*Original Article*

# Surgical Treatment of Left Main Coronary Artery Disease – Off-Pump CABG is a Good Option

Khawaja Nasir Uddin Mahmood[1], Subhash Chandra Mandal[2], Saiful Haque Talukdar[3]

**Abstract:**

**There has been increasing interest in the potential benefit of off-pump coronary artery bypass (OPCAB) surgery when compared to conventional coronary artery bypass (CCAB) using cardiopulmonary bypass (CPB) in the presence of critical left main stem (LMS) Disease. A prospective observational study was conducted from January 2006 to June 2012 in the Department of Cardiac Surgery in the National Institute of Cardiovascular Diseases (NICVD), Dhaka. The study included total 110 patients with LMS disease who underwent CABG. 25 cases were done under CPB and 85 cases were done on beating heart. The two groups had similar baseline characteristics including age, sex, risk-factors, co-morbid conditions and extent of coronary artery disease. There was no difference between the groups with respect to mortality, but the incidence of post-operative bleeding (p≤0.05) , blood requirement (p d"0.05), inotropic and ventilatory support, intensive care unit (ICU) care and post-operative hospital stay (p≤0.05) were significantly reduced when performing off-pump CABG in this high-risk group of patients.**

*Key words: Coronary artery disease, Coronary artery bypass, Off-pump.*

*(Bangladesh Heart Journal 2015; 30(2) : 61-67)*

**Introduction:**

Over the past decades, coronary artery bypass graft (CABG) surgery has generally been regarded as the "gold standard'' therapy for significant left main stem stenosis because of the proven survival benefit. Indeed, recently updated ACC/AHA guideline for CABG states that "the benefit of surgery over medical treatment in patients with significant left main stenosis (LMS) stenosis (≥50%) is little argued". Over the past three decades, several randomized trials and prospective cohort studies have consistently demonstrated marked survival benefit of CABG over medical therapy in patients with LMS.

In the CASS registry after following for up to 16 years, the median survival was almost 7 years longer in CABG group in comparison to medical treatment group (13.3 vs. 6.6 years).

1. Professor of Cardio-vascular Surgery, Ex Head of the Department of Cardio-vascular Surgery, National Institute of Cardiovascular Diseases, Dhaka.
2. Associate Professor, Department of Cardio-vascular Surgery, National Institute of Cardiovascular Diseases, Dhaka.
3. Associate Professor, Department of Cardio-vascular Surgery, National Institute of Cardiovascular Diseases, Dhaka.

Surgical mortality in left main disease is 3%, which is in sharp contrast to 1.8% mortality in patients undergoing surgery but without LMS. However, in lower risk cases of LMS, the mortality is only 0.8%.

Surgical result can be further improved with the use off-pump CABG (OPCAB) and composite arterial graft and bilateral internal mammary artery (IMA) grafts. Avoiding use of cardio-pulmonary bypass (CPB) and no-touch aortic technique reduces the risk of stroke. Once CABG became the standard care for left main disease, the terms "protected" and "unprotected" left main were coined. The term "protected left main" means patent grafts to either left anterior descending (LAD) or left circumflex system (LCX) or one of these two vessels is abundantly supplied with rich collaterals. The term "unprotected left main" (UPLM) means there are neither patent bypass grafts nor collateral. UPLM disease occurs in 3-5% of patients with coronary artery disease. Present guidelines consider this finding a major indication for CABG based mostly on the CASS (Coronary Artery Surgery Study)[2] and ECSS (European Coronary Surgery Study) [3] trials. These trials have shown that in comparison to medical therapy CABG

improves survival in patients with UPLM during a 5-year follow-up period.

