The Heart Surgery Forum #2003-91103
7 (1), 2004 [Epub December 2003] Online address: www.hsforum.com/vol7/issue1/2003-91103.html

# Avoidance of Cardiopulmonary Bypass Improves Early Survival in Multivessel Coronary Artery Bypass Patients with Poor Ventricular Function

(#2003-91103 . . . October 3, 2003)

**Todd M. Dewey**,[1] Morley A. Herbert,[2] Syma L. Prince,[1] Mitchell J. Magee,[1] James R. Edgerton,[1] Gregory Trachiotis,[3] E. P. Alexander,[3] Michael J. Mack[1]

[1]Cardiopulmonary Research Science and Technology Institute, Dallas, Texas; [2]Medical City Dallas Hospital, Dallas, Texas; [3]George Washington University/Veterans Affairs Medical Center, Washington, District of Columbia, USA

## ABSTRACT

**Background:** Patients with diminished ventricular function represent an increasing percentage of candidates for coronary artery bypass grafting (CABG). We have reviewed our recent experience in CABG in patients with ejection fractions (EF) ≤30% to identify factors leading to improved outcomes in this high-risk group.

**Methods:** Between January 1997 and September 2002, 990 patients with EF ≤30% underwent CABG. Univariate and logistic regression analysis was used to analyze data from 204 patients who underwent revascularization off-pump and 713 patients who underwent grafting with cardiopulmonary bypass (CPB) for differences in mortality, morbidity, and length of stay (LOS).

**Results:** Compared with the on-pump patient cohort, patients with depressed ventricular function who underwent revascularization without the use of CPB had a lower operative mortality rate that trended toward significance (2.9% versus 6.3%; $P = .06$) and a significantly lower risk-adjusted mortality rate (1.47% versus 4.13%; $P < .001$), despite a higher predicted risk (5.4% ± 5.5% versus 4.3% ± 3.7%; $P = .01$). Additionally, patients who underwent off-pump bypass grafting had a significantly lower incidence of reoperation for bleeding (1.0% versus 4.6%; $P = .02$), lower blood product use (39.6% versus 66.6%; $P < .001$), decreased postoperative ventilation times (11.3 ± 37.4 hours versus 46.1 ± 156.1 hours; $P < .001$), and fewer days in the intensive care unit (2.6 ± 3.8 days versus 4.2 ± 6.5 days; $P < .001$). Logistic regression analysis showed that CPB use ($P = .048$; odds ratio [OR], 2.4; 95% confidence interval [CI], 1.0-5.8) and previous CABG ($P = .015$; OR, 2.6; 95% CI, 1.2-5.7) were independent risk factors for mortality. A trend toward a shorter LOS (7.6 ± 7.9 days versus 8.9 ± 9.6 days; $P = .06$) was also seen in the off-pump patients.

**Conclusion:** Avoidance of CPB in patients with reduced ventricular function undergoing multivessel bypass improves early survival rates and decreases the incidence of reoperation for bleeding, blood product use, and postoperative ventilatory times.

*Presented at the Sixth Annual Meeting of the International Society for Minimally Invasive Cardiac Surgery, San Francisco, California, USA, June 19-21, 2003.*

*Received September 17, 2003; accepted October 3, 2003.*

*Address correspondence and reprint requests to: Todd M. Dewey, Cardiopulmonary Research Science and Technology Institute, 7777 Forest Ln, Suite C-742, Dallas, Texas, USA; 1-972-566-7219; fax: 1-972-490-5457 (e-mail: tdewey@CSANT.com).*

## INTRODUCTION

Reduced left ventricular function has been identified as a predictor of adverse outcomes after coronary artery bypass grafting (CABG) [Christakis 1992, Milano 1993]. Initial studies that evaluated operative morbidity and mortality with CABG concluded that the risk of revascularization in patients with severe left ventricular dysfunction was prohibitively high [Oldham 1972]. Other reports, however, have demonstrated that patients with reduced ejection fractions show not only a long-term survival benefit from CABG but also an improved functional status [Luchi 1987]. The optimal surgical approach for patients with impaired ventricular function has been unclear. Off-pump coronary artery bypass (OPCAB) grafting has emerged as a viable technique for the management of high-risk patients undergoing revascularization. Proinflammatory cytokines generated by extracorporeal support and cardioplegic arrest have been reported to lead to myocardial dysfunction and hemodynamic instability that may be poorly tolerated in patients with reduced ventricular function [Wan 1999]. The avoidance of cardiopulmonary bypass (CPB) and its associated release of inflammatory mediators promise significant potential benefits in patients with poor ejection fractions. We have reviewed our recent experience in CABG in patients with ejection fractions less than or equal to 30% to ascertain if OPCAB leads to improved outcomes in patients with poor ventricular function.

## MATERIALS AND METHODS

### *Patient Population*

Between January 1997 and September 2002, 12,126 patients underwent isolated CABG within our 22-surgeon multispecialty group practice. Prospectively collected data from the Society of Thoracic Surgeons database were analyzed to identify 990 patients who underwent operations during this period and who had a recorded ejection fraction of 30% or less as determined by echocardiography or contrast ventriculography. Patients who underwent revascularization while in cardiogenic shock or while being resuscitated or who underwent salvage procedures were excluded from the data set. Additionally, all patients having single-vessel bypass or beating heart revascularization on bypass were removed from the analysis. Of these patients, 917 who met these criteria were identified, with 204 patients having undergone revascularization off-pump and 713 patients having received on-pump arrested-heart CABG.

### *Technique of Off-Pump CABG*

OPCAB procedures were performed via a median sternotomy with or without the use of the left internal mammary artery, depending on the operating surgeon's discretion. Patients underwent heparinization at a dose of 1.5 to 2.0 mg/kg to achieve an activated coagulation time of ≥300 seconds. Early in the series, mobilization of the heart was achieved by the use of deep pericardial traction sutures. These sutures allowed access to targets on all aspects of the heart with acceptable hemodynamic indices. More recently, suction devices, such as the Guidant Expose device (Guidant, Santa Clara, CA, USA), were used in lieu of pericardial traction sutures to manipulate the heart. These devices provide superior exposure with improved hemodynamics secondary to reduced distortion and compression of the heart. The right pleura was occasionally opened to allow the heart to shift into the right chest to improve visualization of the posterior-lateral vessels. Stabilization of the target vessels was achieved with either the Guidant tissue stabilizer or the Medtronic Octopus II stabilization system (Medtronic, Minneapolis, MN, USA). A misted carbon dioxide blower was used to improve visualization during the anastomoses. Hemodynamic monitoring was performed by means of a pulmonary artery catheter with continuous cardiac output and mixed venous saturation capability. Transesophageal echocardiography was used in each patient to monitor global and regional wall motion during the procedure.

The left anterior descending artery was generally grafted first if flow-limiting disease was present. The grafts subsequently performed depended on the pattern of occlusion and surgeon preference. Generally, proximal anastomoses were performed prior to construction of the distal anastomosis to provide immediate reperfusion of the myocardium. Anticoagulation therapy was reversed with protamine sulfate at the conclusion of the procedure.

### *Technique of On-Pump CABG*

On-pump revascularization was likewise performed through a median sternotomy with or without use of the left internal mammary artery, depending on the operating surgeon's discretion. CPB was accomplished by cannulating the ascending aorta and right atrium. Myocardial protection was achieved by the use of antegrade and/or retrograde delivery systems with either crystalloid or blood cardioplegia, depending on the surgeon's preference. Patients were actively cooled to an average of 28°C to 32°C. Mean arterial pressures were maintained in the range of 60 to 80 mm Hg. Bypass grafts were then constructed in accordance with the operator's standard practices. Besides transesophageal echocardiography, monitoring was performed by means of a pulmonary artery catheter with continuous cardiac output and mixed venous saturation capability. Patients were delivered to the intensive care unit intubated for later weaning and extubation.

Table 1. Analysis of Patient Demographics*

| Variable | Off-Pump Beating Heart (n = 204) | On-Pump Arrested Heart (n = 713) | *P* |
|---|---|---|---|
| Female sex, n (%) | 37 (18.1) | 130 (18.2) | NS |
| Age, y | 65.7 ± 11.3 | 63.1 ± 10.4 | .002 |
| Diabetes, n (%) | 89 (43.8) | 269 (37.7) | NS |
| BSA, $m^2$ | 2.03 ± 0.26 | 2.06 ± 0.26 | NS |
| Renal failure on dialysis, n (%) | 10 (5.0) | 2 (0.3) | <.001 |
| Stroke, n (%) | 18 (8.9) | 58 (8.1) | NS |
| Peripheral vascular disease, n (%) | 33 (16.3) | 123 (17.3) | NS |
| Cerebrovascular disease, n (%) | 31 (15.3) | 91 (12.8) | NS |
| Previous CABG, n (%) | 16 (7.8) | 59 (8.3) | NS |
| Myocardial infarction, n (%) | 136 (66.7) | 520 (73.0) | NS |
| Angina, n (%) | 173 (84.8) | 647 (90.7) | .02 |
| Congestive heart failure, n (%) | 88 (43.1) | 300 (42.1) | NS |
| Ejection fraction, % | 25.1 ± 4.9 | 26.6 ± 4.2 | <.001 |
| Left main disease >50%, n (%) | 39 (19.1) | 177 (24.9) | NS |
| Preoperative IABP use, n (%) | 12 (5.9) | 142 (19.9) | <.001 |
| Triple-vessel disease, n (%) | 173 (84.8) | 640 (89.8) | .05 |
| Elective status, n (%) | 81 (39.7) | 263 (36.9) | NS |
| Urgent/emergent status, n (%) | 123 (60.3) | 450 (63.1) | NS |
| Predicted risk of mortality (STS) | 0.0536 ± 0.0548 | 0.0432 ± 0.0373 | .01 |

*Data are presented as the mean ± SD where appropriate. NS indicates not significant; BSA, body surface area; CABG, coronary artery bypass graft; IABP, intra-aortic balloon pump; STS, Society of Thoracic Surgeons.

### *Statistical Analysis*

All statistical analyses were performed with the SAS software, version 8.2 (SAS Institute, Cary, NC, USA). Categorical variables were analyzed with chi-square statistics, and continuous variables were analyzed with the Student *t* test. All differences with a *P* value of .05 or less were considered statistically significant. Logistic regression analysis was used to assess the effect of measured variables on operative mortality.

## RESULTS

In the off-pump cohort, there were 167 (81.9%) men and 37 (18.1%) women with a mean age of 65.7 ± 11.3 years (Table 1). The on-pump group consisted of 583 (81.8%) men and 130 (18.2%) women with a mean age of 63.1 ± 10.4 years. The groups differed with regard to ejection fraction, with the off-pump cohort having a mean ejection fraction of

Table 2. Analysis of Outcomes*

| Variable | Off-Pump Beating Heart (n = 204) | On-Pump Arrested Heart (n = 713) | *P* |
|---|---|---|---|
| Length of stay, d | 7.6 ± 7.9 | 8.9 ± 9.6 | NS (.06) |
| Distal arterial anastomoses, n | 1.38 ± 0.85 | 0.86 ± 0.72 | <.001 |
| Distal vein anastomoses, n | 1.85 ± 0.91 | 2.66 ± 1.04 | <.001 |
| Total anastomoses, n | 3.23 ± 0.89 | 3.53 ± 0.99 | <.001 |
| Cross-clamp time, min | 0 | 59.1 ± 21.4 | N/A |
| Perfusion time, min | 0 | 113.2 ± 39.5 | N/A |
| Ventilator time, h | 11.3 ± 37.4 | 46.1 ± 156.1 | <.001 |
| ICU stay, d | 2.6 ± 3.8 | 4.2 ± 6.5 | <.001 |

*Data are presented as the mean ± SD. NS indicates not significant; N/A, not applicable; ICU, intensive care unit.

