

**Original Article**

***Circulatory Support for Repair of Cerebral Aneurysms Using Heparin-Bonded Bypass Circuits and Low-Dose Heparin***

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**ABSTRACT**

Modern advances in neurosurgical technique and improvements in cardiopulmonary bypass technology have facilitated a renewed interest in the ligation of giant cerebral aneurysms utilizing deep hypothermia and low-flow conditions. The widespread introduction of biocompatible heparin-bonded bypass circuits presents perfusionists with the opportunity to curtail sharply the need for heparin and protamine in these patients. We briefly discuss the merits of this procedure and describe our clinical experience.

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## INTRODUCTION

Neurosurgeons first used cardiopulmonary bypass (CPB) as early as 1959, when a team at the Duke University Medical Center reported using deep hypothermia and circulatory arrest (DHCA) to excise a metastatic cranial tumor (1). Interest in bypass-assisted neurosurgery has waxed and waned over the years, and a variety of open and closed chest approaches have been reported. An excellent detailed review of the evolution of this procedure was published by Mongero and Sistino (2). Early successes were tempered with reports of sequelae attributed to the bypass procedure itself, such as hypoperfusion and coagulopathy (3, 4).

The introduction of heparin-bonded bypass circuits has generated considerable interest in the potential for lower heparin and protamine usage, increased biocompatibility, and decreased activation of the complement cascade. Reported success of reduced blood loss using coated circuits and low-dose heparin during coronary bypass (5) and hypothermic neurosurgery (6, 7) demonstrated that the techniques could safely be used concomitantly to improve postoperative coagulation function.

During 1991 and 1992, cardiopulmonary bypass with full systemic heparinization and femoral cannulation for intracranial vascular repair was successfully used on four occasions at our institution. Because of unsatisfactory postoperative bleeding, nine subsequent repairs were performed during the period 1993 to 1998 using Carmeda® heparin-bonded bypass circuits with very low doses of systemic heparin. The results with these nine Carmeda® patients are discussed in this report.

## MATERIALS AND METHODS

### PATIENT CHARACTERISTICS

All patient data were collected prospectively. Mean age of the nine patients was  $51.6 \pm 12$  (SD) years and four (44%) were female. Eight patients had saccular basilar artery aneurysms; one of these had an associated lesion of the anterior communicating artery and another an associated lesion of the middle communicating artery. The ninth patient had an isolated saccular anterior communicating artery aneurysm. Six presented with acute subarachnoid hemorrhage. Patients were considered for CPB-assisted neurosurgery when the size of the aneurysmal sac and the physical structure of its vascular connection to the normal circulation were such that prolonged mechanical decompression was judged to be the safest method for applying the ligature clips. Three patients underwent elective repair of their lesions, and the other six were done on an urgent basis (i.e., their medical condition warranted keeping them in hospital until their surgery could be performed). This technique was not employed for emergency repair of ruptured cerebral aneurysms.

All patients, regardless of urgency, received a full neuro-

logic work-up, including computerized axial tomography and cerebral angiography, and were screened for pre-existing coagulopathy, lower extremity peripheral vascular disease, aortic insufficiency greater than 1+, and clinical evidence of coronary artery disease. Presence of any of these four conditions was grounds for not using CPB, and, indeed, one other candidate for this procedure was refused because of severe aortoiliac occlusive disease. In-house patients were typically maintained on antifibrinolytics until the time of surgery.

### EQUIPMENT SELECTION AND SURGICAL MANAGEMENT

A standard closed Carmeda®<sup>a</sup> heparin-bonded circuit with Maxima® oxygenator,<sup>a</sup> MVR-1600 venous reservoir bag,<sup>a</sup> and BioMedicus BP-80 centrifugal pump<sup>b</sup> was used. A cardiomy reservoir was used for ease of priming, but was then clamped off to eliminate the air-blood interface. All shed blood was harvested into either a Haemonetics Cell Saver 4<sup>c</sup> or COBE BRAT 2<sup>d</sup> for salvage and reinfusion using standard techniques for heparinization of aspirated blood. Standard prime consisted of 1000 ml of Normasol-R<sup>e,e</sup> or Plasma-Lyte,<sup>f</sup> 1000 ml of 5% albumin, and 75 g of mannitol. No heparin was added to the prime.