The proximal location and large size of the left main are favorable factors for percutaneous coronary intervention (PCI). As PCI has progressed from balloon angioplasty to use of bare metal stents and now drug-eluting stents (DES), the rate of procedural complication and restenosis have reduce and this encouraged cardiologists to treat LMS stenosis with PCI. However, there are many concerning factors that have limited the role of PCI in LMS stenosis. First of all, 90% of all stenosis of the left main extend from the distal left main into proximal LAD artery and / or the LCX artery. Such bifurcation lesions are at notoriously high-risk of restenosis.[25-30] Secondly, almost half of the lesions in the left main are calcified . The outcome in such cases may be less than optimal. Thirdly, nearly 80% of the patients with LMS have multivessel coronary diseases, where result of surgery are distinctly superior. Moreover, the complexity and anatomy of the lesion play an important role in PCI, whereas these factors are not relevant to CABG since bypass grafts are to the mid or distal coronary arteries. These factors have restricted suitability of PCI to a small number of cases. Moreover, in Bologna Registry[2], at a median follow-up of 14 months, the rates of repeat revascularization in CABG and PCI groups were 3% and 26% respectively.

The 5-year follow up result of the LMS subgroup of the SYNTEX trial showed a benefit of CABG for all cause death (9.2% vs. 14.6%, p<0.001), cardiac death (4.0% vs. 9.2%, p<0.001), and myocardial infarction (MI) (3.3% vs. 10.6%, p<0.001). The need for target vessel revascularization (TVR) was significantly higher for the PCI group in all 5 years of follow up.

CABG is regarded as better than PCI in LMS stenosis in respect of mortality and need for repeat revascularization, though morbidity is more in CABG. Minimally invasive direct coronary artery bypass (MIDCAB) and off-pump coronary artery bypass (OPCAB) without using CPB and no-touch technique of aorta, will reduce post-operative morbidity.

Recently there has been renewed interest in the potential benefits of OPCAB surgeryy , with encouraging reports of clinical, angiographic and economic superiority when compared to conventional coronary artery bypass (CCAB) using CPB.[10-6] The presence of critical left main stem disease was once considered as a relative contraindication to OPCAB surgery. However, the development in exposure and stabilization techniques, the introduction of intra-coronary shunts and the increasing understanding of the hemodynamic changes which occurs during off-pump surgery, enables patients with critical left main lesions to undergo OPCAB surgery. The present study aims to determine the short-term effects of OPCAB compared with CCAB, in patients with LMS disease on mortality and morbidity.

## Materials and Methods:

### Patient population

Between January 2006 and June 2012, 110 consecutive patients with LMS disease underwent CABG in my surgical team in NICVD. Significant LMS disease was defined as LMS with stenosis equal to or greater than 50%. Among them 85 cases underwent OPCAB surgery. Any conversion to CPB was classified as off-pump cases on the basis of 'intention to trial' analysis. In the early period of study, CCAB surgery was done mostly in patients with LMS disease. With the Increase of proficiency with OPCAB surgery almost all patients in the later part of study underwent OPCAB surgery.

### Anaesthesia and anticoagulation

A standard anaesthesia technique was used for all patients. This consisted of premedication by intravenous midazolam followed by total intravenous anaesthesia (3mg/kg/h propofol). Neuromuscular blockade was achieved by administering pancuronium (0.15mg/kg). Intravenous heparin 300 IU/kg with a target activated clotting time (ACT) of 480 seconds was administered to the CCAB patients immediately prior to the cannulation for CPB. OPCAB patients received 100 IU/kg heparin prior to commencing the distal anastomosis with a target ACT of 250-350 seconds. Protamine sulphate was used to reverse the heparin effect at the completion of the surgical procedure.[13,41,42]

### Surgical procedure

#### CCAB group:

Standard CPB techniques were used with a median sternotomy approach using an ascending aortic perfusion cannula, a single two-stage right atrial cannula and a pulsatile flow of 2.4 L/min/$m^2$. Membrane oxygenator and roller pump heads were used for the CPB. Mild hypothermia (34-36 °C) was maintained and myocardial protection was achieved with antegrade induction of blood cardioplegia followed by intermittent antegrade cold blood cardioplegia.

#### OPCAB group:

OPCAB procedure was performed through either median sternotomy incision or anterolateral thoracotomy approach. Following exposure, approach to target

coronary arteries was eased either lifting and/or pulling the heart with a suction device or by placing cotton gauge on the posterior aspect to lift the heart. Site of anastomosis of coronary artery was stabilized using Octopus II tissue stabilizing system. Bleeding from coronary artery after incision was controlled by pressing proximal part of coronary artery with De Bakey forceps and appropriate size intracoronary shunts were introduced through coronary arteriotomy in all cases to maintain distal perfusion and to achieve a bloodless operative field. Oxygen blower was used for visualization of anastomotic field by removing blood if collected.

