n=198), PCI was the only therapeutic strategy predictive of combined outcomes (HR 2.14; 95% CI 1.25 to 3.63).

Conclusion: In this observational study of stable coronary artery disease, there was no difference in overall mortality between initial medical therapy or revascularization surgery strategies. Patients initially treated with PCI had greater chance to develop combined major cardiovascular events. (Int J Cardiovasc Sci. 2017;30(5):408-415)

Keywords: Coronary Artery Disease / surgery; Myocardial Revascularization; Medication Therapy Management; Percutaneous Coronary Intervention; Cohort Studies.

Introduction

Coronary artery bypass grafting (CABG) surgery and percutaneous coronary intervention (PCI) are widely used strategies in the management of coronary artery disease (CAD), associated with optimized medical therapy (MT). However, in the last years, evidence has narrowed the indication of revascularization procedures in stable patients, with conflicting results regarding the benefits and impact on mortality when comparing the initial treatment options.[1-9] Prior studies have suggested that PCI decreases symptoms without a long-term prognostic effect, even when compared to medical treatment alone.[7,8] More recent data reinforced the superiority of CABG in preventing major cardiac events in patients with multivessel disease, especially in patients with more complex coronary artery disease and diabetes.[10-12] However, these studies showed similar results between CABG and PCI when patients with less complex disease were evaluated.[10,12]

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Between 2005 and 2008, 166,514 PCIs were performed in Brazil by the Brazilian Public Health System (Sistema Único de Saúde - SUS), an annual average of 41,628 procedures or 22/100,000 inhabitants. Of these, 37% were elective in patients with stable CAD. Drug-eluting stents (DES) are not covered by SUS, and probably a significant proportion of the Brazilian patients do not have optimized medical therapy and access to revascularization procedures, with differences among geographic regions of Brazil.[13] Therefore, the results of many clinical trials might not be generalizable to real-world clinical practice.

Even in developed countries, there are gaps in literature regarding the effectiveness of treatment strategies in patients with stable CAD. There are few clinical trials comparing the therapeutic options and this lack of knowledge brings complexity to the decision-making process. The purpose of this study was to evaluate the long-term prognosis of patients with stable CAD treated with medical therapy alone as the initial treatment option, compared with patients submitted to PCI or CABG in a public hospital in Brazil.

Methods

Study population

This was a prospective cohort study in patients from an outpatient clinic in a tertiary care university hospital in Southern Brazil. Between 1998 and 2011, 560 consecutive patients with stable CAD were enrolled. All patients had documented CAD, which was defined by the presence of at least one of the following: documented history of acute myocardial infarction (AMI), surgical or percutaneous myocardial revascularization, a lesion > 50% in at least one coronary artery assessed by angiography, or the presence of angina and positive noninvasive testing of ischemia.[14]

Patients were divided into three groups, according to the baseline intervention strategy: MT, PCI, or CABG, which was adopted prior to study enrollment. During follow-up, patients were managed by a multidisciplinary team according to current guidelines and at the discretion of attending physicians. Patients who underwent PCI or CABG during follow-up were identified, although they were analyzed as originally classified. All enrolled patients had complete clinical and laboratory data at baseline, at least three visits and one year of follow-up. This study was approved by the Institutional Research and Ethics Committee.

Follow-up and endpoints

Stable patients were periodically assessed every 3-6 months. At each visit, a standardized register was filled in, which included the current disease history, cardiovascular risk factor control, new cardiac events (including admission data and invasive procedures), laboratory and cardiac exams and pharmacological and non-pharmacological treatment. Relevant comorbidities were evaluated by questionnaire and chart review.

The primary outcomes of interest were death from any cause and occurrence of a major adverse cardiovascular event (MACE), defined as acute coronary syndrome (ACS), stroke and death. Acute coronary syndrome was defined as a hospital admission for chest pain or related symptoms and a discharge diagnosis by a physician of AMI or unstable angina. All-cause mortality and need for revascularization (either surgical or percutaneous) were also assessed.

