Advantages of Off-Pump Coronary Bypass Surgery in High-Risk Patients

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Introduction and objectives. Myocardial revascularization without cardiopulmonary bypass has been shown to reduce operative morbi-mortality. We report our recent experience with this novel technique in order to evaluate its theoretical advantages in comparison with conventional surgery.

Patients and methods. This retrospective analysis included 547 consecutive patients undergoing isolated myocardial revascularization from December 1997 through November 2000. One hundred twenty-one off-pump patients were compared to 426 undergoing cardiopulmonary bypass. Logistic regression analysis was performed to find predictors of mortality, transfusion, postoperative hospital stay. Cardiopulmonary bypass was an independent predictor of blood transfusion and longer hospital stay.

Results. Off-pump patients were at greater risk: they were older, with a lower ejection fraction and a higher prevalence of unstable angina, heart failure and associated comorbidity. Off-pump surgery reduced transfusions (1 ± 1 vs 1.9 ± 2 blood units; p < 0.0001) and postoperative hospital stays (8.9 ± 5 vs 11.3 ± 7 days; p < 0.001). The off-pump group showed a trend toward reduced morbidity but the technique did not decrease hospital mortality. Cardiopulmonary bypass was an independent predictor of blood transfusion and longer hospital stay. Short-term follow-up revealed no significant differences in recurring angina or patency rates.

Conclusions. Off-pump coronary bypass surgery is a good option in high-risk patients because it reduces the incidence of perioperative transfusion and the length of hospitalization. Furthermore, it showed a trend toward reduced morbidity. Mortality was not significantly higher in spite of the higher risk of the patients. Long-term longitudinal follow-up is mandatory to assess the true effectiveness of this technique.

Key words: Cardiopulmonary bypass. Coronary disease. Revascularization.

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INTRODUCTION

The spread of myocardial revascularization in a beating heart (with or without cardiopulmonary bypass [CPB]) has made clear the problems associated with CPB physiopathology. This «new» technique is a sur-
Aortoconary bypass intervention without CPB

The usual procedure was mid-sternotomy, although in some patients left anterior mini-thoracotomy was used. In most patients, the left internal mammary artery was used as the first choice for the graft, although other arterial grafts were used (right mammary or left radial artery). Optimum exposure was achieved with the use of pericardial traction points (Lima points). Positioning the operating table in the right lateral decubitus Trendelenberg position improved the exposure of the circumflex area. A C.T.S. stabilizer was used (Cardiothoracic Systems Inc., Cupertino, CA, USA); the Octopus I and II system was used most often. After system heparinization (dose: 1.5 mg/kg) control of the coronary artery to be bridged was achieved with a prolene 6/0 double slip-stitch proximal and distal to the arteriotomy. In 1 patient who had poor hemodynamic tolerance when the artery was occluded, it was necessary to use an intracoronary shunt. In 70% of patients the permeability of the graft was tested in situ with a flow meter (Medi-Stim Butterfly Flowmeter, Medi-Stim AS, Oslo, Norway). After the intervention, an early extubation protocol was followed (the first at 4 hours post-surgery).

Aortocoronary bypass intervention with CPB

In all patients, mid-sternotomy was carried out and the left internal mammary artery was used in the majority, but other arterial grafts were also used. After cannulating the ascending aorta and the right atrium, and heparinizing the patient (3 mg/kg), cardiopulmonary bypass was initiated. In all patients a membrane oxygenator and roller centrifuge pump was used. System hypothermia of 30 to 32 °C was induced, and retrograde and antegrade cryoatrioanuloplasty (cold shot) was used with grafts. Before aortic cross-clamping, a hot shot was administered. All patients were extubated at 8 hours as is customary.

Statistical analysis

Statistical analysis was performed with the Windows SPSS 6.0.1 statistics program. The quantitative values were expressed as mean and standard deviation, and the qualitative values as percentages. After a descriptive study, the variables between the groups were compared through χ² tests for the analysis of qualitative variables, and the Student t test for numerical data (previous verification of supposition of normality). The corresponding logistical regression analyses were carried out to estimate whether surgery with CPB was 1 of the independent variables associated with mortality, longer hospital stay, and post-surgery.
cal AV failure. The variable «surgery with CPB» was included, as were all those with a value of P ≤ 0.2, in a previous univariate analysis. The variables age, sex, previous ejection fraction, NYHA, and unstable angina were also considered in the models, given their clinical significance.