Patient preparation included placement of intra-arterial and pulmonary arterial catheters, external electrodes for cardioversion and cardiac pacing, and introduction of a transesophageal echocardiography (TEE) probe to monitor ventricular distention during asystole. Eventually, use of the TEE was discontinued at the anesthesiologist's discretion. Core temperatures were monitored with a nasopharyngeal temperature probe. During bypass, the temperature of the brain was monitored directly using a standard myocardial temperature probe<sup>g</sup> placed into the cerebrum. Patients were placed in either a supine or modified lateral position as dictated by the neurosurgical approach (anterior versus lateral), and both groins were prepared for vascular access.

Following the initial neurosurgical dissection, the cardiothoracic team established bypass. Patients were given an initial heparin loading dose of 2500 units to achieve an activated clotting time (ACT) of 200 sec or greater. Supplemental heparin was given throughout the procedure as needed if the ACT fell below 200 sec. No upper limit for the ACT was established.

The right femoral artery and vein were preferentially cannulated to provide a less tortuous path for advancement of the cannulae. Cannula sizes can be roughly correlated with patient body surface area, but final selection of cannula sizes was

<sup>a</sup> Medtronic Cardiopulmonary, Anaheim, CA 92807

<sup>b</sup> Medtronic Bio-Medicus, Eden Prairie, MN 55344

<sup>c</sup> Haemonetics, Braintree, MA 02184

<sup>d</sup> COBE Cardiovascular, Arvada, CO 80004

<sup>e</sup> Abbott Laboratories, North Chicago, IL 60064

<sup>f</sup> Baxter Healthcare, Deerfield, IL 60015

<sup>g</sup> Sorin BioMedical, Irvine, CA 92623

made after visual inspection of the femoral vessels. We used either a 17 or 19 Fr cannula<sup>h</sup> in the artery and either a 27 or 29 Fr cannula<sup>h</sup> in the vein. Once inserted, cannulae were flushed with heparinized saline solution, and CPB was initiated within 2–3 min so that thrombus would not form in the lumens, as recommended in the literature (6). Because of the possibility of arterial dissection during femoral arterial cannulation, the cannulae were carefully checked using a test infusion before initiation of bypass. The final positions of the venous cannulae were determined by manipulation until the maximal gravity drainage rate was achieved. Only then was active cooling begun to a target core temperature of 15°C.

Target bypass flows were 2.4 L/min/m<sup>2</sup> during normothermia and were generally reduced as the patient cooled. Flow was reduced to 500 ml/min during deep hypothermia. Ligation of the lesion was performed during the low flow period while the sac of the aneurysm was decompressed. Adequacy of the clipping and general hemostasis were carefully observed during rewarming and bypass was terminated once a core temperature of 37°C was reached. The cannulae were again flushed with heparinized saline until they could be removed. Protamine was given using a 1:1 dosing regimen to counteract any remaining circulating heparin.

Fibrinogen levels and platelet counts were drawn prebypass, as well as approximately 45 min before the anticipated termination of bypass. This allowed our clinical laboratory sufficient time to perform the required analyses and prepare either platelets or cryoprecipitate for infusion.

## RESULTS

Average maximum sustained flow for all patients was 4.14 ± 0.33 (SD) L/min, with a mean cardiac index of 2.20 ± 0.26 (SD) L/min/m<sup>2</sup>. Although a target flow rate of 2.4 L/min/m<sup>2</sup> had been established by protocol, these flows under gravity venous drainage were judged to be adequate on the basis of blood gases and mixed venous oxygen saturation. Augmented venous drainage may be warranted for unusually large patients. Our largest patient was 2.29 m<sup>2</sup>.

Five of the nine patients required only the heparin loading dose of 2500 units to achieve and maintain ACTs of 200 sec or more for the entire procedure. Four patients required supplemental heparin to maintain the desired ACT. The average total heparin dose for all nine patients was 3667 ± 1640 (SD) units. The average recorded ACT on bypass was 273 ± 86 (SD) sec. No clot formation could be detected in the circuit at any time. Six patients required an intravenous bolus of 20–40 mEq of potassium during the cooling phase to achieve asystole and to allow the neurosurgeons to continue their dissection. All patients spontaneously defibrillated during the rewarming phase.

Mean cooling time was 33 ± 7 (SD) min, with 95 ± 21 (SD)

min to rewarm. Eight patients spent an average of 23 ± 11 (SD) min under low-flow hypothermia. One patient was clipped at 15°C without the need for low-flow conditions. Average duration of bypass was 185 ± 54 (SD) min. The average brain temperature during low-flow was 13.2 ± 1 (SD) °C.

