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The Octopus II™ Stabilizing System: Biochemical and Neuropsychological Outcomes in Coronary Artery Bypass Surgery

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ABSTRACT

Background: The aim of this study was to determine if coronary artery bypass graft (CABG) surgery performed utilizing the Octopus II™ stabilizing system provides myocardial and cerebral protection comparable to traditional CABG surgery utilizing cardiopulmonary bypass (CPB).

Methods: Elective patients requiring surgery for double or triple vessel disease were randomized to receive either conventional CABG with CPB (n = 14) or OPCAB using the Octopus II™ stabilizing system (n = 12), after receiving institutional approval and written consent. Exclusion criteria included previous cardiac surgery, recent myocardial infarction, and previous cerebrovascular disease. Troponin T (TnT) was measured preoperatively and at 2, 4, 6, 8, 10, 12, 24, and 72 hours after initiation of grafting. Neuropsychological assessments (10 measures) were performed in the week prior to surgery, one week, and six months after surgery.

Results: Troponin T release was reduced in the OPCAB patients at all time points (repeated measures ANOVA p = 0.043), reaching significance at 8, 10 and 12 hours (p = 0.033, 0.038, 0.019). Other factors (composite clinical end point (prolonged LOS or ICU stay or 30-day mortality), infarction, and intubation time) did not show any significant differences between the two groups. The incidence of neuropsychological deficits was not different between the two groups at both seven-day and six-month follow-up assessments.

Conclusions: Decreased TnT release suggests a myocardial benefit for the OPCAB procedure. A neuropsychological benefit remains to be demonstrated.

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INTRODUCTION

The adoption of new technologies for the performance of beating heart surgery has revitalized the interest in performing coronary artery bypass graft surgery without the use of cardiopulmonary bypass (CPB). In order for alternative surgical methods to be widely accepted, the comparison with current techniques is mandatory. An early concern which hindered the widespread use of off-pump coronary artery bypass surgery (OPCAB) was the question of graft patency. A recent paper by Jansen et al. described angiographic findings in 100 consecutive OPCAB cases that showed similar results to coronary grafting on pump [Jansen 1998].

There are now many clinical papers reporting series of patients in varied settings which show initial excellent results of off-pump surgery [e.g., Hart 1999]. In addition, recent reports have demonstrated reduced hospital length of stay [Gulielmos 1998, Spooner 1998], improved neurological outcomes [Murkin 1999, Diegeler 2000], and reduced inflammatory response and myocardial injury [Czerny 2000]. Boyd et al. and Ricci et al. have reported reduced morbidity in high risk geriatric groups, while Stamou et al. demonstrated benefits of OPCAB in operations for coronary artery bypass grafting [Boyd 1999, Ricci 2000, Stamou 2000]. A recent paper by Kshettry et al. challenged the clear advantage associated with OPCAB techniques [Kshettry 2000]. In a retrospective analysis of 135 off-pump cases compared to 609 on-pump cases they could not demonstrate any advantage in morbidity associated with the OPCAB technique beyond reduced blood loss and less blood transfusions in the OPCAB patients.

It is hypothesized that one of the major advantages seen with off-pump surgery is the avoidance of CPB. However, most reports are limited by their retrospective nature and their non-randomized design. In this preliminary report we assess the efficacy of coronary artery grafting utilizing the Octopus II™ stabilizing system in a prospective randomized manner. Specifically, we will address the neuropsychological and myocardial effects of the procedure by direct comparison with conventional coronary artery grafting utilizing CPB.

MATERIALS AND METHODS

Patients

Elective coronary artery bypass patients requiring surgery for double or triple vessel disease, who were considered suitable for revascularization either with or without CPB, were randomized to receive either conventional CABG surgery with CPB (Group 1, n = 14), or OPCAB utilizing the Octopus II™ retraction stabilising system (Group 2, n = 12). Patients were randomized following informed consent to participate in the trial.

All elective patients admitted for surgery for double or triple vessel disease were considered for inclusion in the trial. The following exclusion criteria were adopted:

1. Ejection fraction (EF) <40%.
2. Non-English speaking.
3. Previous cerebrovascular disease including cerebrovascular accident, reversible ischaemic neurological deficit, or transient ischaemic attack anytime prior to planned surgery.
4. All emergency and urgent coronary artery surgery including patients with unstable angina pectoris (requiring heparin or glycerine trinitrate prior to surgery) or myocardial infarction within six weeks of surgery.
5. Previous open heart surgery.
6. More than three distal anastomoses.
7. Chronic renal failure (Cr >0.3) or severe chronic obstructive airways disease (with pulmonary function test evidence).

