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 < 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.

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) >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).

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. 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, 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 surgery, with encouraging reports of clinical, angiographic and economic superiority when compared to conventional coronary artery bypass (CCAB) using CPB. 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.

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/m². 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 vessel revascularization (TVR) was significantly higher for the PCI group in all 5 years of follow up.
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<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 differences 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.
Discussion:
In 1967, Kolessov, working in the Soviet Union, reported the use of the IMA to bypass coronary arteries off-pump, which was abandoned following the development of CPB. Though CABG is the gold standard in the treatment of LMS disease, 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%. The internal mammary artery performs best when used to bypass the left anterior descending artery. 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

Table-I
Patient characteristics based on procedure performed.

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

*Significant p>0.05

Table-II
Post-operative data based on procedure performed.

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

*Significant (p<0.05)
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. Recently, however, few groups have reported encouraging preliminary data with OPCAB surgery with LMS stenosis.

Dewey and colleagues' 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' 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:


