MID-TERM RESULTS OF THE ON-PUMP VS OFF-PUMP CORONARY ARTERY BYPASS GRAFTING SURGERY

Romel Mani, MD
Paolo Nardi, MD
Emanuele Bovio, MD
Carlo Bassano, MD
Antonio Pellegrino, MD
Luigi Chiariello, MD
Cardiac Surgery Unit, Policlinico Tor Vergata, Tor Vergata University of Rome, Rome, Italy

Abstract

Objective. To evaluate the fate of ON-pump vs. OP-CABG surgery at mid-term follow-up.
Methods. Data from 166 consecutive OP-CABG patients compared with those of 203 ON-pump CABG patients operated on the same time of OP-CABG operations were retrospectively analyzed.
Results. As compared to OP-CABG, in the ON-pump CABG patients mean value of Logistic EuroSCORE (8.1%±7.8% vs. 6.2%±5.9%; P<0.05), more extended coronary disease (2.7±0.5 vs. 2.5±0.7 diseased vessels/patient; P<0.001) consequently requiring a greater number of grafts/patient (2.9±0.9 vs. 2.3±0.9; P<0.0001), and emergency surgery (12% vs. 6%; P<0.05) were more frequently observed. Operative mortality was 1.9% in ON-pump CABG vs. 1.2% in OP-CABG (P=NS), incidence of stroke 2.4% vs. 1.8% (P=NS). Incidence of stroke by using OP-CABG PAS-Port system technique was reduced at 1.2%.
Intraoperatively, costs per patient were higher for OP-CABG vs. ON-pump CABG (1.930,00 € + 1.050,00 €, if PAS-Port system was included, vs. 1.060,00 € for ON-pump surgery). ICU stay (1.9±1.0 vs. 1.4±0.7 days) and total postoperative in-hospital stay (5.3±3.3 vs. 5.5±3.5 days) were similar in both groups (P≥0.1, for both comparisons).
At 4 years, survival (91%±13% in the ON-pump CABG vs. 84%±19% in the OP-CABG) and freedom from MACE (composite end-point of all-cause death, myocardial infarction, repeat coronary revascularization of the target lesion) (82%±9% vs. 76%±14%) were not significantly different (P≥0.1, for both comparisons). Freedom from late cardiac death was slightly significant higher after ON-pump CABG (98%±4% vs. 90%±10%; P=0.05).
Conclusions. Mid-term freedom from composite end-points are substantially similar after ON-pump CABG and OP-CABG. OP-CABG techniques required higher intra-operative costs. Freedom from cardiac death appears to be better after ON-pump CABG.

Keywords: CABG, coronary revascularization, OPCAB

Introduction

Coronary artery bypass surgery (CABG) improves ischemic symptoms and prognosis in patients with coronary artery disease. For more then three decades, surgical coronary revascularization has been primarily performed with the use of cardiopulmonary bypass (ON-pump CABG) with cardioplegic arrest, and is considered the standard for surgical coronary revascularization in patients affected by multivessel coronary artery disease, providing a motionless, bloodless field for an optimal construction of the distal coronary anastomoses.

However in the last years, off-pump (OP-CABG) coronary artery bypass grafting has gained increased interest of cardiac surgeons, in order to reduce post-operative complications associated with the use of CPB and to avoid any potential detrimental effects of cardiopulmonary bypass, especially the inflammation response, adverse neurological outcome, and the multi-system organ failure that may occur.[1,2] Advances in surgical techniques, myocardial protection, perioperative anaesthesiology management have led to improved outcomes of ON-pump CABG, as well as the development of modern stabilizers has made the OP-CABG more technically feasible and safe. Therefore, a greater number of patients affected by several co-morbid diseases undergo CABG with low in-hospital mortality rate.[3,4] Several studies have compared ON-pump CABG with OP-CABG with respect to short-term mortality, complications, costs, and short-term follow-up. Generally, majority of the studies found no substantial differences for both types of revascularization .[5-7] However, other studies evidenced lower graft patency rates for OP-CABG, higher rates of cardiac events and need of revascularization following OP-CABG. [8-9]

In fact, OP-CABG, is a difficult surgical procedure, and operating with a beating heart would lead to a less complete and a less effective revascularization and, consequently, to a worse follow-up outcome.[10-11] These are the reasons, that the enthusiasm for off-pump surgery decreased rapidly, and the proportion of OP-CABG procedures remains at 20-25% of the total CABG surgery performed in Europe and USA.

