Beating Heart Surgery Reduces Utilization of Blood Products in Coronary Revascularization

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ABSTRACT

Background: The purpose of this study was to compare patients who had coronary artery bypass (CABG) without cardiopulmonary bypass (CPB) with a group of patients with comparable risk who had CPB used during CABG. The elimination of CPB to perform CABG appears to improve the clinical outcomes of surgical patients. Elimination of CPB may reduce hemodilution and coagulation dysfunction, thus reducing the need for blood transfusion.

Methods: Between January 1, 1995 and December 31, 2000, 3,744 patients underwent isolated CABG. Of these, 245 patients were operated on without the use of CPB (NOCPB). Risk scores based on pre-surgical factors related to surgical mortality were calculated for each of the 3,744 patients in the study using a logistic regression model. Stratified risk scores were then used to randomly match a set of

245 CPB patients with those in the NOCPB group. Statistical analysis was carried out on the two matched groups.

Results: In the NOCPB group, 3 (1.2%) patients died in-hospital, similar to the 1.6% death rate in the CPB cases. There was a trend towards a lower stroke rate in the NOCPB group (0.8% vs. 2.9%; p=0.06). Two patients (0.8%) of the NOCPB patients were re-explored for bleeding, 2 (0.8%) had perioperative myocardial infarctions, and there were no deep sternal wound infections. NOCPB patients received an average of 1.5 $\pm$ 1.2 saphenous vein graphs compared to 2.6 $\pm$ 1.1 for the CPB group (p<0.000). In addition, 90 % of NOCPB patients received an internal mammary artery graft compared to 95 % of the CPB group (p<0.077). The CPB group had similar outcomes. 66 (26.9%) of the NOCPB patients received blood or blood products, which was significantly lower than the 42% rate in the CPB group (p<0.001). The NOCPB patients who did require blood needed on the average only 2 units compared to the 6 units required in the CPB group (p<0.001).

Conclusion: Mortality outcomes for risk-matched groups of off-pump and pump patients were comparable. Significantly fewer patients in the off-pump group required blood products, and those who did required fewer units of blood.

INTRODUCTION

The purpose of this study was to compare patients who had CABG without CPB with a group of patients with comparable risk who had CPB used during CABG. Numerous observations suggest that the elimination of cardiopulmonary bypass in the performance of coronary artery bypass surgery may improve clinical outcomes [Edmunds 1995, Buffolo 1996, Hill 1998, Ascione 1999, Pompilio 1999, Taylor 1999, Arom 2000, Ascione 2000, Kshettry 2000, Stamuo 2000, Newman 2001, Pompilio 2001, Puskas 2001] . Despite these observations, the methods have come under criticism because all of the studies have been retrospective in nature and thus subject to selection bias [Wait 2001]. The presence of a relatively large, detailed, and prospectively assembled patient database affords an opportunity to utilize modern risk adjustment methods. Such patient group matching is the next best thing to a prospective randomized trial that nowadays would be prohibitively expensive and would raise many difficult ethical issues [Pliam 1997, D'Agostino 1998, Peterson 2000].

MATERIALS AND METHODS

Between January 1, 1995 and December 31, 2000, 3,744 patients underwent isolated CABG. Of these, 245 patients were operated on without the use of CPB (NOCPB). Fifty-one (20.8%) patients had their operation done via a left mini-thoracotomy (MIDCAB) and 194 (79.2%) were done via sternotomy (OPCAB). One hundred seventy-five (71%) were male and 70 (29%) were female. Fifty-one (20.8%) patients had their operation done via a left mini-thoracotomy (MIDCAB) and 194 (79.2%) were done via sternotomy (OPCAB). One hundred seventy-five (71%) were male and 70 (29%) were female.

A risk score based on pre-surgical factors related to surgical mortality was calculated for each patient by the application of a risk model that was developed using stepwise logistic regression on the entire set of study patients. The underlying risk model that was used to stratify all patients in the study was a logistic regression model which has been described previously [Pliam 1997]. The preoperative risk factors that were used as input to our logistic regression program were: age greater than 75 years, female gender, low ejection fraction (below 35%), reoperation, hypertension, hypercholesterolemia, smoking status (current, previous, or none), diabetes, chronic obstructive pulmonary disease, prior myocardial infarction, emergency, failed catheter intervention emergency, intraaortic balloon pump, congestive heart failure, cardiogenic shock, morbid obesity, triple vessel disease, left main disease, small physical stature, prior stroke, acute evolving myocardial infarction, anemia (hct below 35%), peripheral vascular disease, renovascular disease, and cerebrovascular disease. Using this input, a logistic regression model was generated that included 9 significant predictors of hospital mortality: low ejection fraction, chronic obstructive pulmonary disease, emergency, intraaortic balloon, left main disease, congestive heart failure, morbid obesity, peripheral vascular disease, and renal disease. The area under the receiver operating charactertic curve (C-Index) was 0.796 for the model when run on the total number of study patients.

In the NOCPB group, three risk strata (low, medium, and high) were developed by dividing the cumulative percentages of risk into tritiles. These NOCPB subgroups contained 143, 37, and 65 patients respectively. Using the same model, risk scores were also calculated on 3,499 patients that had CABG using

cardiopulmonary bypass during the same time period. These risk scores were similarly stratified into tritiles, using the same cutoff points that were used to stratify the NOCPB group. A group of 245 patients were then selected from the 3,499 patients who had cardiopulmonary bypass used, and samples drawn randomly from each risk strata to exactly match the numbers of patients in the NOCPB group. The resulting group of 245 patients was designated as the CPB group.