Statistical Analyses

Continuous variables were expressed as mean ± 1 Standard Deviation (SD) and non-continuous ones were expressed as median and interquartile range (IQR) and were compared using paired t-test or the Wilcoxon signed-rank test, as appropriate. Categorical data were presented as frequencies and were compared by Qui-square or Fisher's exact test. All tests were two-sided. Long-term outcomes were compared for those who initially underwent medical treatment, with the outcomes for those who underwent CABG and PCI, irrespective of stent type. The primary analysis evaluated the time to the first MACE. Survival curves were derived by Kaplan–Meier analysis and compared using log-rank tests. Multivariate Cox analyses were used to compare event-free survival among groups. In the multivariate analyses, parameters that were clinically or significantly associated with main outcomes were included in the models. Outcomes were adjusted for gender, age, diabetes, smoking, ventricular dysfunction, chronic kidney disease and presence of comorbidities such as peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disease (COPD), liver disease and cancer. Variables that had any effect on the variable of interest were selected by the manual and stepwise method ($p < 0.10$). All data

were analyzed using SPSS program (version 11.0.0; SPSS, Chicago, Illinois, USA) and P values less than 0.05 were considered significant.

Results

The mean follow-up of the study was 5.1 years. Of the 560 patients, 288 (51.4%) were initially managed with MT, 159 (28.4%) with PCI and 113 (20.2%) with CABG. Baseline characteristics of patients according to the management strategy are shown in Table 1. Patients in the PCI group were more likely to have previous AMI than the other two groups. Patients in the CABG group had more hypertension, dyslipidemia, left ventricular dysfunction and, as expected, greater proportion of patients with three-vessel coronary disease.

All-cause mortality occurred in 69 patients (12.3%), with an annual mortality incidence of 2.5%/year (13 events/year). The cumulative survival rates for patients assigned to each group were 89% for MT, 88% for PCI, and 84% for CABG (p = 0.82). During follow-up, 115 patients (20.5%) underwent PCI and 56 patients (10%) underwent CABG. The rate of events and comparisons between groups are shown in Table 2. Patients from PCI and CABG groups had more ACS (22.6% and 23.9% respectively) when compared with MT group (14.9%, p = 0.04). On the other hand, the rate of CABG revascularization during the follow-up was higher in the MT (14.2%) and PCI (6.9%) groups when compared to CABG (3.5%) (p < 0.01).

At the end of follow-up, there was no significant difference in adjusted mortality between groups (hazard ratio [HR] for the PCI group, 1.05; 95% confidence interval [CI], 0.59 to 1.84; and HR for the CABG group, 1.20; 95% CI 0.68 to 2.15), with virtually identical survival curves (Figure 1A). In the multivariate Cox-model analysis, age, male gender, diabetes, and cerebrovascular disease were predictive of overall mortality (Table 3). Considering the occurrence of combined major events, PCI was independently associated with worse prognosis (HR 1.50, 95% CI 1.05 to 2.14), with no difference between MT and CABG (HR 1.24, 95% CI 0.84 to 1.83) (Figure 1B). Ventricular dysfunction, diabetes and cerebrovascular disease were also predictive of major events (Table 3).

Both groups of MT and PCI were more likely to require further revascularization (PCI or CABG)

Table 1 – Baseline Characteristics of the Patients

	Total n = 560	MT n = 288	PCI n = 159	CABG n = 113	p Value
Age, years	62 ± 11	62 ± 11	61 ± 12	63 ± 10	0.16
Male	329 (58.8)	170(59)	85 (53.5)	74 (65.5)	0.14
Diabetes Mellitus	198 (35.4)	110 (38.2)	47 (29.6)	41 (36.3)	0.18
Hypertension	438 (78.2)	226 (78.5)	114 (71.7)	98 (86.7)	0.01
Dyslipidemia	355 (63.4)	178 (61.8)	96 (60.4)	81 (71.7)	0.05
Smoking (current)	83 (14.8)	45 (15.6)	31 (19.5)	7 (6.2)	0.02
Smoking (previous)	264 (47.1)	132 (45.8)	67 (42.1)	65 (57.5)	0.02
Myocardial infarction	289 (51.6)	130 (45.1)	108 (67.9)	51 (45.1)	< 0.001
Cerebrovascular disease	58 (10.4)	33 (11.5)	15 (9.4)	10 (8.8)	0.67
Renal failure	86 (15.4)	36 (12.5)	25 (15.7)	25 (22.1)	0.06
LVEF (%)	54 ± 13	55 ± 14	54 ± 13	50 ± 11	0.01
LVEF < 50%	188 (33.6)	94 (32.6)	43 (27)	51 (45.1)	< 0.01
Three-vessel disease	81 (14.5)	30 (17.3)	14 (10.8)	37 (41.6)	< 0.001