Aim of our study was to retrospectively analyzed a single-center experience obtained by two strategies of revascularization in terms of clinical results, efficacy, impact on intraoperative costs, and in particular in terms of early neurological outcome. Survival, freedom from cardiac death, MACE were also investigated up to 4 years of follow-up.

Main Text

Methods

From January 2008 to December 2010, 369 patients affected by multivessel coronary artery disease underwent surgical myocardial revascularization in our Division, 166 using OP-CABG techniques and 203 with the aid of cardiopulmonary bypass.

The study was approved by our local Institutional Review Board, which waived the need for patient consent.

Chronic renal dysfunction, was present in 67 (18%); chronic obstructive pulmonary disease was present in 82 (22%). Emergency CABG, namely, ought to be performed before the beginning of the next working day after coronary angiography, was needed in 34 patients (9%). Patients requiring coronary surgery reoperation or concomitant procedures (valvular or ablation surgery, replacement of ascending aorta, ventricular resection) were excluded from the study.

Criteria to choose OP-CABG

Most of OP-CABG procedures (90%) were performed by one expert surgeon (CB) in beating heart surgery. Exclusion criteria to perform OP-CABG were: left ventricular ejection fraction less than 0.30, left ventricular end-diastolic diameter greater than 60 mm, distal diffuse narrowing of coronary arteries, intra-myocardial course of the left descending coronary artery, emergency or urgency surgery in presence of perioperative hemodynamic instability.

Surgical strategy and safety measures

Access to the heart was obtained through a complete median longitudinal sternotomy in all patients.

ON-pump CABG was performed by means of normothermic cardiopulmonary bypass and intermittent antegrade blood cardioplegia (600 ml the first dose, 400 ml the others administered every 20-25 minutes). Cardiopulmonary bypass was performed by means of a

Sorin Monolyth-Pro (Sorin Biomedica; Turin, Italy) or Capiox (Terumo Cardiovascular System; Borken, Germany) membrane oxygenator and a Stockert roller pump (Stockert Instrumente; Munich, Germany).

In OP-CABG patients, left anterior descending artery and its diagonal branches were bypassed as first vessel, followed by the right coronary artery and finally the left circumflex artery system. Proximal anastomoses of the saphenous grafts were always performed before distal ones, either handsewn or with the aid of an automated device that avoided aortic clamping (PAS-Port; Cardica; PAS-Port® Proximal Anastomosis System, USA) (n=84, 51% of OP-CABG procedures).

Stabilization was obtained with the aid of suction stabilizers (Octopus and Starfish; Medtronic Inc; Minneapolis, MN; USA in the early phase, and Acrobat and X-pose; Guidant Co; Boston Scientific, Boston, MS, USA later on). Distal perfusion was maintained after arteriotomy by means of intravascular shunts (Clearview, Medtronic Inc; Minneapolis, MN; USA).

Monitoring of cardiac function was obtained with transesophageal echocardiography and insertion of a Swan-Ganz pulmonary artery catheter. Other safety measures included perfusionist's stand-by on a ready-dry state (mounted, non-primed cardiopulmonary bypass circuit).

Internal thoracic artery as in situ graft, was the conduit of choice for the left anterior descending artery revascularization in all cases. In the last 2 years of the reported study (2009-2010), OP-CABG was routinely performed using PAS-port system.