Table 3. Analysis of Complications*

| Variable | Off-Pump Beating Heart | On-Pump Arrested Heart | *P* |
|---|---|---|---|
| Operative mortality, n (%) | 6 (2.9) | 45 (6.3) | NS (.06) |
| Risk-adjusted mortality | 0.0147 | 0.0413 | <.001 |
| Cardiac arrest, n (%) | 2 (1.0) | 14 (2.0) | NS |
| Reoperation for bleeding, n (%) | 2 (1.0) | 33 (4.6) | .02 |
| Reoperation for graft occlusion, n (%) | 0 (0.0) | 3 (0.4) | NS |
| Perioperative MI, n (%) | 0 (0.0) | 10 (1.4) | NS |
| Neurologic complications, n (%) | 1 (0.5) | 15 (2.1) | NS |
| Prolonged ventilation, n (%) | 14 (6.9) | 130 (18.2) | <.001 |
| Renal failure, n (%) | 9 (4.4) | 59 (8.3) | NS (.06) |
| Atrial fibrillation, n (%) | 44 (21.6) | 196 (27.5) | NS |
| Readmitted to hospital, n (%) | 14 (7.9) | 37 (6.3) | NS |
| Intra/postoperative IABP use, n (%) | 2 (1.0) | 55 (7.7) | <.001 |
| Transfusion requirement, n (%) | 80 (39.6) | 472 (66.6) | <.001 |

*NS indicates not significant; MI, myocardial infarction; IABP, intra-aortic balloon pump.

25.1% ± 4.9% versus 26.6% ± 4.2% for the on-pump group ($P < .001$). Additionally, the predicted risk of mortality for the off-pump group was higher than for the on-pump patients (5.36% versus 4.32%; $P = .01$). The off-pump group also had a significantly greater percentage of patients with renal failure requiring dialysis (5% versus 0.3%; $P < .001$). There were no differences between the two groups with respect to the incidences of previous bypass grafting or myocardial infarction, the occurrence of chronic obstructive pulmonary disease, or the prevalence of left main stenosis greater than 50%. The on-pump group was more likely to have had preoperative placement of an intra-aortic balloon pump (IABP) and an increased frequency of triple-vessel disease. Both groups demonstrated an equivalent requirement for preoperative inotropic support (6.4% for the off-pump group versus 5.2% for the on-pump group, not significantly different). The rates of preoperative stroke for the groups were not statistically different and were consistent with previously reported populations of patients who underwent coronary artery bypass [Almassi 1999].

The perioperative results of the two cohorts are shown in Tables 2 and 3. Patients with compromised ventricular function who underwent off-pump revascularization showed a trend toward a reduced operative mortality rate, compared with the patients who underwent bypass operations using CPB (2.9% versus 6.3%; $P = .06$), despite a higher preoperative predicted risk of mortality in the former group. The risk-adjusted mortality rates of the two groups were 1.47% in the off-pump patients and 4.13% in the on-pump group and were significantly different ($P < .001$). There was also a significantly greater need for an intraoperative or postoperative IABP in the on-pump group than in the off-pump patients (7.7% versus 1.0%; $P < .001$). Patients in the off-pump group were significantly less likely to require reoperation for bleeding (1.0% versus 4.6%; $P = .02$), to need prolonged ventilation postoperatively (6.9% versus 18.2%; $P < .001$), or to receive blood products (39.6% versus 66.6%; $P < .001$).