Data are expressed as mean ± Standard Deviation or as a number (%).
P-values were obtained through chi-square test for categorical variables and Student's t-test for continuous variables.
MT: medical therapy; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; LVEF: left ventricular ejection fraction.

Table 2 – Primary and secondary outcomes

	Total n = 560	MT n = 288	PCI n = 159	CABG n = 113	p Value
Combined Outcomes	168 (30)	77 (26.7)	52 (32.7)	39 (34.5)	0.21
Death	69 (12.3)	32 (11.1)	19 (11.9)	18 (15.9)	0.41
ACS	106 (18.9)	43 (14.9)	36 (22.6)	27 (23.9)	0.04
Stroke	14 (2.5)	9 (3.1)	5 (3.8)	0	0.16
Cardiovascular death	40 (7.1)	23 (9)	7 (4.4)	10 (8.8)	0.27
Heart failure	24 (4.3)	10 (3.5)	6 (3.8)	8 (7.1)	0.26
Subsequent revascularization*					
PCI	115 (20.5)	54 (18.8)	37 (23.3)	24 (21.2)	0.51
CABG	56 (10)	41 (14.2)	11 (6.9)	4 (3.5)	< 0.01

Data are expressed as total number of events (%).
P-values were obtained through Fisher`s exact test for categorical variables.
ACS: acute coronary syndrome; MT: medical therapy; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting
Some patients had a nonfatal myocardial infarction or stroke before their subsequent death, so the number of combined events is lower than the sum of each single event. In the survival analyses, the time until the first event was used.
** Values represent the first revascularization procedure in patients who were originally assigned to the medical therapy group.*

during the follow-up, after the multivariate analysis (HR =1.55, 95% CI 1.01 to 2.41 and HR = 1.85, 95% CI 1.13 to 3.02, respectively) (Figure 1C). The median time to subsequent revascularization was 32 months (IQR - 11 to 79) in the MT, 32 months (IQR - 8 to 79) in PCI and 38 months (IQR - 24 to 83) in the CABG group (P=0.019). Ventricular dysfunction and diabetes were also predictive of additional revascularization and previous acute myocardial infarction was inversely associated with this outcome (Table 3).

Subgroup analyses

We also analyzed rates of combined major events in patients with diabetes and three-vessel coronary disease, factors identified as determinants in the choice of therapy in patients with stable CAD. There was no significant difference in outcome between initial management strategy in patients with 3-vessel coronary disease (HR = 1.22, 95% CI 0.36 to 4.15 in the PCI group and HR = 1.05, 95%, CI 0.40 to 2.73 in the CABG group). However, in patients with diabetes, the PCI group was predictor of combined major events in the multivariate analyses (HR = 2.14, 95% CI 1.26 to 3.63).

Discussion

The present study reports the results of a cohort from an outpatient clinic in a tertiary care university hospital in Southern Brazil. Developing countries are characterized by a limited access to therapies and difficulties in incorporating new technologies, where the gap in applying the results of clinical trials is even more evident.