Data collection

Perioperative myocardial infarction was defined as an increase of post-operative troponine I higher than 5 ng/ml associated with a CK-MB above normal values and more than 10% of total CK, and the onset of ECG new anomalies. Major non-cardiac complications were also analyzed: a pulmonary complication was defined as an episode of primary lung failure requiring mechanical ventilation for more than 48 hours, re-intubation, or intermittent application of positive end-expiratory pressure by mask; a neurological complication was defined as an episode of stroke due to a focal or general cerebral lesion; renal insufficiency was defined as a two-fold increase of preoperative serum creatinine level or oliguria necessitating continuous veno-venous hemodiafiltration. Operative mortality included death in hospital after operation at anytime or within 30 days after discharge. MACE (Major Adverse Cardiac Events) was defined as composite of all-cause death, documented myocardial infarction, or repeat coronary revascularization of the target lesion).

The mean duration of follow-up was similar in the ON-pump CABG vs. OP-CABG (35±13 vs. 34±15 months, p=NS). Four patients were lost (n=3 in ON-pump CABG group, n=1 in OP-CABG group), and follow-up was 99% complete.

All causes of operative and at follow-up death, data of pre- and postoperative echocardiography exams were analyzed. Need for in-hospital readmission for cardiovascular causes and functional status of the patients were also recorded, at the outpatient clinic visit or by telephone interview. Collected data of functional tests and echocardiographic exams during the follow-up were also analysed.

Statistical analysis

Analysis was performed with Stat View 4.5 (SAS Institute Inc, Abacus Concepts, Berkeley, CA). Student's t test for continuous data and the χ^2 or Fisher's exact test for categorical data were used. Twenty-six preoperative and perioperative variables were analyzed including age, gender, Logistic EuroScore I Risk Stratification System [12] expressed and percent risk of death plus or minus 1 standard deviation, previous myocardial infarction, smoking habit, co-morbidity (arterial hypertension, diabetes mellitus, chronic renal dysfunction, chronic obstructive pulmonary disease, hyperlipidemia, peripheral vascular disease, obesity), previous percutaneous coronary revascularization, previous cerebrovascular accidents (stroke or TIA), Canadian Cardiovascular Society (CCS) grade of angina, New York Heart Association (NYHA) functional class, preoperative left ventricular ejection fraction (LVEF), severely depressed LVEF (equal to or less than 0.35), number of diseased coronary artery vessels, need of emergency or urgent CABG, number of grafts per patient, cardiopulmonary bypass and aortic cross-clamp times, calcification of the aorta (so defined when intra-operatively detected at the inspection and/or palpation, or by transesophageal echocardiography), and "aortic clamp-less" technique. Risk factors analysis to detect independent predictor/s for postoperative stroke was performed using the Logistic Regression analysis. Overall survival (not including operative mortality), freedom from late cardiac death and from MACE were expressed as mean values plus or minus 1 standard deviation, and computed by using the Kaplan-Meier method; the log-rank test was used to compare survival estimates among subgroups, and the Cox proportional hazards methods was used to evaluate the influence of variables on time to death in the entire population of CABG patients. All other continuous values were expressed as mean plus or minus 1 standard deviation of the mean. All p values less than 0.05 were considered statistical significant.

Results

Preoperative, angiographic, intra-operative and postoperative variables of the ON-pump CABG and OP-CABG patients are reported in Tables 1-4. Due to the exclusion criteria to perform OP-CABG, the retrospective analysis showed that in the ON-pump CABG group Logistic EuroSCORE, incidence of diabetes mellitus, hyperlipidemia, peripheral vascular disease, and the number of patients with a LVEF =/<0.35 were higher in comparison with OP-CABG group (Table 1). As well as, emergency and urgent CABG were more frequently performed in the ON-pump CABG group (Table 1) (P<0.05, for all comparisons). Number of diseased coronary vessel per patients was higher in the ON-pump CABG as compared with OP-CABG (Table 2), consequently requiring a greater number of grafts per patient (2.9±0.92 vs. 2.3±0.96) (Table 3).