The average perfusion time for the on-pump group was 113.2 ± 39.5 minutes, and the mean cross-clamp time was 59.1 ± 21.4 minutes. Patients in the on-pump group had a greater total number of anastomoses performed at the time of operation than the patients in the off-pump group (3.53 ± 0.99 versus 3.23 ± 0.89; $P < .001$). However, more arterial anastomoses were performed in the off-pump group than in the on-pump cohort (1.38 ± 0.85 versus 0.86 ± 0.72; $P < .001$). The patients who underwent revascularization with CPB tended to spend significantly longer times in the intensive care unit than did the patients in the off-pump group (4.2 ± 6.5 days versus 2.6 ± 3.8 days; $P < .001$). Additionally, a trend toward a shorter hospital length of stay was seen in the off-pump patients (7.6 ± 7.9 days versus 8.9 ± 9.6 days; $P = .06$).

There were no differences between the groups with regard to the incidences of postoperative neurologic complications, myocardial infarction, or sternal wound infections. Logistic regression analysis identified CPB use as an independent risk factor for death in the considered patient population ($P = .048$; odds ratio, 2.4; 95% confidence interval, 1.0-5.8). Previous bypass surgery was also identified as an independent risk factor for death.

## CONCLUSIONS

Severe left ventricular dysfunction prior to surgical revascularization is a noted risk factor for increased morbidity and mortality [Edwards 1997]. Despite improvements in myocardial protection, oxygenator design, and perioperative care, mortality can range anywhere from 2 to 3 times that seen in patients with normal ventricular function [Nollert 1997, Bouchart 2001, Carr 2002]. This study demonstrates reduced risk-adjusted mortality rates and selected morbidity in patients with off-pump revascularization, compared with a contemporaneous cohort of patients with a lower predicted risk of mortality who underwent on-pump arrested-heart bypass grafting. We posit that the elimination of CPB and cardioplegia explains the improved perioperative outcomes in this high-risk group.

Recent investigations have described well the cascade of proinflammatory mediators released in response to CPB. Myocardial dysfunction and hemodynamic instability may be the consequence of the release of cytokines such as tumor necrosis factor α (TNF-α), interleukin 6 (IL-6), and IL-8 [Wan 1997, Hennein 1994]. The myocardium has previously been demonstrated to be capable of generating TNF-α, IL-6, and IL-8 during CPB and after reperfusion of the ischemic myocardium [Wan 1996b]. Furthermore, the degree of surgical trauma and the extent of dissection can influence the production of IL-6 in addition to CPB [Fransen 1998]. Studies have suggested that IL-6 can play a role in neutrophil-mediated myocardial ischemia-reperfusion injury [Sawa 1998].

Another significant cytokine involved with attracting and activating T-lymphocytes and neutrophils, as well as controlling their migration, is IL-8 [Finn 1993, Rollins 1997]. Animal models have shown that IL-8 release is induced after reperfusion of the ischemic myocardium [Ivey 1995, Kukielka 1995]. Likewise, clinical investigations have identified the myocardium as a major source of IL-8 after extended periods of ischemia and subsequent reperfusion [Oz 1995, Wan 1996a]. IL-8 has also been identified after acute myocardial infarctions [Neumann 1995]. The dissimilarity between the transient regional ischemia caused by off-pump bypass grafting and the extended global ischemia caused by arrested-heart revascularization may explain the reduced level of IL-8 production seen in off-pump procedures compared with conventional approaches [Wan 1999]. A strong correlation has been identified between IL-8 levels and the liberation of troponin-I after on-pump revascularization, implying the significance of this cytokine in inducing myocardial injury [Wan 1999]. Patients with limited ventricular reserve would be expected to poorly tolerate any significant degree of myocardial injury associated with revascularization. Reducing the myocardial injury and dysfunction due to cytokine release by avoiding CPB and cardioplegic arrest may provide insight into the finding in this study that the use of extracorporeal circulation was an independent risk factor for mortality.