**Postoperative management**

At the end of surgery, patients were transferred to the ICU. The lungs were ventilated with 70% oxygen using volume-controlled ventilation and a tidal volume of 10 ml/kg with less than 5 cm H, O of positive end-expiratory pressure (PEEP). Adjustment in FiO, and respiratory rate were made according to routine blood gas analysis, in order to maintain PaO, between 80 and 100 mmHg, PaCO, between 35 and 40 mm Hg. Patients were extubated as soon as they met the following criteria: hemodynamic stability, no excessive bleeding (<80 ml/h), normothermia, and consciousness with adequate return of muscle power and control of pain. Fluid management postoperatively consisted of 5% dextrose infused at a rate of 1 ml/kg/h with additional blood to maintain normovolemia and hematocrit greater than 24%. Potassium and Sodium deficiency was promptly treated as necessary to maintain an electrolyte balance within the normal range.

**Data collection**

Data were collected prospectively during the patient's admission from non-randomized patients with critical LMS disease and retrospectively analyzed.

**Outcome definitions**

Operative mortality was defined as any death that occurred within 30 days of operation. Re-exploration for bleeding was defined as bleeding that required surgical reoperation after initial departure from the operating theatre. Post-operative blood loss was measured as the total chest tube drainage starting immediately after closure of the chest in the operating theatre. Ventilatory failure was defined by the requirement for mechanical ventilation of more than 12 hours. Postoperative stroke was defined as a new focal neurological deficit and comatose states occurring postoperatively that persisted for greater than 24 hours after their onset and were noted before discharge. Renal failure defined as patients with a postoperative creatinine level greater than 200 mmol/L or patient requiring dialysis. Sternal wound infection was defined in accordance with the published evidence-based guidelines by the Center for Disease Control and Prevention.[17] Chest infection was defined as exacerbation of chronic bronchitis or a culture proven diagnosis of pneumonia. Gastrointestinal complications were defined in accordance with the Society of Cardio-thoracic Surgeons of Great Britain and Ireland.[18] Postoperative atrial arrhythmias was defined as the occurrences of new atrial arrhythmia in the absence of preoperative persistent or paroxysmal atrial arrhythmias.

**Statistical analysis**

Statistical analyses were performed using SPSS. Continuous variables were presented as the mean± standard deviation and categorical variables were presented as either absolute numbers or percentages. Data were checked for normality prior to statistical analysis. Categorical variables were analyzed using the Chi-square-test. Differences between study groups were considered statistically significant when $p \leq 0.05$.

**Results:**

A total of 110 patients with LMS disease underwent CABG during the study period. OPCAB procedure was performed in 85 (77.27%) cases and CCAB was done in 25 (22.73%) cases. Baseline and intra-operative characteristics are summarized in Table I and post-operative data based on procedure performed are summarized in Table II. There were no difference between the OPCAB and CCAB groups in terms of age, sex, body mass index, risk-factors and incidence of co-morbid conditions. In hospital mortality was comparable between groups and consisted of 4 (4.71%) death in OPCAB group and 2 (8%) death in CCAB group. No statistically significant difference between the 2 groups was observed with regard to the effect of both techniques on the occurrence of myocardial complications like myocardial infarction and arrhythmias.

There was significant difference in total blood loss in the two groups. Transfusion requirements were also significantly lower in the OPCAB group in comparison to the CCAB group. The incidence of renal failure and transient stroke were higher in CCAB group but was not significant statistically. The overall inotropic requirement was significantly higher in the CCAB group, as was the requirement of prolonged ICU and total post-operative stay. There were significant differences between the two groups in the periods of ventilatory support required but minimal differences between the incidences of sternal wound infection.