Patients were eligible for withdrawal after randomization only if one or more of the following criteria were met: intramuscular coronary artery, coronary artery deeply embedded in fat, any patient unable to tolerate vessel occlusion or heart elevation, and aortic calcification making routine cardiopulmonary bypass techniques unsuitable.

Surgical Technique

Group 1: Patients underwent conventional coronary artery grafting with CPB. Cardiopulmonary bypass was instituted after positioning of a single two-stage atrial cannula and an ascending aortic cannula. Standard management was instituted, including use of a membrane oxygenator, arterial line filtration, non pulsatile flow, and alpha stat pH management. Patients were allowed to drift to a temperature of 34°C. After placement of the aortic cross clamp, cardioplegic arrest was induced with tepid blood cardioplegia (32°C) and intermittent bolus cardioplegia as required. Proximal anastomoses were performed with after-application of a partial aortic clamp (side-biting). Patients were separated from bypass when nasopharyngeal temperatures in excess of 36.5°C were achieved.

Group 2: OPCAB was performed through a median sternotomy. In all patients, stabilization was achieved utilizing the Octopus II™ stabilizing device. Prior to placement of the Octopus II™, one or two deep pericardial sutures were placed to aid in visualization of the left posterior pericardium. Distal anastomoses were performed with either transient snaring of the target vessel or the use of flow-through stents. Proximal anastomoses were performed with partial aortic clamping. Temperatures were maintained throughout the procedure by utilizing a combination of a bair hugger, warming blanket, hot line fluid warmer, humidified ventilation circuit, and increased theater temperatures.

All distal anastomoses were performed in a similar manner in each group with 6-0 or 7-0 polypropylene sutures utilizing a single suture continuous technique.

Anesthetic Technique

All patients received a standardized anesthetic management protocol identical for both treatment arms, consisting of lorazepam premedication, induction with midazolam, pancuronium and fentanyl, and maintenance with isoflurane, nitrous oxide and/or propofol as required. Hemodynamic control was maintained by altering depth of anesthesia or administration of vasoactive drugs.

Group 1 patients had a standard heparinization protocol, with 3mg/kg heparin bolus prior to cannulation, 10,000 IU in pump prime, with a target ACT of >400 pre-bypass. Group 2 received 1.5mg/kg of heparin prior to commencement of coronary grafting, with a target ACT of >200 pre-bypass.

Biochemical Sampling

Plasma samples were collected at 2, 4, 6, 8, 10, 12, 24 and 72 hours after commencement of coronary grafting for the assessment of the Troponin T (TnT) release profile. Plasma TnT was measured using a one-step enzyme-linked immunoassay (Boehringer Mannheim) on a Boehringer Mannheim ES300 immunoassay analyzer. The detection limit of this assay is 0.05 ng/ml. The upper reference limit is 0.2 ng/ml.

Neuropsychological Assessment

Neuropsychological testing was performed utilizing our established test battery on all patients preoperatively, postoperatively prior to discharge, and six months after surgery [Andrew 1998, Kneebone 1998]. Neuropsychological test selection was based substantially on the Statement of Consensus and includes measures of memory, attention, and psychomotor speed [Murkin 1995]. Tests included in order of administration are the California Verbal Learning Test (CVLT), Purdue Pegboard, Trail Making Test Trials A and B, and Digit Symbol Substitution. Neuropsychological deficits were defined using reliable change criteria [Kneebone 1998].

Data Analysis

Statistical analyses were performed using the SPSS® statistical software package (SPSS Inc., Chicago, IL), with an

Table 1. Demographics and pre-existing disease

	Group 1 On pump (N = 14)	Group 2 OPCAB (N = 12)
Demographics		
Age	65.9 ± 8.3	61.7 ± 11.7
Education (yrs)	10.7 ± 2.8	10.9 ± 3.6
Gender (M/F)	10/4	11/1
FSIQ	102.3 ± 9.4	103.2 ± 6.1
Pre-existing disease (%)		
Cerebrovascular disease	0%	0%
Hypertension	70%	55.6%
Hypercholesterolemia	77.8%	75%
Diabetes mellitus	30%	11.1%
Elevated creatinine	40%	33.3%
Family history	80%	77.8%