Many investigators have emphasized the role of preoperative prophylactic placement of an IABP in providing hemodynamic support to patients with reduced ejection fractions who undergo surgical revascularization. Numerous reports have established the beneficial effects of preoperative IABP placement in high-risk patients undergoing coronary artery bypass with CPB [Gunstensen 1976, Christakis 1992, Christenson 1997]. Additionally, Craver and Murrah [2001] demonstrated favorable results with elective IABP placement in a small selected group of high-risk patients who underwent OPCAB. In this study, 12 balloon pumps were placed preoperatively in the off-pump cohort, and patients in this group who received an IABP had no survival advantage. In the on-pump group, 142 balloon pumps were placed preoperatively. The operative mortality rate in the patients without a preoperative IABP was 6.0%, compared with 7.8% in the patients with an IABP (not significantly different). Again, no obvious survival benefit for preoperative IABP placement was seen within the on-pump group. These results reflect the fact that most balloon pumps were placed for hemodynamic instability or ongoing ischemia instead of being electively placed. We do agree, however, that elective preoperative placement of an IABP can be of significant benefit for high-risk patients undergoing OPCAB and in whom a conversion to CPB would be particularly detrimental. The on-pump cohort had an appreciably increased need for IABP placement in the operating room or in the postoperative period. Within this group, patients who received an IABP intraoperatively or postoperatively had a significantly greater mortality rate (34.6% versus 4.0%; $P < .001$) than those patients who did not receive the device. Failure to wean from CPB and post-bypass hemodynamic instability were the most frequent reasons for insertion. Based on this study, we conclude that the need for an IABP to separate the patient from CPB or to leave the operating room is a marker for an increased perioperative risk of mortality.

Inherent in the performance of off-pump bypass grafting is the potential for conversion to mechanical support to complete the procedure. This is especially true in a population with limited hemodynamic reserve and cardiomegaly, which can make visualization and grafting of the posterior and lateral wall problematic. Multiple factors can contribute to the downward hemodynamic spiral that ultimately leads to conversion. Significant hemodynamic deterioration may result from a number of mechanical alterations to the normal geometry of the heart, such as right ventricular compression, right ventricular outflow tract obstruction, mitral annular deformation causing regurgitation, and impaired left ventricular filling. Our experience has demonstrated that larger hearts are more difficult to position and more likely to develop mechanically unfavorable geometries. Moreover, coexistent ischemia magnifies the effects of mechanical dysfunction, resulting in the need to transition to pump support. In the present series, data regarding conversions from off-pump to on-pump support were only collected beginning in 2000. Of the 8 patients who underwent conversions, 6 were placed on pump support but without cardioplegic arrest. In this subgroup of 6 patients, there were 2 deaths that were attributable to cardiac complications resulting from conversion from off-pump bypass. The remaining 2 conversion cases, one an operative death, were converted to pump support with cardioplegic arrest. Because this study was not an intention-to-treat inquiry, conversion cases were not included in the study analysis. Only 1 of the 8 conversions was recorded as emergent in nature. Reasons for nonemergent conversion included the presence of intramyocardial vessels, difficult exposure of target arteries, and hemodynamic or rhythm changes that made proceeding with OPCAB problematic. If the cardiac deaths involving conversions are counted as off-pump deaths, a survival benefit is still seen with OPCAB. The off-pump group now has an observed mortality rate of 4.4% and a risk-adjusted mortality rate of 2.16%. This result is still significantly better than the risk-adjusted mortality rate of 4.13% seen in the on-pump group ($P < .001$).

On the basis of previous work, we recommend an early transition to pump support for this patient population once a patient becomes refractory to pharmacologic

Table 4. Variation in Mean Number of Grafts per Patient from 1997 to 2002*

| | Off-Pump Beating Heart | On-Pump Arrested Heart | *P* |
|---|---|---|---|
| Overall | 3.23 ± 0.89 (204) | 3.53 ± 0.99 (713) | <.001 |
| 1997 | N/A (0) | 3.56 ± 1.05 (178) | N/A |
| 1998 | 2.50 ± 0.67 (12) | 3.44 ± 0.89 (161) | <.001 |
| 1999 | 3.11 ± 0.89 (47) | 3.54 ± 1.08 (120) | .01 |
| 2000 | 3.44 ± 0.84 (72) | 3.61 ± 0.96 (111) | NS |
| 2001 | 3.38 ± 1.01 (42) | 3.59 ± 0.87 (101) | NS |
| 2002 | 3.00 ± 0.68 (31) | 3.43 ± 0.91 (42) | .03 |