**Table-I**

*Patient characterstics based on procedure performed.*

| | OPCAB (no-85) | Conventional (n-25) | p-value |
|---|---|---|---|
| Age at operation (Yr.) | 41 -64 | 39-66 | 0.0016 |
| Body mass index (Kg/m²) | 22.10 | 22.21 | 0.0087 |
| Female sex | 11(12.9%) | 6(24%) | 0.0162 |
| Diabetes | 35(41.86%) | 11(44%) | 0.0113 |
| Current smoker | 12(13.9%) | 3(12%) | 0.0097 |
| Hypercholesterolemia | 25(30.23%) | 7(28%) | 0.0088 |
| Hypertension | 41(51.16%) | 13(52%) | 0.0014 |
| Peripheral vascular Diseases | 13(16.28% | 4(16%) | 0.0011 |
| Renal dysfunction | 23(27.90%) | 6(24%) | 0.0147 |
| Respiratory disease | 29(34.88%) | 8(32%) | 0.0096 |
| Ejection fraction <30% | 11(12.90%) | 5(20%) | 0.0185 |
| Triple vessel disease | 69(81.39% | 21(84%) | 0.0177 |
| Number of grafts | 3 | 3 | |

*Significant p>0.05

**Table-II**

*Post –operative data based on procedure performed.*

| | OPCAB (no-85) | Conventional (no -25) | p values |
|---|---|---|---|
| In hospital mortality (%) | 4(4.71%) | 2(8%) | 0.0162 |
| Renal failure (%) | 2(2.34%) | 1(4%) | 0.0041 |
| Transient stroke (%) | 6(7.05%) | 2(8%) | 0.0016 |
| Troponin (%) | 8(9.41%) | 3(12%0 | 0.0106 |
| Atrial arrhythmia (%) | 22(25.98%) | 7(28%) | 0.0087 |
| Ventricular arrhythmia (%) | 4(4.71%) | 1(4%) | 0.0064 |
| Post operative bleeding & blood requirement (%) | 2(2.34%) | 6(24%) | 2.53* |
| Sternal wound infection (%) | 2(2.34%) | 1(4%) | 0.0041 |
| Inotropic support more than two(%) | 10 (11.75%) | 22(88%) | 8.57* |
| Ventilator support >12 hours (%) | 4(4.71%) | 15(60%) | 4.57* |
| ICU stay > 3days (%) | 2(2.34%) | 16(64%) | 5.59* |
| Post operative stay >14 days (%) | 2 (2.34%) | 15(60%) | 4.48* |

*Significant ($p \leq 0.05$)

**Discussion:**

In 1967, Kolessov, working in the Soviet Union, reported the use of the IMA to bypass coronary arteries off-pump[35], which was abandoned following the development of CPB. Though CABG is the gold standard in the treatment of LMS disease, but PCI with DES is now being done in a particular subset of patients. Disadvantage of CABG is its increased morbidity. To reduce post-operative morbidity, newer techniques like OPCAB and MIDCAB surgery and composite arterial grafts based on bilateral IMA grafts to simultaneously avoid the use of CPB and to permit a non-touch aortic technique (thereby reducing the risk of stroke). Furthermore, greater use of aspirin, statins and arterial grafts demonstrated two-thirds reduction in mortality with CABG at 5 years with the benefit persisting at 10 years, shown in a meta-analysis of the randomized controlled trials.

In contrast to the saphenous vein grafts, the internal mammary artery grafts appear to be remarkably resistant to atherosclerotic involvement, for it yields 10 year patency rates approaching 95%.[3] The internal mammary artery performs best when used to bypass the left anterior descending artery.[3] In other positions, it may be no better than the saphenous veins.

The deleterious effect of CPB, however have prompted a renewed interest in beating heart coronary revascularization and OPCAP surgery has been shown

to confer significant advantage in terms of morbidity and cost when compared to CCAB. However, the presence of critical LMS disease has been considered risky and was a relative contraindication to OPCAB surgery due to concern over the well demonstrated hemodynamic changes that occur during displacement of the heart.[20] Recently, however few groups have reported encouraging preliminary data with OPCAB surgery with LMS stenosis.[3]

Dewey and colleagues[3] original work involved 100 LMS patients who received off-pump CABG. They performed a multivariate logistic regression analysis, which concluded that, the use of CPB was a significant risk factor for inhospital mortality.