Operative mortality was 1.9% (n=4/203) for ON-pump CABG and 1.2% (n=2/166) for OP-CABG (P=NS). Postoperative complications and outcomes are reported in Table 4.
In particular, incidence of postoperative stroke was 2.5% in ON-pump CABG group vs. 1.8% in OP-CABG group (Table 4). Independent predictors for postoperative stroke were the advanced age of patients (76 vs. 67 years) (P=0.005), preoperative peripheral vascular disease (P=0.01), and obesity (P<0.05). At the univariate analysis also the association of carotid artery disease and diabetes was recognized as risk factor for stroke (P<0.05). Using the aortic "clamp-less" technique (i.e. achieved either with total arterial revascularization or using PAS-port system avoiding completely aortic manipulation) the incidence of stroke was reduced from 1.8% in the entire group of patients undergone OP-CABG at 1.2% in this subgroup of OP-CABG (P=0.06, marginally significant vs. ON-pump CABG).

Intra-operative costs per patient of OP-CABG techniques with or without use of PAS-Port System were higher in comparison with those of ON-pump CABG.

Follow-up Results

At 4 years, survival rate was 91%±13% for ON-pump CABG vs. 84%±19% for the OP-CABG (P=NS) (Figure 1); freedom from late cardiac death was 98%±4% vs. 90%±10% (P=0.05) (Figure 2), from MACE 82%±9% vs. 76%±14% (P=NS) (Figure 3). Thirty-four out of 358 patients (9.4%) surviving at operation with completed follow-up (not including 4 patients lost) died. Causes of late death were cardiac events in 16 patients (sudden death=13, acute myocardial infarction=2, congestive heart failure=1), malignancy in 6, gastric

hemorrhage in 2, stroke in 2, renal failure in 4, septicemia in 1, and unknown in 3.
On multivariate Cox Regression analysis, independent predictors of overall late mortality were advanced age at operation ($P<0.01$), a lower mean value of preoperative LVEF ($P<0.01$), peripheral vascular disease ($P<0.01$), chronic obstructive pulmonary disease ($P=0.05$) and patients affected by postoperative major complications ($P<0.05$).
Independent predictors of late cardiac mortality remained advanced age at operation ($P<0.05$), a lower mean value of preoperative LVEF ($P<0.05$), peripheral vascular disease ($P<0.05$), and patients who experienced postoperative major complications ($P=0.05$).
Clinical and Functional Status

At 4 years, freedom from reintervention either for coronary revascularization than for graft occlusion documented by means of coronary angiography or coronary angiography 64-slice CT-scan, were 90%±7% and 90%±7% in the ON-pump CABG and 95%±2% and 93%±3% in the OP-CABG patients (P=NS, for both comparisons). Follow-up echocardiography obtained on 250 patients showed a preserved value of LVEF either in the ON-pump than in the OP-CABG patients 0.53±0.08 vs. 0.56±0.7 (P=NS). Stress tests were examined in 243 patients. CCS anginal class markedly improved from 2.9±1.2 preoperatively to 1.2±0.6 in the ON-pump CABG and from 2.9±1.1 preoperatively to 1.4±0.5 in the OP-CABG group ($P<0.0001$).

Discussion

Off-pump CABG have been increasingly used in Western world since the 1990s, when Benetti and Buffolo and their colleagues[1,2] demonstrated potential benefit associated with the avoidance of cardiopulmonary bypass.[13,14] However, the preferable technique remains unclear: the supposed superiority of OP-CABG in terms of short term results can be counterbalanced by more frequent lack of completeness revascularization and low graft patency rate, both conditioning a worse follow-up outcome.