*Data are presented as the mean number of grafts per patient (number of patients). N/A indicates not applicable; NS, not significant.

manipulation or repositioning [Edgerton 2003]. Full CPB is preferred to isolated right or left heart support because of the ability to simultaneously support both ventricles and completely decompress and unload the heart. Grafting should then be completed with off-pump techniques with the heart supported but beating. We advise against cardioplegic arrest in this situation, if possible, to limit global myocardial ischemia.

The mortality benefit in the off-pump group is notable given that the mean number of anastomoses during the study period was significantly greater in the on-pump cohort. Recently, there have been no differences between the groups with respect to the mean number of anastomoses performed in 2000 and 2001, but there is still a significant difference in 2002 (Table 4). This finding suggests a nonrandomized unmatched comparison rather than incomplete revascularization in the off-pump group, especially given the improved perioperative mortality rate in the off-pump patients. However, the question of complete revascularization will be determined only from long-term follow-up with regard to the return of symptoms or the need for reintervention.

This study is limited by its nonrandomized retrospective nature in evaluating two different surgical approaches to revascularization of patients with severely reduced ejection fractions. Patient stratification into the two cohorts was left solely to the discretion of the operating surgeon. Experience with off-pump bypass grafting varies across our 22-surgeon practice, but this variation most likely reflects that of cardiac surgery as a whole. The inability to identify conversions before the year 2000 limits our ability to calculate a conversion rate for the entire study period. However, the observed rate of conversion for the last 3 years of the study was 5.5%. Given the relatively few patients in this category, attempting to identify risk factors leading to conversion would be speculative.

In summary, OPCAB grafting shows a mortality and morbidity benefit compared with conventional techniques in patients with severe left ventricular dysfunction. We believe that despite revascularization the production of proinflammatory cytokines initiated by CPB and intervals of global myocardial ischemia are poorly tolerated in these patients. Long-term follow-up regarding survival, adverse cardiac events, and the need for reintervention is essential to ensure that the perioperative benefits of OPCAB translate into long-term survival and improved quality of life for these patients.

## REFERENCES


Almassi GH, Sommers T, Moritz TE, et al. 1999. Stroke in cardiac surgical patients: determinants and outcomes. Ann Thorac Surg 68:391-8.

Bouchart F, Tabley A, Litzler PY, Haas-Hubscher C, Bessou JP, Soyer R. 2001. Myocardial revascularization in patients with severe ischemic left ventricular dysfunction: long-term follow-up in 141 patients. Eur J Cardiothorac Surg 20:1157-62.

Carr JA, Haithcock, BE, Paone G, Bernabei AF, Silverman NA. 2002. Long-term outcome after coronary artery bypass grafting in patients with severe left ventricular dysfunction. Ann Thorac Surg 74:1531-6.

Christakis GT, Weisel RD, Fremes SE, et al. 1992. Coronary artery bypass grafting in patients with poor ventricular function: Cardiovascular Surgeons of the University of Toronto. J Thorac Cardiovasc Surg 103:1083-92.

Christenson JT, Simonet F, Badel P, Schmuzier M. 1997. Evaluation of preoperative intra-aortic balloon pump support in high risk coronary patients. Eur J Cardiothorac Surg 11:1097-104.

Craver JM, Murrah CP. 2001. Elective intraaortic balloon counterpulsation for high-risk off-pump coronary artery bypass operations. Ann Thorac Surg 71:1220-3.

Edgerton JR, Dewey TM, Magee MJ, et al. 2003. Conversion in off-pump coronary artery bypass grafting: an analysis of predictors and outcomes. Ann Thorac Surg 76:1138-43.