RESULTS

Of a total of 547 patients, surgery without CPB was used in 121 (28.4%). The usual method was mid-sternotomy, except in 14 patients in the group without CPB in which left anterior mini-thoracotomy was used (11.6% of the group). The most common stabilization system used was the Octopus (115 patients; 95%).

Comparison between surgery with and without CPB in all patients

The 121 patients who underwent coronary intervention without CPB were compared to the group of 426 patients who underwent surgery with CPB. The principal pre-surgery variables analyzed were similar in both groups with regard to age, presence of unstable angina, NYHA grade IV, previous ejection fraction, number of vessels affected, single-vessel disease, 3-vessel disease, and circumflex involvement (Table 1). Those in the group without CPB were older and had a more severe clinical course (the differences were statistically significant); a greater number with unstable angina and NYHA functional grade IV. The previous EF was lower in this group, although 3-vessel coronary disease was more frequent in the group with CPB. Chronic obstructive bronchopneumopathy (COBN) co-morbidity, previous cerebral accident (CVA), arterial hypertension, chronic renal insufficiency, and diabetes mellitus type 1 were more frequent in the group without CPB. Peripheral vascular disease was much more frequent in the group without CPB (almost significant) (Table 1). The greater initial risk of the group without CPB was confirmed by the Higgins, Tuman, and Euroscore morbidity-mortality scores (Table 2).

For post-surgery complications (Table 3), hemorrhage was clearly the greatest in the group with CPB, who had more transfusions and re-operations. In the group without CPB the number of new episodes of post-surgical AF, sepsis, deep sternal infection or mediastinitis, and significant pleural drainage (a third or more of the hemithorax) was lower, but was not significant. We did not differentiate between this group and that with CPB as far as transitory phrenic paralysis, transitory AV block, or respiratory distress.

There was no difference between the 2 groups with regard to acute peri-operative myocardial infarction, maximum CPK-Mb levels, pneumonia and post-operative CVA, prolonged intubation (>48 h), re-intubation, or episodes of severe bronchospasm requiring bronchodilator treatment or measures involving positive pressure ventilator assistance (PPVA). The lower incidence of complications translated into a shorter post-operative hospital stay in the group without CPB (statistically significant). On the other hand, despite the lower morbidity, nosocomial mortality was greater in the group without CPB (Table 3). We also assessed the percentage of incomplete revascularization (some coronary territory with stenosis not revascularized); 29.7% (36 patients) in the group without CPB vs 13.3% (57 patients) in the conventional group (P < 0.01).

At 1 year followup, 4 patients (3% of the group) presented with typical unstable angina in the group without CPB; angiography was performed in 1 patient, revealing the occlusion of a saphenous graft on the
right coronary artery. In the group with CPB, 24 patients (5.6%) developed angina during the first year; 18 patients (4.2%) had significant ischemia on dobutamine echocardiography. Eleven (2.6%) of these patients were catheterized, and graft occlusion was found in 6 (1.4%).

A later comparison between the group with and the group without CPB was performed to risk subgroup: patients of 75 years of age, EF=35%, NYHA grade IV cardiac insufficiency, grade IV angina, and patients with a history of COBN, CVA, and peripheral vascular disease. Although it is a redundant analysis and increases multiple comparison errors, we obtained some interesting results.

The most outstanding difference was the greater number of transfusions in the group with CPB in older patients with severe ventricular dysfunction (subgroups EF=35% and age=75 years old). In addition, we observed a slight tendency for a greater number of episodes of post-operative bronchospasm in patients without CPB in the distinct subgroups, but with an almost significant difference in the COBN group. In this group, we observed a greater incidence of pneumonia and post-operative AF and even prolonged ventilation in 1 patient. All this resulted in a longer hospital stay.

### Comparison of surgery with or without CPB and with CPB factors in the subgroups per Euroscore

Comparisons were carried out per the Euroscore scores (European scores of surgical morbidity-mortality) (Table 4). Three subgroups of patients were established: low risk (0-2), medium risk (3-5), and high risk (6), corresponding to a median expected mortality rate of 1.28%, 2.92%, and 4.8%, respectively. Among the differences found was the greater need for transfusions in patients with CPB, especially in the low and high risk groups. The maximum post-operative CPK-Mb numbers were also greater with CPB, especially in the low-risk group. Surgery without CPB resulted in shorter hospital stays in all 3 subgroups.