Yeatman and colleagues[3] had a slightly smaller cohort of only 75 off-pump CABG with significant LMS stenosis. The pre-operative characteristics were relatively well matched between off-pump and on-pump patients. Off-pump patients had a lower incidence of inotropic support, temporary pacing, blood transfusion and chest infection, plus a short post-operative length of stay.

The results of the present study suggest that myocardial revascularization in the presence of critical LMS stenosis can be safely and effectively achieved using OPCAB techniques. OPCAB patients required less post-operative inotropic support, less blood transfusion, less ventilatory support, less post-operative ICU stay and inhospital stay compared to CCAB group.

Advantage of this study is that the operations in both groups were done by single surgeon. But there are some limitations, which may affect the conclusions drawn from the study. First, this is an observational study and by its retrospective nature, cannot account for the unknown variables affecting the outcome. Second, the study is spread over a period of 6 years with most of the patients on CPB being from the early part of the study period, and with most belonging to the off-pump group from the later part of the study period. Also, the off-pump patients include the period during the “learning curve”, may be indicating a degree of selection bias. Third, multivariate analysis and propensity scoring of the collected data was not done.

**Conclusion:**

Advances in procedural techniques, devices and operator experience have greatly expanded the scope of OPCAB surgery for LMS stenosis in the modern days. Off-pump CABG is feasible and safe to perform in patients with significant LMS stenosis. There is no difference between the groups with respect to mortality and there is significant reduction of post-operative morbidity like the incidence of post-operative bleeding, blood requirement, inotropic and ventilatory support and ICU and post-operative hospital stay can be significantly reduced when performing off-pump CABG in this high risk group.

OPCAB surgery in LMS stenosis not only shows better outcome in terms of morbidity than CCAB but also diverts patients from PCI to OPCAB surgery, considering the risk involved in PCI in distal third and bifurcation of LMS stenosis.

**References:**

1. Eagle KA, Guyton RA, Davidoff R, et al.; American College of Cardiology; American Heart Association. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). *Circulation*. 2004 Oct 5;110(14):e340-437.
2. Coronary Artery Surgery Study (CASS): a randomized trial of coronary artery surgery, Survival data. *Circulation* 1983; 68: 939-50.
3. Varnauskas E. Twelve-year follow-up of survival in the randomized European Coronary Surgery Study. *N Eng J Med* 1988;319: 332-7.
4. Caracciolo EA, Davis KB, Sopko G et al. Comparison of surgical and medical group survival in patients with left main equivalent coronary disease. Long term CASS experience. *Circulation* 1995;91: 2335-44.
5. Yusuf S, Zucker D, Peduzzi P et al. Effects of coronary artery bypass graft surgery on survival: Overview of 10 year results from randomized trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet* 1994; 344: 563-70.
6. Keogh BE, Kinsman R. *Fifth National Adult Cardiac Surgical Database Report 2003.* Dendrite Clinical System (Henley-on Thames, Oxfordshire, UK) 2004.
7. Zhang Z, Mahoney EM, Spertus JA, et al. The impact of age on outcomes after coronary artery bypass surgery versus stent-assisted percutaneous coronary intervention: one-year results from the Stent or Surgery (SoS) trial. *Am Heart J*. 2006 Dec;152(6):1153-60.
8. Taggart DP, Lees B, Gray A, Altman DG, Flather M, Channon K; ART Investigators. Protocol for the Arterial Revascularisation Trial (ART). A randomised

trial to compare survival following bilateral versus single internal mammary grafting in coronary revascularisation [ISRCTN46552265]. *Trials*. 2006 Mar 30;7:7.

9. Buffolo E, de Andrade CS, Branco JN, Teles CA, Aguiar LF, Gomej WJ. Coronary artery bypass grafting without cardio-pulmonary bypass. *Ann Thorac Surg* 1996; 61(1): 63-6.

10. Puskas JD, Wright CE, Ronson RS, Brown WM, Gott JP, Guyton RA. Off-pump multivessel coronary bypass via sternotomy is safe and effective. *Ann Thorac Surg* 1998; 66(3): 1068-72.