Edwards FH, Grover FL, Shroyer AL, Schwartz M, Bero J. 1997. The Society of Thoracic Surgeons National Cardiac Surgery Database: current risk assessment. Ann Thorac Surg 63:903-8.

Finn A, Naik S, Klein N, Levinsky RJ, Strobel S, Elliott MM. 1993. Interleukin-8 release and neutrophil degranulation after pediatric cardiopulmonary bypass. J Thorac Cardiovasc Surg 105:234-41.

Fransen E, Maessen J, Dentener M, Senden N, Geskes G, Buurman W. 1998. Systemic inflammation in patients undergoing CABG without extracorporeal circulation. Chest 113:1290-5.

Gunstensen J, Goldman BS, Scully HE, Huckell VF, Adelman AG. 1976. Evolving indications for preoperative intraaortic balloon pump assistance. Ann Thorac Surg 22:535-45.

Hennein HA, Ebba H, Rodriguez JL, et al. 1994. Relationship of the proinflammatory cytokines to myocardial ischemia and dysfunction after uncomplicated coronary revascularization. J Thorac Cardiovasc Surg 108:626-35.

Ivey CL, Williams FM, Collins PD, Jose PJ, Williams TJ. 1995. Neutrophil chemoattractants generated in two phases during reperfusion of ischemic myocardium in the rabbit: evidence for a role of C5a and interleukin-8. J Clin Invest 95:2720-8.

Kukielka GL, Smith CW, LaRosa GJ, et al. 1995. Interleukin-8 gene induction in the myocardium after ischemia and reperfusion in vivo. J Clin Invest 95:89-103.

Luchi RJ, Scott SM, Deupree RH. 1987. Comparison of medical and surgical treatment for unstable angina pectoris: results of a Veterans Administration Cooperative Study. N Engl J Med 316:977-84.

Milano CA, White WD, Smith LR, et al. 1993. Coronary artery bypass grafting in patients with severely depressed ventricular function. Ann Thorac Surg 56:487-93.

Neumann FJ, Ott I, Gawaz M, et al. 1995. Cardiac release of cytokines and inflammatory responses in acute myocardial infarction. Circulation 92:748-55.

Nollert G, Schmoekel M, Markewitz A, et al. 1997. Surgical therapy for coronary artery disease in patients with a left ventricular ejection fraction of 25% or less. J Cardiovasc Surg (Torino) 38:389-95.

Oldham HN Jr, Kong Y, Bartel AG, et al. 1972. Risk factors in coronary artery bypass surgery. Arch Surg 105:918-23.

Oz MC, Liao H, Naka Y, et al. 1995. Ischemia-induced interleukin-8 release after human heart transplantation: a potential role for endothelial cells. Circulation 92:II-428-32.

Rollins BJ. 1997. Chemokines. Blood 90:909-28.

Sawa Y, Ichikawa H, Kagisaki K, Ohata T, Matsuda H. 1998. Interleukin–6 derived from hypoxic myocytes promotes neutrophil-mediated reperfusion injury in myocardium. J Thorac Cardiovasc Surg 116:511-7.

Wan S, DeSmet JM, Barvais L, Goldstein M, Vincent JL, LeClerc JL. 1996. Myocardium is a major source of proinflammatory cytokines in patients undergoing cardiopulmonary bypass. J Thorac Cardiovasc Surg 112:806-11.

Wan S, Izzat MB, Lee TW, Wan IY, Tang NL, Yim AP. 1999. Avoiding cardiopulmonary bypass in multivessel CABG reduces cytokine response and myocardial injury. Ann Thorac Surg 68:52-7.

Wan S, LeClerc JL, Vincent JL. 1997. Cytokine responses to cardiopulmonary bypass: lessons learned from cardiac transplantation. Ann Thorac Surg 63:269-76.

Wan S, Marchant A, DeSmet JM, et al. 1996. Human cytokine responses to cardiac transplantation and coronary artery bypass grafting. J Thorac Cardiovasc Surg 111:469-77.