National and international guidelines for the management of patients with stable CAD recommend revascularization with CABG for symptomatic patients with unprotected left main coronary artery disease, 3-vessel disease with or without proximal left anterior descending artery disease or 2-vessel disease with proximal left anterior descending artery (Class I recommendation). For the same patients, PCI has a Class IIa recommendation to improve survival. However, all revascularization recommendations to improve survival are based on level of evidence B or C.[14-16] Guidelines emphasize the importance of using a Heart Team approach to decide which therapy is best for each patient, demonstrating that the optimal therapeutic strategy in stable CAD patients is not straightforward.[15]

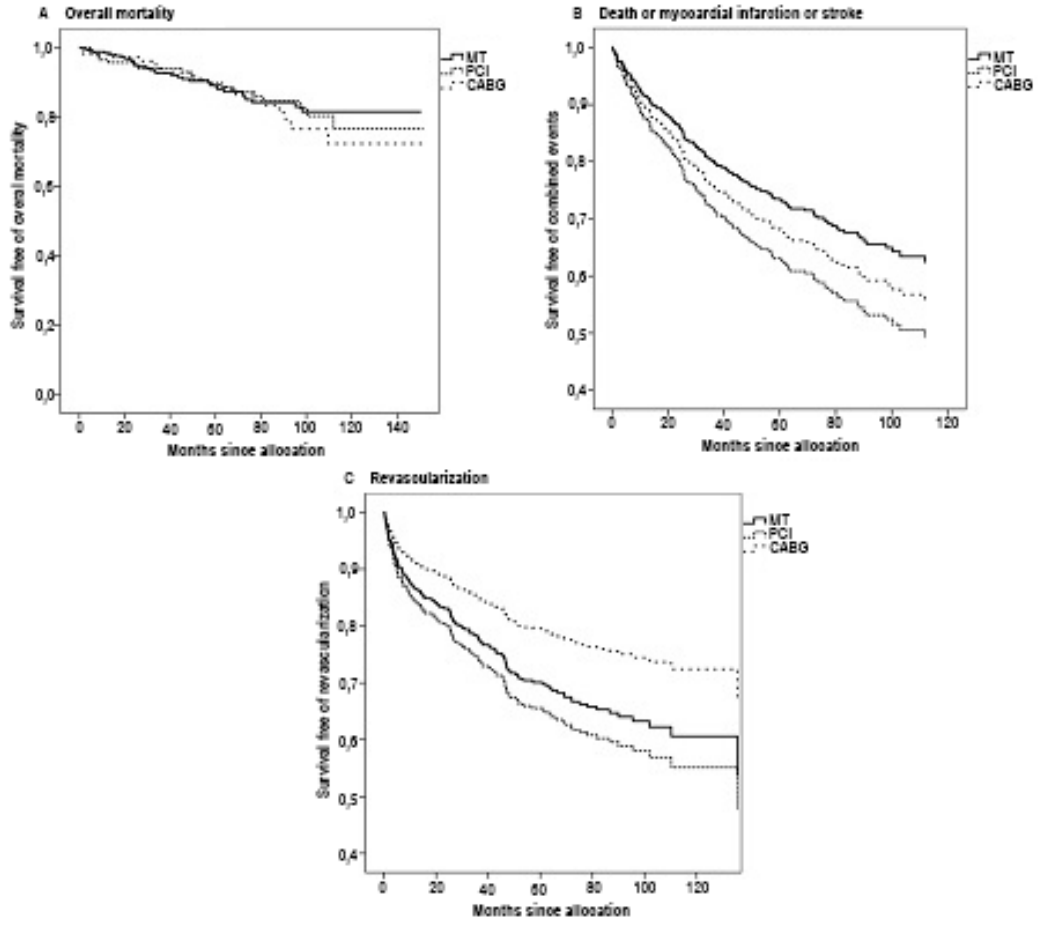

Figure 1 – *Unadjusted probability of event-free survival in patients in the MT, CABG, and treatment groups, adjusted for clinical parameters. A: overall mortality; B: combined events of death, myocardial infarction, and stroke; C: revascularization.*

The Second Medical, Angioplasty, or Surgery Study (MASS II) was the first randomized clinical trial with stable multivessel CAD that compared the 3 current therapeutic strategies: PCI with bare-metal stents versus CABG versus MT alone.[9] The 5-year and 10-year follow-up data showed no differences in overall mortality between the groups. CABG was superior to MT and PCI for the combined endpoints of AMI, additional revascularization and mortality.[17,18] Our study results were consistent with MASS II findings regarding overall mortality and subsequent revascularization, suggesting that the initial strategy with MT can be considered, while acknowledging that during a long-term follow-up a revascularization procedure may be necessary. However, the MASS II 10-year follow-up showed a higher incidence of AMI in MT and PCI compared to CABG patients, which demonstrates the better prognosis of surgical patients.[18]