11. Tasdemir O, Vural KM, Karagoz H, Bayazit K. Coronary artery bypass grafting on the beating heart without use of extra-corporeal circulation: review of 2052 cases. *J Thorac Cardiovas Surg* 1998; 116(1): 68-73.

12. Brasil LA, Gomes WJ, Salomao R, Buffolo E. Inflammatory response after myocardial revascularization with or without cardiopulmonary bypass. *Ann Thorac Surg* 1998; 66(1): 56-9.

13. Ascione R, Lloyd CT, Underwood MJ, Lotto AA, Pistis AA, Angelini CD. Economic outcome of off-pump coronary artery bypass surgery: a prospective randomized study. *Ann Thorac Surg* 1999; 68(6): 2237-42.

14. Ascioni R, Lloyd CT, Underwood MJ, Gomes WJ, Angelini GD. On-pump versus off-pump coronary revascularization: evaluation of renal function. *Ann Thorac Surg* 1999; 68(2): 493-8.

15. Ascioni R, Lloyd CT, Gomes WJ, Caputo M, Brayan AJ, Angelini GD. Beating versus arrested heart revascularization: evaluation of myocardial function in a prospective randomized study. *Eur J Cardio-thorac Surg* 1999; 15(5): 686-90.

16. Arom KV, Emery RW, Flavin TF, Peterson RJ. Cost effectiveness of minimally invasive coronary artery bypass surgery. *Ann Thorac Surg* 2000; 68(4): 1562-6.

17. de Lezo JS, Medina A, Pan M et al. Rapamycin eluting stents for the treatment of unprotected left main coronary disease. *Am Heart J*. 2004 Sep;148(3):481-5.

18. Park SJ, Kim YH, Lee BK, et al. Sirolimus- eluting stent implantation for unprotected left main coronary artery stenosis: comparison with bare metal stent implantation. *J Am Coll Cardiol* 2005; 45: 351-6.

19. Valgimigli M, van Mieghem CA, Ong AT et al. Short and long-term clinical outcome after drug eluting stent implantation for the percutaneous treatment of left main coronary artery disease : insight from the Rapamycin-Eluting and Texas Stent Evaluated At Rotterdam Cardiology Hospital registries (RESEARCH and T-SEARCH). *Circulation* 2005; 111: 1383-9.

20. Price MJ, Cristea E, Sawhney N et al. Serial angiographic follow-up of sirolimus-eluting stents for unprotected left main coronary artery revascularization. *J Am Coll Cardiol* 2006; 47: 871-7.

21. Chieffo A, Morici N, Maisano F, et al. Percutaneous treatment with drug eluting stent implantation versus bypass surgery for unprotected left main stenosis: a single centre experience. *Circulation* 2006; 113: 2542-7.

22. Kim YH, Park SW, Hong MK, et al. Comparison of simple and complex stenting techniques in the treatment of unprotected left main coronary artery bifurcation stenosis. *Am J Cardiol.* 2006 Jun 1;97(11):1597-601. Epub 2006 Apr 7.

23. Lee MS, Kapoor N, Jamal F et al. Comparison of coronary artery bypass surgery with percutaneous coronary intervention with drug eluting stents for unprotected left main coronary artery disease. *J Am Coll Cardiol* 2006; 47 864-70.

24. Palmerini T, Marzocchi A, Marrozzini C, et al . Comparison between coronary angioplasty and coronary artery bypass surgery for the treatment of unprotected left main coronary artery stenosis (the Bologna Registry). *Am J Cardiol* 2006; 98: 54-9.

25. Tanabe K, Hoye A, Lemos PA et al. Restenosis rates following bifurcation stenting with sirolimus-eluting stents for de novo narrowings. *Am J Cardiol* 2004; 94: 115-8.

26. Lemos PA, Hoye A, Goedhart D et al. Clinical, angiographic and procedural predictors of angiographic restenosis after sirolimus-eluting stent implantation in complex patients : an evaluation from the Rapamycin-Eluting Stents Evaluated at Rotterdam Cardiology Hospital (RESEARCH) study. *Circulation* 2004; 109: 1366-70.

27. Hoye A, Iakovou I, Ge L et al. Long-term outcomes after stenting of bifurcation lesions with the “Crush” technique predictors of an adverse outcome. *J Am Coll Cardiol* 2006; 47: 1949-58.

28. Valgimigli M, Malagutti P, Rodriguez-Granillo GA et al. Distal left main coronary disease is a major predictor of outcome in patients undergoing percutaneous intervention in the drug-eluting stent era : an integrated clinical and angiographic analysis based on the Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) and Taxus- Stent Evaluated At Rotterdam Cardiology Hospital (T-SEARCH) registries. *J Am Coll Cardiol* 2006; 47: 1530-7.

29. Hoffman SN, TenBrook JA, Wolf MP, Pauker SG, Salem DN, Wong JB. A meta-analysis of randomized controlled trials comparing coronary artery bypass graft with percutaneous transluminal coronary angioplasty: one- to eight-year outcomes. *J Am Coll* Cardiol 2003; 41: 1293-304.

30. Brener SJ, Lytle BW, Casserly IP, Schneider JP, Topol EJ, Lauer MS. Propensity analysis of long-term survival after surgical or percutaneous revascularization in patients with multivessel coronary artery disease and high-risk features. *Circulation* 2004; 109: 2290-5.

31. Hannan EL, Racz MJ, Walford G et al. Long-term outcomes of coronary artery bypass grafting versus stent implantation. *N Eng J Med* 2005; 352: 2174-83.

32. Malenka DJ, Leavitt BJ, Hearne MJ, et al.; Northern New England Cardiovascular Disease Study Group. Comparing long-term survival of patients with multivessel coronary disease after CABG or PCI: analysis of BARI-like patients in northern New England. Circulation. 2005 Aug 30;112(9 Suppl):I371-6.

33. Smith PK, Califf RM, Tuttle RH, et al. Selection of surgical or percutaneous coronary intervention provides differential longevity benefit. *Ann Thorac Surg* 2006; 82: 1420-8.

34. Taggart DP. Surgery is the best intervention for severe coronary artery disease. *BMJ* 2005; 330: 785-6.

35. Kolessov VL. Mammary artery coronary anastomosis as method of treatment of angina pectoris. *J Thorac Cardiovas Surg* 1967; 54: 535-44.

36. Louagie YA, Gonzalez ME, Schroder E. Off-pump myocardial revascularization for left main stem disease in a high-risk patient. *Acta Chir Belg* 1999; 99(6): 309-11.

37. Cartier R, Brann S, Martineau R, Couturier A. Left main coronary artery stenosis and revascularization in the beating heart: Short and Long-term experience. *Ann Chir* 1999; 53(8): 701-705.

38. Dewey TM, Magee MJ, Edgerton JR, Mathison M, Tennison D, Mack MJ. Off-pump bypass grafting is safe in patients with left main coronary disease. *Ann Thorac Surg* 2001; 72: 788-92.

39. Yeatman M, Caputo M, Ascioni R, Ciulli F, Angelini GD. Off-pump coronary artery bypass surgery for critical left main stem disease : safety, efficacy and outcome. *Eur J Cardiothorac Surg* 2001; 19: 239-44.

40. Mohr FW, Morice MC, Kappetein AP et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary artery disease: 5 year follow up of the randomized, clinical SYNTAX trial. *Lancet*, 2013 Feb; 381(9867): 629-38.

41. Calafiore AM, Teodori G, Mezzetti A, et al. Intermittent antegrade warm blood cardioplegia. *Ann Thorac Surg* 1995, 59(2): 398-402.

42. Caputo M, Bryan AJ, Calafiore AM, Suleiman MS, Angelini GD. Intermittent antegrade hyperkalaemic warm blood cardioplegia supplemented with magnesium prevents myocardial substrate derangement in patients undergoing coronary artery bypass surgery. *Eur J Cardio-thorac Surg* 1998; 14(6): 596-601.

43. Stone PH, Goldschlager N. Left main coronary disease: review and appraisal. *Cardiovasc Med*. 4. 1979: 165-77.