### Logistical regression analysis

The study was completed by determining the principal independent predictors of nosocomial death, longer post-operative hospital stays (cut off point: 9 days), need for blood transfusion, or immediate post-operative AF failure (Table 5).

The type of surgery (with or without CPB) was a significant predictor of peri-operative blood transfusion, with a greater need for transfusion occurring in those patients with surgery with CPB. The other independent variable associated with transfusions was the female sex. The type of surgery (with CPB vs without CPB) was also an independent predictor of longer post-operative hospital stay (greater in patients with CPB), along with post-operative AF failure and the need for transfusion. In a prospective analysis, there was a significant interaction between the type of intervention and the need for transfusion when the dependent variable of longer hospital stay was excluded. The type of operation (with CPB vs without CPB) was not associated with a greater incidence of post-operati-
ve AF, but was associated with age and unstable angina; however, these were not significant predictors of nosocomial death.

DISCUSSION

The advances in CPB have reduced physiopathologic risks, especially the systemic inflammatory response and multi-organ damage caused by ischemia-reperfusion. The repercussions of these deleterious effects are greater in certain at-risk patients: those of advanced age or with bad ventricular function or significant dysfunction of various organs or systems. An attempt to decrease the incidence of these complications has led to the development of myocardial revascularization without CPB, especially in this at-risk type of patient.3-7 The introduction of new surgical techniques requires careful evaluation of the results and short-term, medium-term, and long-term followup. This is the only way to ascertain the most appropriate indication for this type of surgery.10 On the other hand, coronary bypass without CPB, with beating heart, is more difficult and has unavoidable repercussions with regard to the initial learning curve.5,12,17 It also has an effect on complete revascularization, which tends to be inferior when off-pump surgery is used.3

Initial studies have evaluated the efficacy and safety of the technique.12-16 Some studies analyzed the hemodynamic changes induced by heart mobilization and the coronary occlusion to be bridged, evaluating the patient’s level of tolerance.17,18 Other studies have analyzed short-term graft permeability to verify whether there is a significant decrease in this variable. The study by Wiklund et al.19 concluded that the majority of the stenosis present on post-operative coronary angiography was not present on later studies, which brings into question the trustworthiness of early angiographic studies. There are also published studies on intraoperative coronary angiography to confirm the proper function of coronary grafts.20,21 To this end, systematic measurement of intraoperative flow with the Doppler method was used.22 On the other hand, Ömeroglu et al.23 reported promising data on mid-term permeability using angiographic studies in 70 randomly selected patients (total of 696 patients) undergoing surgery without CPB (mean coronary angiography intervention of 36 months). They concluded that the permeability index is comparable to that of conventional surgery, especially with arterial grafts on the anterior descending artery.

Other publications have focused on analysis of the post-operative clinical course in determining the incidence of complications, nosocomial death, and the repercussions of this technique on hospital stays and costs.3,7,24-26 Many investigators have compared these results with those of using conventional surgery, generally showing a lower morbidity-mortality rate, especially in at-risk patients.3-7,24,25 Among the risk subgroups that could benefit from this alternative surgery are COBN patients, those with bad ventricular function, or with risk of peri-operative CVA and, naturally, elderly patients who constitute an ever-growing number of patients treated.27-29 They have also considered as re-operation or in single-vessel intervention as a viable alternative: mono-bypass to the anterior descending coronary artery via mid-sternotomy or anterior mini-thoracotomy, or circumflex branch bypass by mini-thoracotomy.30,31 Similarly, special cases such as non-elective surgery32 and patients with critical left coronary artery trunk stenosis have been studied.33 Our study attempts to prove the possible benefit of analyzing the incidence of significant complications, nosocomial death, and length of hospital stay. Early post-operative surgical course (first year) and all angiographic studies performed during said period have also been evaluated. We collected this data in a retrospective manner, subject to the limits inherent in this type of design. In any case, although global reports are increasing, up to this point there are few prospective random studies on the subject respect,25,34 and they are limited to the immediate post-operative period. The tendency of our service has been to use this technique in the higher surgical risk patients and, even in some with established contraindications for surgery with CPB. This is in addition to positive outcomes with conventional surgery in low- or intermediate-risk patients, in whom we have achieved a very low overall mortality rate (approximately 1%) (Table 3).