The lack of difference in mortality between MT and PCI strategies in our study corroborate the findings of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial which showed death rates of 7.6% in PCI group and 8.3% in MT group.[8] The COURAGE nuclear substudy, however, observed a graded relationship between risk of events and the extent and severity of residual ischemia in the end of follow-up. In addition, revascularization with PCI resulted in a more effective reduction of ischemia than MT alone. Although not evidenced by the clinical trial, a pragmatic interpretation of these data indicates revascularization for patients with more than 10% of ischemia during stress testing.[19] Our study did not evaluate data from stress testing and did not consider the degree of ischemia in the analysis, limiting the ability to identify a subgroup of patients with worse prognosis in the MT group. On the other hand, a sub-analysis of

Table 3 – Multivariate analyses comparing event-free survival between groups, adjusted for clinical parameters

Outcome	HR	95%CI	p
Death			
Age	1.04	1.01 – 1.07	0.005
Male gender	2.17	1.14 – 4.13	0.018
Diabetes	2.22	1.28 – 3.86	0.005
Cerebrovascular disease	5.07	2.89 – 8.90	< 0.001
Renal failure	1.65	0.93 – 2.91	0.086
Death, myocardial infarction, and stroke			
Left ventricular dysfunction	1.43	1.06 – 1.95	0.022
Diabetes	1.58	1.16 – 2.15	0.004
Cerebrovascular disease	1.73	1.16 – 2.59	0.008
PCI group	1.50	1.05 – 2.14	0.026
CABG group	1.24	0.84 – 1.83	0.270
Revascularization			
Left ventricular dysfunction	1.46	1.05 – 2.05	0.025
Diabetes	1.88	1.37 – 2.59	< 0.001
Previous myocardial infarction	0.58	0.42 – 0.82	0.002
PCI group	1.85	1.13 – 3.02	0.015
Medical therapy group	1.55	1.01 – 2.41	0.049

HR: Hazard Ratio; 95% CI: 95% confidence interval; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting

the STICH trial showed that in patients with CAD with severe left ventricular dysfunction (ejection fraction ≤ 35%), inducible myocardial ischemia did not identify patients with worse prognosis or those with greater benefit from CABG revascularization over MT alone.[20]

Similar results concerning overall mortality were observed in the BARI 2D trial, in which cumulative survival did not differ significantly between the revascularization (88.3%) and MT groups (87.8%, p = 0.97).[11] These rates are very similar to those found in our study. However, we observed a worse prognosis in the PCI group when combined events were analyzed, especially in the subgroup of diabetic patients. This difference may be attributable to the use of bare-metal stents in our patients (the option available at the public health system in our country), as opposed to the wide use of drug-eluting stents in BARI 2D. The significantly reduced major cardiovascular events in patients who were selected to undergo CABG when compared to MT differ from our results.

The FREEDOM Trial showed that the combined events of death, AMI and stroke occurred more frequently in patients who underwent PCI compared to CABG (26.6% vs. 18.7%, respectively).[12] These findings are consistent with the ARTS,[21] CARDia[22] and SYNTAX (subgroup analysis)[10] trials, where higher rates of major adverse cardiovascular events were observed in diabetic patients assigned to undergo PCI, rather than CABG. Similar to our results, revascularization rates were significant in the PCI group. Likewise, a recent meta-analysis of six randomized trials using contemporary therapy strategies compared CABG and PCI with DES.[23] Although there were no significant differences in death or AMI rates at 1 or 2 years, these differences were evident after 5 years of follow-up, favoring CABG.