In-hospital Results

Randomized controlled trials, observational studies and most of the meta-analyses recently published generally found no significant difference in peri-operative mortality, but did find a reduced need for blood transfusions and shorter hospital stay.[5,7] Likewise, in our study mortality and major complications rates appeared to similarly occur in ON-pump CABG and OP-CABG patients, as well as the length of intensive care unit and postoperative stay, and the incidence of postoperative atrial fibrillation, although the patients who underwent ON-pump CABG in our series had a preoperative higher EuroScore and required more frequently urgent or emergency surgery.

The incidence of re-exploration for bleeding and the need of blood transfusions were higher in the ON-pump CABG. These findings can be likely related on the one hand to a greater inflammatory response caused to the cardiopulmonary bypass, but on the other to a major rate of patients operated on emergency (12% in ON-pump patients vs. 6% in OP-CABG patients) or on urgency (48% vs. 42%). In these cases platelet anti-aggregation therapy was not always stopped and could lead to a greater peri-operative bleeding.

Relatively to the costs, the use of stabilizer devices during OP-CABG increases the expenditure in comparison with ON-pump CABG surgery (1.930,00 €, vs. 1.060,00 €). Costs further increase over about one third if (+ 1.050,00 €) if PAS-Port system automated systems are used, as we found from our brief cost analysis. Such costs were partly counterbalanced by the minor requirement of blood transfusions in the OP-CABG patients, as well as by the reduced ICU stay of the OP-CABG patients, although without a statistical difference (1.4 vs. 1.9 days) (Table 4).

An important aspect to focalize the attention in our study has been the reduced incidence of postoperative stroke when the manipulation of the aorta was avoided. Afilalo and co-authors[15] in a recent meta-analysis of randomized trials observed 49 strokes among 3,605 OP-CABG procedures compared with 76 among 3,589 ON-pump CABG procedures, representing a 30% relative risk reduction. Borgermann and co-workers[16] found that by using in 395 patients PAS-Port system or total arterial revascularization the incidence of stroke was significantly reduced in comparison with conventional CABG (1.3% vs. 3.6%, $P<0.05$). In our study we have found that the incidence of stroke was similar in the two groups (2.5% in the ON-pump vs. 1.8% in the OP-CABG). However, we found a trend in reduction (1.2%, 1 case /84 OP-CABG procedures using with PAS-Port, $P=0.06$ vs. ON-pump CABG) when OP-CABG was performed without aortic manipulation, i.e. using the PAS-Port. For these reason, the higher costs of "clamp-less" OP-CABG procedures using PAS-Port can be justified, especially in patients at higher risk for stroke (i.e, in presence of peripheral and carotid vascular disease, advanced age, high preoperative serum creatinine level, extent of aortic atherosclerosis and calcification of the aorta). [3,6,17] In our study we recognized as independent predictors for early stroke the advanced age, the peripheral vascular disease, and the obesity.

Follow-Up Outcome

Mid- and long-term efficacy of the off-pump CABG remains unclear.[18] Results from the ROOBY Trial recently published by Hattler and co-workers,[19] indicated that OP-CABG in comparison with ON-pump CABG was associated with a significant lower patency rate at 1 year of follow-up either for arterial (85.8% vs. 91.4%) than for saphenous (72.7% vs. 80.4%) grafts ($P<0.05$). Moreover effective revascularization was significantly worse after off-pump than on-pump. Takagi and Co-workers [6] in a systematic review of randomized trials comparing off-pump and on-pump CABG surgery showed lower rates of revascularization and graft patency in the off-pump coronary surgery, with a 38% increase in repeat revascularization rate. Reduced graft patency and incomplete revascularization can affect long-term results and increase repeat interventions with adjunctive expenditure.[20] Hannan et al.[9] in 13,889 off- pump CABG and 35,941 on-pump CABG patients reported a better freedom from a subsequent revascularization following on-pump CABG (93.6% vs. 89.9%). However, more recent series evidenced that off-pump coronary surgery performed by skilled surgeons may offer the same effective results during follow-up in comparison with a conventional CABG.[21-23] In our analysis we did not find substantial differences in terms of survival and freedom from MACE. These findings can be likely related to the good experience of the surgeon who performed off-pump surgery, as also reported by other studies who have stressed the importance of a necessary experience required in the beating heart coronary surgery.[21-27] Freedom from cardiac death appeared better in the On-pump CABG patients with a discrete statistical relevance (98% vs. 90%, Figure 2). Considering that our follow-up was based on clinical records, we did not have definitive data about the cause of death, details of angiographic status of the grafts or of the native coronary tree, such that to draw a clear evidence that mortality could be related to a graft failure or to an incomplete revascularization. However, in a recent publication, Filardo and colleagues[28] showed a significantly higher risk of death at 10 years of follow-up in OP-CABG patients in comparison with ON-CABG patients.