Table 2. Surgical and outcome data

	Group 1 On pump (N = 14)	Group 2 OPCAB (N = 12)
No. of grafts	2.5 ± 0.5	2.2 ± 0.6
% LIMA	100%	83.3%
CPB time (min)	35.6 ± 8.6	–
X-clamp time (min)	20.1 ± 4.8	–
Octopus in position (min)	–	20 ± 7.6
Graft time (min)	–	12 ± 7.6
Procedure time (min)	123.7 ± 29.4	109.1 ± 23.3
Intubation time (hr)	10.1 ± 4.5	10.9 ± 4.9
ICU time (hr)	25.7 ± 5.2	27.5 ± 13.0
LOS (days)	5.6 ± 1.5	5.5 ± 0.9
Perioperative infarction	0	1
Combined clinical endpoint	4	2

alpha value of 0.05 or less considered statistically significant. Quantitative data was compared with one-way analysis of variance (ANOVA). Categorical data was analyzed with the chi-square statistic, with Fisher's 2-tailed exact test used if the expected cell sizes were small. Group differences were examined on incidence of deficits on each neuropsychological measure at both seven-day and six-month assessment (analyzed as per categorical data), and number of measures per patient showing a statistically significant deficit (analyzed with the Mann-Whitney U tests). Preoperative, perioperative, and postoperative variables which differed significantly between the two surgical groups were transformed to conform with assumption of normal distribution and then tested for associations with the change score variable using Pearson correlation coefficients (continuous variables) or one-way ANOVA (categorical variables). A combined clinical endpoint was determined for each patient. This was defined as having either a prolonged length of stay or intensive care stay (> mean + 1 SD) or death within 30 days. Data are displayed as mean ± SD.

RESULTS

We report findings from the first 26 patients enrolled in an ongoing prospective randomized study. This represents less than 30% of the patients to be enrolled.

Preoperative and Surgical Variables

As shown in Table 1 (◎), both groups were comparable in demographics and comorbidities. The two groups were also comparable on surgical and outcome data (see Table 2, ◎). To establish the potential myocardial injury time for the Octopus group we have recorded both the time taken to perform the graft (graft time) and the total time that the Octopus stabilizing system was in contact with the surface of the heart (Octopus in position).

Troponin T

TnT release profiles were assessed for all patients and individual release profiles are shown in Figure 1 (◎). The release profile for the one patient with myocardial infarction has not been plotted. This patient's peak TnT value occurred at the 72-hour sampling interval (3.6 ng/ml). All of the remaining Group 2 patients (n = 11) demonstrated a peak release at 6 or 8 hours. Twelve of 14 Group 1 patients demonstrated a peak at six or eight hours.

Figure 2 (◎) displays the mean data for TnT release at each time interval. The release of TnT was significantly reduced in Group 2 ($p = 0.043$, repeated measures ANOVA) compared to Group 1 At the individual sampling times of 8, 10 and 12 hours after commencement of grafting, the TnT release was significantly lower in Group 2 ($p = 0.033$, 0.038 and 0.019 respectively, t-test).

Incidence of Neuropsychological Deficits

At the seven-day assessment there were no differences between the groups in the incidence of deficits on each neuropsychological measure (see Table 3, ◎). Similarly, as shown in Figure 3 (◎), there were no differences between the patients in each group when the number of tests per patient displaying a deficit were examined. The tests most susceptible to deficits in Group 1 were Pegs R, Trail Making B, and Digit Symbol Substitution. Conversely, the most susceptible tests for Group 2 were verbal memory (CVLT Total, Long Free and Long Cued) and also Digit Symbol.

The six-month follow-up results indicate an almost total reduction in the incidence of deficits in both Group 1 and Group 2 patients.

DISCUSSION

The last five years have seen rapid progress in the area of minimally invasive cardiac surgery. There now appears to be wide acceptance for so-called off-pump procedures in

Table 3. Percentage of patients showing deficits on each neuropsychological measure at the seven-day and six-month assessment

Variable	7 days Group 1 On pump (N = 14)	7 days Group 2 OPCAB (N = 12)	6 months Group 1 On-pump (N = 10)	6 months Group 2 OPCAB (N = 8)
CVLT Total	7.1 (1)	25.0 (3)	0	0
CVLT Long Free	7.1 (1)	16.7 (2)	0	0
CVLT Long Cued	7.1 (1)	33.3 (4)	0	0
CVLT Disc	7.1 (1)	0 (0)	0	0
Peg R	21.4 (3)	0 (0)	0	0
Peg L	0 (0)	0 (0)	0	0
Peg RL	7.1 (1)	0 (0)	0	0
TMT A	7.1 (1)	0 (0)	10 (1)	0
TMT B	28.6 (4)	8.3 (1)	10 (1)	25 (2)
Dig. Symb	21.4 (3)	16.7 (2)	0	0

Data presented as percentages (number of patients).

the execution of coronary artery bypass procedures. Reports attesting to the safety of this approach and the good short and intermediate term results seem compelling. However, aspects of myocardial and neurological injury have not been well assessed.