The subgroup analysis performed in our patients with three-vessel disease showed no difference in combined events between initial management strategies. Although multivessel disease is considered a complex CAD, results of the SYNTAX trial demonstrated the importance of estimating lesion severity, and showed that major cardiac events did not significantly differ between PCI and CABG in patients with low SYNTAX score.[10] The present study did not measure coronary disease complexity, limiting its ability to provide comparative data regarding better optimum revascularization strategy for multivessel-disease patients. In a large North-American observational study, patients older than 65 years with multivessel CAD had a better long-term survival when submitted to CABG, when compared to patients who underwent PCI.[24] Similar results were found in a pooled database of three large randomized trials that compared long-term outcomes between these groups,[25] showing lower rates of AMI and repeated revascularization in patients with multivessel or left main CAD and previous AMI. We have also demonstrated a worse prognosis in PCI group in overall patients, but could not show any differences in the multivessel-disease subgroup.

Our study had limitations inherent to observational studies. Moreover, it used data from a single center in a reference hospital, in which the results may not be generalized. However, our results represent the real-world practice in a public health system.

Conclusion

The present study shows that stable CAD patients who are initially treated with medical therapy instead of coronary revascularization have similar rates of death from any cause and major cardiovascular events compared to those initially treated invasively.

Author contributions

Conception and design of the research: Furtado MV, Telo GH, Polanczyk CA. Acquisition of data: Furtado MV, Araújo GN, Jost MF, Américo AD, Peruzzo N, Nasi G. Analysis and interpretation of the data: Furtado MV, Araújo GN, Jost MF, Américo AD, Peruzzo N, Telo GH, Borges FK, Polanczyk CA. Statistical analysis: Furtado MV, Araújo GN, Jost MF, Américo AD, Peruzzo N, Nasi G. Obtaining financing: Furtado MV, Telo GH, Polanczyk CA. Writing of the manuscript: Furtado MV, Araújo GN, Jost MF, Borges FK. Critical revision of the manuscript for intellectual content: Furtado MV, Américo AD, Peruzzo N, Nasi G, Telo GH, Borges FK, Polanczyk CA.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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References

1. Pursnani S, Korley F, Gopaul R, Kanade P, Chandra N, Shaw RE, et al. Percutaneous coronary intervention versus optimal medical therapy in stable coronary artery disease: a systematic review and meta-analysis of randomized clinical trials. Circ Cardiovasc Interv. 2012;5(4):476-90.
2. Serruys P, Daemen J, Morice MC, De Bruyne B, Colombo A, Macaya C, et al. Three-year follow-up of the ARTS-II— sirolimus-eluting stents for the treatment of patients with multivessel disease. EuroIntervention. 2008;3(4):450-9.
3. Rodriguez A, Bernardi V, Navia J, Baldi J, Grinfeld L, Martinez J, et al. Argentine randomized study: coronary angioplasty with stenting versus coronary bypass surgery in patients with multiple vessel disease (ERACI II): 30 days results and one-year follow-up results. J Am Coll Cardiol. 2001;37(1):51-8. Erratum in: J Am Coll Cardiol. 2001;37(3):973-4.
4. Booth J, Clayton T, Pepper J, Nugara F, Flather M, Sigwart U, et al; SoS Investigators. Randomized, controlled trial of coronary artery bypass surgery versus percutaneous coronary intervention in patients with multivessel coronary artery disease: six-year follow-up from the Stent or Surgery Trial (SoS). Circulation. 2008;118(4):381-8.
5. Hannan EL, Wu C, Walford G, Culliford AT, Gold JP, Smith CR, et al. Drug-eluting stents vs. coronary-artery bypass grafting in multivessel coronary disease. N Engl J Med. 2008;358(4):331-41.
6. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al; SYNTAX Investigators. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Eng J Med. 2009;360(10):961-72. Erratum in: N Engl J Med. 2013;368(6):584.
7. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, et al; COURAGE Trial Research Group. Optimal medical therapy with or without PCI for stable coronary disease. N Engl J Med. 2007;356(15):1503-16.

8. Shaw LJ, Berman DS, Maron DJ, Mancini GB, Hayes SW, Hartigan PM, et al; COURAGE Investigators. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. Circulation. 2008;117(10):1283-91.