Overall, we compared the results obtained with surgery with and without CPB. Diverse systemic scores predicting morbidity-mortality were applied3-10 to determine the risk to the patients in our study, who were followed for a pre-determined period of time. As has been shown in other studies,3,7,24,25 we have achieved a decrease in morbidity in patients who undergo surgery without CPB, in spite of this being a high-risk group.

| TABLE 5. Predictors of longer hospital stay, need for transfusion, and post-operative AF |
|---------------------------------|----------------|-----------------|
|                                 | Odds ratio | 95% CI | P     |
| Longest stay:                   | Surgery with CPB | 2.3 | 1.4-3.7 | <.001 |
|                                 | Need for transfusion | 2.5 | 1.5-4.2 | <.05  |
|                                 | Post-operative AF failure FA | 2.9 | 1.8-4.7 | <.001 |
| Need for transfusion:           | Surgery with CPB | 2.2 | 1.3-3.7 | <.001 |
|                                 | Female sex | 4.8 | 2.4-9.4 | <.0001|
| Post-operative AF               | Age | 0.95 | 0.93-0.98 | <.005 |
|                                 | Unstable angina | 0.5 | 0.2-0.9 | <.04  |

CPB indicates cardiopulmonary bypass; AF, atrial fibrillation; 95% CI, 95% confidence interval.
The need for transfusion has been much lower and hospital stays have been significantly shortened. Of special note is the greater, although not significant, incidence of post-operative CAV in patients in the non-CPB group (Table 3), which is different from the findings in other studies.\(^6,24,33\) The decrease in episodes of CAV has been associated with surgery without CPB and without aortic cross-clamping (no pump-no touch technique), as found by Ricci et al.\(^24\) In a setting like, Cuenca et al\(^25\) described their experience with complete arterial double mammary artery revascularization without CPB. This is based on the use of a T-form (or Y-form) graft in both mammary arteries, using the Tector technique,\(^36,37\) but stripped down and without using CPB. They thereby avoided proximal anastomosis and cross-clamping in the aorta, achieving, according to their published series, a zero incidence of CAV. In our case, we performed proximal anastomosis of the ascending aorta in the majority of the revascularized patients with 2 or more grafts, although partial cross-clamping of the aorta was done during controlled hypertension. For us, the Tector technique has not, so far, shown a clear long-term benefit, and we are not sure it is important to make the complete revascularization of the heart dependent on the flow and permeability of a single mammary artery. On the other hand, although a study of the costs has not been performed, as in other published studies,\(^25,38\) a significant cost-reduction is foreseen. In spite of the low incidence of complications, however, we have not found a decrease in nosocomial death, which is opposite to the data published by other authors.\(^4,5,30\) Arom et al\(^3\) have also shown a decrease in the morbidity rate, but a comparable mortality rate in both groups. A possible explanation for our results may be found in the excessive risk of the 4 patients who died (in 2 we may have underestimated the indication for conventional surgery). Of note are the excellent results regarding mortality in patients who underwent surgery with CPB. The Arom study also introduces us to 1 of the potential risks of off-pump surgery: incomplete revascularization (with 1 less anastomosis than in the group with CPB) and the greater number of early re-operations for graft occlusions. In our series, the index of recurrent angina and angioplasty in the first year was 24% and 10% after surgery without CPB vs 9% and 2% after conventional surgery. In our study, these differences were not as notable in followup. Our experience was that revascularization without CPB is a safe technique with results on recurrent angina and graft permeability comparable to those that occur with conventional surgery. Longer followup is needed, however, especially to evaluate the effects of this minor complete revascularization.

In the analysis of the risk subgroups, the patients with COBN had more respiratory problems and supraventricular arrhythmias, resulting in longer hospital stays, which is not the case in other studies. It is difficult to find a coherent explanation for this phenomenon, but it could be related to early extubation and more complete early post-operative management in patients with COBN. Having an adequate fast-track protocol in place could be beneficial, with the use of low-dose narcotics or ultrashort action narcotics (remifentanil) and optimizing post-operative analgesia. On the other hand, re-operations for hemorrhage were more frequent in patients who had CPB (table 3), particularly those with unstable angina. This subgroup primarily underwent emergency surgery, and therefore in many patients prior antiagregant treatment was impossible.