Limitations of the study

The study was retrospective observational, not randomized; 2) the power of statistical analysis in detecting differences in the two groups of CABG patients had been affected by the selection criteria to perform OP-CABG. However, the aim of the study mainly was to analyze the results of each type of CABG, focalizing the interest on the effectiveness of CABG techniques in the current clinical practice.

Conclusion

In conclusion, ON-pump CABG remains an effective surgical strategy for the treatment of extended multivessel coronary disease, in patients affected by co-morbid disease, with a high EuroScore. Mid-term freedom from cardiac death observed after ON-pump CABG appears to be very satisfactory. Off-pump surgery needs for more expensive technology and more demanding technique, requiring expertise surgical practice.

References:

Buffolo E, de Andrade CS, Branco JN, Teles CA, Aguiar LF, Gomes WJ. Coronary artery bypass grafting without cardiopulmonary bypass. Ann Thorac Surg 1996;61:63-6.

Benetti FJ, Naselli G, Wood M, Geffner L. Direct myocardial revascularization without extracorporeal circulation: experience in 700 patients. Chest 1991;100:312-6.

Dalén M, Ivert T, Holzmann MJ, Sartipy U. Long-term survival after off-pump coronary artery bypass surgery: a Swedish Nationwide Cohort Study. Ann Thorac Surg 2013; doi: 10.1016/j.athoracsur.2013.07.014.

Lamy A, Devereaux PJ, Prabhakaran D, et al. CORONARY Investigators. Off-pump or on-pump coronary-artery bypass grafting at 30 days. N Engl J Med 2012;366:1489-97.

Lemma MG, Coscioni E, Tritto FP, et al. On-pump versus off-pump coronary artery bypass surgery in high-risk patients: operative results of a prospective randomized trial (on-off study). J Thorac Cardiovasc Surg 2012;143:625-31.

Møller CH, Perko MJ, Lund JT, et al. No major differences in 30-day outcomes in high-risk patients randomized to off-pump versus on-pump coronary bypass surgery: the best bypass surgery trial. Circulation 2010;121:498-504.

Hueb W, Lopes NH, Pereira AC, et al. Five-year follow-up of a randomized comparison between off-pump and on-pump stable multivessel coronary artery bypass grafting. The MASS III Trial. Circulation 2010;122(11 Suppl):S48-52.

Takagi H, Mizuno Y, Niwa M, Goto S, Unemoto T. A meta-analysis of randomized trials for repeat revascularization following of off-pump versus on-pump coronary artery bypass grafting. Interact CardioVasc Thorac Surg 2013; doi:10.1093/icvts/ivt316.

Hannan EL, Wu C, Smith CR, et al. Off-pump versus on-pump coronary artery bypass graft surgery: differences in short-term outcomes and in long-term mortality and need for subsequent revascularization. Circulation 2007;116:1145-52.

Ivanov J, Borger MA, Tu JV, Rao V, David TE. Mid-term outcomes of off-pump versus on-pump coronary artery bypass graft surgery. Can J Cardiol 2008;24:279-84.