9. Hueb W, Soares PR, Gersh BJ, César LA, Luz PL, Puig LB, et al. The Medicine, Angioplasty, or Surgery Study (MASS-II): a randomized, controlled clinical trial of three therapeutic strategies for multivessel coronary artery disease: one-year results. J Am Coll Cardiol. 2004;43(10):1743-51.

10. Mohr FW, Morice MC, Kappetein, Feldman TE, Ståhle E, Colombo A, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. Lancet. 2013;381(9867):629-38.

11. Frye RL, August P, Brooks MM, Hardison RM, Kelsey SF, MacGregor JM, et al; BARI 2D Study Group. A randomized trial of therapies for type 2 diabetes and coronary artery disease. N Engl J Med. 2009;360(24):2503-15.

12. Farkou ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M, et al; FREEDOM Trial Investigators. Strategies for multivessel revascularization in patients with diabetes. N Engl J Med. 2012;367(25):2375-84.

13. Piegas LS, Haddad N. Percutaneous coronary intervention in Brazil: results from the Brazilian Public Health System. Arq Bras Cardiol. 2011;96(4):317-24.

14. Guimarães JI, César LA, Mansur AP, Armaganijan D, Amino JG, Souza AC, et al; Sociedade Brasileira de Cardiologia. Diretriz de angina estável. Arq Bras Cardiol. 2004;83(supl 2):6-44.

15. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines; American College of Physicians; American Association for Thoracic Surgery; Preventive Cardiovascular Nurses Association.; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2012;60(24):e44-164.

16. Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, et al; Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS); European Association for Percutaneous Cardiovascular Interventions (EAPCI). Guidelines on myocardial revascularization. Eur Heart J. 2010;31(20):2501-55.

17. Hueb W, Lopes NH, Gersh BJ, Soares P, Machado LA, Jatene FB, et al. Five-year follow-up of the Medicine, Angioplasty, or Surgery Study (MASS II): a randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease. Circulation. 2007;115(9):1082-9.

18. Hueb W, Lopes NH, Gersh BJ, Soares PR, Ribeiro EE, Pereira AC, et al. Ten-year follow-up 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.

19. Shaw LJ, Berman DS, Maron DJ, Mancini GB, Hayes SW, Hartigan PM, et al; COURAGE Investigators. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the clinical outcomes utilizing revascularization and aggressive drug evaluation (COURAGE) trial nuclear substudy. Circulation. 2008;117(10):1283-91.

20. Panza JA, Holly TA, She L, Pellikka PA, Velazquez EJ, Lee KL, et al. Inducible myocardial ischemia and outcomes in patients with coronary artery disease and left ventricular dysfunction. J Am Coll Cardiol. 2013;61(18):1860-70.

21. Serruys PW, Ong AT, van Herwerden LA, Sousa JE, Jatene A, Bonnier JJ, et al. Five-year outcomes after coronary stenting versus bypass surgery for the treatment of multivessel disease: the final analysis of the Arterial Revascularization Therapies Study (ARTS) randomized trial. J Am Coll Cardiol. 2005;46(4):575-81.

22. Kapur A, Hall RJ, Malik IS, Qureshi AC, Butts J, de Belder M, et al. Randomized comparison of percutaneous coronary intervention with coronary artery bypass grafting in diabetic patients: 1-year results of the CARDia (Coronary Artery Revascularization in Diabetes) trial. J Am Coll Cardiol. 2010;55(5):432-40.

23. Fanari Z, Weiss SA, Zhang W, Sonnad SS, Weintraub WS. Comparison of percutaneous coronary intervention with drug eluting stents versus coronary artery bypass grafting in patients with multivessel coronary artery disease: meta-analysis of six randomized controlled trials. Cardiovasc Revasc Med. 2015;16:70–77.

24. Weintraub WS, Grau-Sepulveda MV, Weiss JM, O'Brien SM, Peterson ED, Kolm P, et al. Comparative effectiveness of revascularization strategies. N Engl J Med. 2012;366(16):1467-76.

25. Chang M, Lee CW, Ahn JM, Cavalcante R, Sotomi Y, Onuma Y, et al. Coronary artery bypass grafting versus drug-eluting stents implantation for previous myocardial infarction. Am J Cardiol. 2016;118(1):17-22.