When the subgroups are compared according to Euroscore (Table 4), transfusion requirements showed a tendency to increase with an increase risk, but were always lower than in the group with CPB. The enzymes also increased (maximum post-operative CPK-Mb numbers) in the successive risk group, and were always greater than in the patient who underwent CPB (there were significant differences in the low-risk group). Finally, the length of hospital stay was also longer with increased risk and lower in the group who underwent surgery without CPB. The difference length hospital stay between the group with CPB and the group without CPB was more notable in the higher risk subgroup. Then the principal independent predictors of longer hospital stay, need for transfusion, AF post-operative failure, and nosocomial death were determined. This analysis confirmed that surgery with CPB resulted in a greater rate of transfusion and longer hospital stays. It was also significantly associated longer stays, the need for transfusion, and post-operative AF. On the other hand, female gender was a potent predictor of need for transfusion, possibly because of greater hemodilution during CPB due to smaller body surface. Age and unstable angina are associated with post-operative AF, but not the type of intervention. Finally, we did not encounter significant predictors of mortality. The results are contradictory; some studies show a lesser incidence of immediate post-operative FA,\(^3,30,31\) while others conclude that surgery without CPB had no effect on the occurrence of this arrhythmia, as myocardial ischemia is the substrate responsible in all coronary interventions.\(^35,36,39\) The same contraindication is advanced for nosocomial death: some propose a clear benefit with revascularization without CPB,\(^4,5,30\) while others do not demonstrate any improvement.\(^3,7,25,31,33,38\) There are recent published studies which document the possible morbidity-mortality rates associated with this technique.\(^40,41\) In fact, several studies have found the indications for of this surgery are limited, warning of the potential complications that can present, or simply showing the lack of an obvious benefit. Studies note are those of Locker et al\(^42\) and Sternik et al.\(^43\) In Locker et al’s
study, revascularization without CPB decreased early mortality in patients without CPB with acute myocardial infarction in comparison with CPB (5% vs 24%, respectively); but the results were different at 2-year followup: long-term mortality was inverted (23% vs 3%), and more symptoms were evident in patients in the group with CPB (40% vs 19%) and along with a higher re-operation rate (15% vs 0%). Sternik et al evaluated the progress of patients with severe ventricular dysfunction who underwent myocardial revascularization without CPB and found less early mortality and less mortality at 2-year followup (3% vs 13% and 9% vs 15%, respectively), but found functional deterioration and a higher re-operation rate (14% vs 10% and 3% vs 0%, respectively). In both studies, the negative results appear to be related to the greater initial in-complete revascularization achieved with the technique without CPB. Czerny et al44 analyzed this aspect in their study, comparing the rate of revascularization achieved with the use of CPB or without it. Bull et al38 were not able to find a significant reduction in the morbidity or costs of surgery without CPB; on the other hand, Ascione et al45 concluded that the costs were lower. Some researchers report on the potential risk associated with surgery without CPB: Hangler et al41 found evidence of endothelial damage through local occlusion of the coronary artery, and Chavanon et al40 observed a greater incidence of aortic dissection in interventions with CPB.

After years of study, the conclusions reached in various studies have been recapitulated, and the pros and cons of myocardial revascularization without CPB have been established. Cooley45 and Mack46 discuss the advantages and disadvantages of this surgical technique, which limits our using this surgery extensively or indiscriminately. We must review the specific indications for it, which requires further randomized prospective studies, since most comparative studies are flawed in their selection of sample patients. Until further studies are completed, we cannot advise systematic myocardial revascularization with CPB in patient without compromising the clinical outcome.

CONCLUSIONS

Myocardial revascularization without CPB is a valid alternative in high-risk surgical patients, as it reduces overall morbidity, the need for transfusions, and the length of hospital stay. It does not reduce mortality but there is not a significant increase in mortality in the group without CPB, in spite of their greater risk at the outset.

A limitation of our study is the lack of patient randomization. In each case, the surgeon responsible chose one procedure or the other based on their own personal criteria, which may result in selection error. Prospective and randomized studies and long-term followup studies are needed to determine if there are differences in the need for re-operation, the appearance of later cardiac events, and above all graft impermeability. Significantly reduced permeability could be a large price to pay in certain patients, especially those with low surgical risks. We are on the brink of determining the relevancy and most ideal indication for surgery without CPB through further studies.

REFERENCES