Our study looks at patients undergoing bypass surgery for double and triple vessel disease, randomizing them into traditional or off-pump (OPCAB) arms. Specifically, we have chosen to look at TnT release and neuropsychological dysfunction following surgery.

The release profile of TnT following coronary artery bypass surgery utilizing CPB has been demonstrated [Mair 1993, Baker 1998, Bonnefoy 1998]. Our findings in this study show substantially diminished earlier release of TnT in the OPCAB group compared with those patients who underwent CPB surgery. The avoidance of CPB and its attendant problems, aortic cross-clamping and relative myocardial ischemia, surely contribute to the lower level of insult to the myocardium in the OPCAB group. This may well imply a more straightforward perioperative course for the patient. Furthermore, the acutely injured heart presenting for surgery may well be better off undergoing OPCAB revascularization if hemodynamic stability can be maintained during the procedure. This contention has some support in the recently published results in octogenarians and in reoperative coronary artery bypass cases, in which there were clear benefits associated with OPCAB surgery in these otherwise high risk groups [Boyd 1999, Ricci 2000, Stamou 2000].

While there have been significant improvements in cardiopulmonary bypass technology over the last three decades, the incidence of neuropsychological complications following traditional open heart surgery has remained alarmingly high [Newman 1987, McKhann 1997]. These sequelae are presumed to be the result of a series of factors, including systemic inflammatory response, loss of pulsatile flow, relative hypotension, and aortic manipulation, including cannulation, resulting in embolic showers.

To determine whether OPCAB surgery utilizing the Octopus stabilizing system results in a different or altered pattern of neuropsychological deficits requires a larger sample than presented in this preliminary report. By avoiding cardiopulmonary bypass and still maintaining hemodynamic stability, it would be anticipated that resultant neuropsychological dysfunction would be lessened. In the small number of patients we have investigated, this has not been the case when the two groups were compared with respect to total deficits in the immediate postoperative period. However, the pattern of deficits does show some differences. At the initial postoperative assessment, the patients undergoing CPB demonstrated a susceptibility to deficits in the cognitive domains of motor speed and dexterity, attention and visual-motor speed. Conversely in the OPCAB group the domain of verbal memory appeared to be most susceptible to early deficits.

We concur with other authors that the most relevant time to make an assessment of specific effects of surgery on neuropsychological functioning is at a longer time interval after the operation. We have found that at six months postoperatively there does not appear to be any significant difference between the on-pump and OPCAB groups. This finding is somewhat unexpected, as an early report from a non-randomized study was highly suggestive of a substantial beneficial effect associated with surgery that avoided CPB [Murkin 1999]. However, this study, as the authors acknowledged, compared two quite disparate groups, with the on-pump group receiving 3.2 grafts and the OPCAB group only 1.1 grafts.

Our inability to demonstrate any difference in the neuropsychological deficits between the on-pump and OPCAB groups may be a function of the low number of grafts performed in each group (mean number of grafts was 2.5 and 2.0 for Group 1 and Group 2 respectively), and the brief exposure to CPB in the on-pump group (mean CPB time 35.6 min.). This finding supports our previous work which demonstrated no clear neuropsychological benefits of off-pump surgery when compared to on-pump single graft surgery; however, significant benefits were evident when the off-pump group were compared with patients undergoing multiple-graft surgery [Andrew 1998]. Our finding is supported by two previous non-randomized studies that demonstrated no early or late neurological or neuropsychological benefit associated with coronary artery graft surgery performed without CPB [Malheiros 1995, Taggart 1999].

Although both our previous study and the current data are based on small samples, the findings taken in combination suggest that the neuropsychological benefits of off-pump surgery are minimal when compared to patients undergoing surgery for single or double vessel disease with relatively short CPB times. However, the OPCAB procedure may have the potential to reduce the incidence of neuropsychological deficits in patients undergoing multiple graft surgery and/or requiring extensive exposure to CPB.

In conclusion OPCAB surgery utilizing the Octopus II™ system clearly provides a myocardial benefit as assessed by

TnT release. Neuropsychological benefits, however, cannot be demonstrated.

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