RESULTS

The average age was 67 years (range: 39 to 92). Seventy-four (30.2%) patients presented with diabetes mellitus, 160 (65.6%) had hypertension, 148 (60.4%) had elevated cholesterol and 15 (6.2%) had a history of stroke. Left main coronary disease was present in 44 (18%). After selection, analysis showed that the overall risk score was nearly identical between the groups. Pre-operative hematocrit and body surface area were comparable, as were the number of grafts performed in each group. In the NOCPB group, 3 (1.2%) patients died in-hospital, similar to the 1.6% death rate in the CPB cases. There was a trend towards a lower stroke rate in the NOCPB group (0.8% vs. 2.9%; p=0.06). Two (0.8%) of the NOCPB patients were re-explored for bleeding, 2 (0.8%) had perioperative myocardial infarctions, and there were no deep sternal wound infections. The CPB group had similar outcomes. Sixty-six (26.9%) of the NOCPB patients received blood or blood products, which was significantly lower than the 42% rate in the CPB group ($p<0.001$). NOCPB patients received an average of 1.5 ± 1.2 saphenous vein graphs compared to 2.6 ± 1.1 for the CPB group ($p<0.000$). In addition, 90 % of NOCPB patients received an internal mammary artery graft compared to 95 % of the CPB group ($p<0.077$). The NOCPB patients who did require blood needed on the average only 2 units compared to the 6 units required in the CPB group ($p<0.001$).

DISCUSSION

All non-randomized clinical studies can be criticized to the extent that patient selection criteria was in some manner biased. The current study is no exception, but we have taken a number of measures in order to address this criticism. We recognize the following. The present study was carried out over a six-year period, during which time the numbers of NOCPB procedures steadily increased. In fact, in 1995 we

performed 756 isolated CABG procedures, only 1 of which was a NOCPB procedure. The percentages of NOCPB for each year subsequent to 1995 were 3.0, 2.9, 3.8, 11.8 and 27.9 percent. The NOCPB patients in the earliest stages of our experience were selected for the NOCAB procedure because the exhibited good left ventricular function, required fewer bypass grafts, had good target vessels, and had generally fewer co-morbidities. As our experienced grew, our selection criteria for NOCPB expanded. So did the number of grafts per patient performed. Since the risk stratification model that we developed only took into account preoperative variables, it did not take into account the number of bypass conduits received by a patient. As noted above, there was a difference in the number of bypass grafts received by NOCPB and CPB patients, suggesting that there exist some risk factors that we were not entirely accounted for by the statistical methods that we employed.

Most medical decision-making is based on nonrandomized clinical studies rather than formal, randomized clinical trials. Until recently, the only way to study nonrandomized treatments has been through the use of carefully performed multivariate analysis. But multivariate analysis does not always result in a correct assessment [Rosenbaum 1983, Pliam 1997, D'Agostino 1998, Peterson 2000, Blackstone 2001, Wait 2001]. One set of statistical techniques for making improved inferences from nonrandomized comparisons is known as *balancing scores* [Rosenbaum 1983]. A balancing score is a simply a matching technique which allows placement of similar patients into groups which tend to eliminate bias and selection factors. The differences in outcomes of such similar patient groups can then be assessed more objectively with respect to the differences in treatments given. Over the past five years, statistical balancing scores have been used increasingly to analyze clinical data in lieu of expensive and often impractical prospective randomized clinical trials. [D'Agostino 1998, Blackstone 2001]. The present study utilizes a balancing score technique to match potentially dissimilar groups, allowing the *simulation* of prospective randomized trial. The greatest potential limitation of this method appears to be the predictive capability of the logistic regression risk model that was employed. Since this model had a C-Index 0.796, we felt reasonably confident that the model had relatively strong predictive capability.

The results of the present study appear to be consistent with those of others. Puskas et al. [Puskas 2001] used a matched set of CABG and OPCAB patients to

demonstrate improved clinical results in the OPCAB group. The OPCAB group exhibited a markedly diminished incidence of perioperative transfusion (70% vs 33). Similar results have been observed by others [Buffolo 1996, Ascione 1999, Pompilio 1999, Arom 2000, Kshettry 2000, Stamuo 2000, Pompilio 2001] .

There are a number of obvious advantages to reducing the number of blood product s transfused incident to CABG. Elimination of CPB may reduce hemodilution and coagulation dysfunction, thus improving surgical results [Edmunds 1995, Hill 1998, Ascione 2000]. Diminishing the number of transfusions should reduce the transmission of blood-borne viruses, the risk of allergic transfusion reactions, and immune sensitization. In addition, this should contribute to an overall improvement in resource utilization [Ascione 1999, Puskas 2001].

There is considerable evidence that cardiopulmonary bypass can have a deleterious effect on a patient's central nervous system [Edmunds 1995, Hill 1998, Taylor 1999, Newman 2001]. This risk may have two components, the short-term immediate effect of perioperative stroke, and the longer-term phenomenon of intellectual impairment [Newman 2001]. It is not clear whether or not these two entities share a common mechanism. But it seems certain that a few patients, who are afflicted with a heavily calcified or "lead pipe" ascending aorta, have a very high risk of experiencing a stroke if their aorta is cross-clamped. We, and others, have managed a number of such cases using complete arterial revascularization off-pump with excellent results.

We, and others, have observed that older patients undergoing CABG have a greater propensity to perioperative blood product transfusion. As older, sicker patients are referred for coronary bypass operations, an increasing proportion of patients may have relative contraindications to cardiopulmonary bypass [Pliam 1999, Stamuo 2000].

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