Thourani VH, Guyton RA. Graft patency after off-pump coronary artery bypass surgery. Circulation 2012;125:2806-8.

Roques F, Nashef SA, Michel P, et al. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. Eur J Cardiothorac Surg 1999;15:816-23.

Lytle BW. On-pump and off-pump coronary bypass surgery. Circulation 2007;116:1108-9.

Mohr F-W. To beat or not to beat? From one size fits it all to an individual coronary revascularization strategy. Eur Heart J 2012;31:2441-3.

Afilalo J, Rasti M, Ohayon SM, Shimony A, Eisenberg MJ. Off-pump vs. on-pump coronary artery bypass surgery: an updated meta-analysis and meta-regression of randomized trials. Eur Heart J 2012;33:1257-67.

Börgermann J, Hakim K, Renner A, et al. Clampless off-pump versus conventional coronary artery revascularization: a propensity score analysis of 788 patients. Circulation 2012;126(11 Suppl 1):S176-82.

Hedberg M, Boivie P, Engstroem KG. Early and delayed stroke after coronary surgery- an analysis of risk factors and the impact on short- and long-term survival. Eur J Cardiothorac Surg 2011;40:379-87.
Shroyer AL, Grover FL, Hattler B, et al. Veterans Affairs Randomized On/Off Bypass (ROOBY) Study Group. N Engl J Med 2009;361:1827-37.
19. Hattler B, Messenger JC, Shroyer AL, et al. Veterans Affairs Randomized On/Off Bypass (ROOBY) Study Group. Off-Pump coronary artery bypass surgery is associated with worse arterial and saphenous vein graft patency and less effective revascularization: Results from the Veterans Affairs Randomized On/Off Bypass (ROOBY) trial. Circulation 2012;125:2827-35.
Khan NE, De Souza A, Mister R, et al. A randomized comparison of off-pump and on-pump multivessel coronary-artery bypass surgery. N Engl J Med 2004;350:21-8.
Angelini GD, Culliford L, Smith DK, et al. Effects of on- and off-pump coronary artery surgery on graft patency, survival, and health-related quality of life: long-term follow-up of 2 randomized controlled trials. J Thorac Cardiovasc Surg 2009;137:295-303.
Widimsky P, Straka Z, Stros P, et al. One-year coronary bypass graft patency: a randomized comparison between off-pump and on-pump surgery angiographic results of the PRAGUE-4 trial. Circulation 2004;110:3418-23.
Raja SG, Husain M, Popescu FL, Chudasama D, Daley S, Amrani M. Does off-pump coronary artery bypass grafting negatively impact lon-term survival and freedom from reintervention? Hindawi Publishing Corporation; 2013: doi 10.1155/2013/602871.
Kobayashi J, Tashiro T, Ochi M, et al. Japanese Off-Pump Coronary Revascularization Investigation (JOCRI) Study Group. Early outcome of a randomized comparison of off-pump and on-pump multiple arterial coronary revascularization. Circulation 2005;112(9 Suppl):I338-43.
Sousa Uva M, Cavaco S, Oliveira AG, et al. Early graft patency after off-pump and on-pump coronary bypass surgery: a prospective randomized study. Eur Heart J 2010;31:2492-9.
Sarin EL, Kayatta MO, Kilgo P, et al. Short- and long-term outcomes in octogenarian patients undergoing off-pump coronary artery bypass grafting compared with on-pump coronary artery bypass grafting. Innovations (Phila.) 2011;6:110-5.
Wu C, Camacho FT, Culliford AT, et al. A comparison of long-term mortality for off-pump and on-pump coronary artery bypass graft surgery. Circ Cardiovasc Qual Outcomes 2012;5:76-84.
Filardo G, Grayburn PA, Hamilton C, Hebeler RF Jr, Cooksey WB, Hamman B. Comparing long-term survival between patients undergoing off-pump and on-pump coronary artery bypass graft operations. Ann Thorac Surg 2011;92:571-8.