Eight patients had satisfactory surgical repair of their lesions. Five were discharged directly home, and three went to skilled nursing facilities. Mean postoperative length of stay was 12.9 ± 7 (SD) days. All patients had a quantifiable neurological complication postoperatively, the most common being transient third nerve palsy secondary to the surgical approach used. None of the observed complications was attributable to CPB technique. Mild transient left hemispheric paresis occurred in three patients. One patient suffered a left superior communicating artery infarct and a deep vein thrombosis (DVT) and was left permanently disabled. Another patient underwent a complex staged repair of both left middle communicating and basilar artery aneurysms; she suffered postoperative general paresis and is also disabled.

There was one death in the nine patients, a 72-year-old female who underwent elective repair of a large (approximately 19 mm) anterior communicating artery aneurysm. Control of her lesion proved to be unsatisfactory, and she sustained a massive cerebral infarct, expiring on postoperative day four.

Although a prime motivation for use of this technique was reduction of bleeding and associated complications, no comparable group exists for objective data analysis. We can only report a subjective impression by the staff neurosurgeon involved that hemostasis was much better with Carmeda<sup>®</sup> than his earlier experience with full systemic heparinization and CPB. Estimated blood loss during the operations was 700 ± 340 (SD) milliliters. Intraoperative blood product usage included 1.0 ± 0.9 (SD) units of cryoprecipitate, 2.2 ± 3.1 (SD) units of fresh frozen plasma, 2.3 ± 1.9 (SD) units of packed red blood cells and 0.4 ± 0.5 (SD) units of pooled platelets.

## DISCUSSION

Any surgical team considering neurosurgery with CPB must make some basic decisions, starting with the choice of open- or closed-chest cannulation. We elected to use the closed-chest approach with femorofemoral bypass, thereby avoiding another significant surgical procedure, as well as more raw surfaces for bleeding and heat loss via the open chest cavity. Open-chest techniques would offer the surgical team easier cannulation access and unfettered access to the heart for decompression and defibrillation. Both approaches are still in use in the modern literature.

Proper patient evaluations should be made if one is to use the closed-chest technique. We screened all patients for significant (>1+) aortic valve insufficiency because of the risk of left ventricular distention during ventricular fibrillation. Routine placement of external cardiac pacing provides some facility for

<sup>h</sup> DLP-Medtronic, Grand Rapids, MI 49501

ventricular unloading should distention occur. However, we have not found ventricular distention to be a problem, and so we have discontinued the use of both TEE and external pacing. Cardiac histories were evaluated because of the cardiodepressant effects of thiopentothal given for cerebral protection. Examinations were performed for lower extremity peripheral vascular disease to identify candidates that might not be able to be cannulated femorally. Coagulation profiles were drawn to identify potential bleeding problems, and most in-house patients were placed on intravenous antifibrinolytics to help maintain normal coagulation function.

Some centers using the closed-chest technique employ kinetically assisted femoral venous return with a centrifugal pump and percutaneous venous catheters in the 17–21 Fr range (8). However, we had considerable earlier experience using the larger-bore thin wall “te-do” venous cannulae, such as those from Medtronic-BioMedicus,<sup>1</sup> under gravity venous drainage with quite satisfactory flows.

Any patient subjected to CPB is at risk for the complications of thrombocytopenia, platelet dysfunction, and defibrination, largely because of the interaction of the blood with the foreign surfaces of the bypass circuit. The heparin coating of the Carmeda<sup>®</sup> circuit is said to provide a biocompatible surface that should ameliorate these potential problems, along with the potential for reduced activation of the complement system (9–12). We were also interested in a low-dose heparin protocol to avoid the heparin-protamine complex required for hemostasis at the end of bypass and further reduce the risk of complement activation. After reviewing the experience of Bennett et al (6), we decided to use an initial loading dose of 2500 units of heparin and a target ACT of 200 sec. More recent works on low-dose heparin strategies have been published by Bennett (13) and Hollingsed (14). Our surgeons subjectively noted improved hemostasis using the Carmeda<sup>®</sup> system and a low-dose heparin protocol, and we have been unable to detect any clot formation in our bypass circuits.

We had established a goal of minimizing no-flow conditions while on bypass to avoid static areas in the circuit where blood might start to coagulate. When some patients required periods of no-flow in order to complete the placement of ligature clips, the bypass loop of the oxygenator was used for recirculation purposes, and cannulae were flushed with heparinized saline to help insure patency.

Although it is our normal perfusion practice to use open venous reservoirs, we adopted the use of a closed circuit for these procedures to reduce the air-to-blood interface inherent in an open system, as well as electing not to return any shed blood to the bypass circuit. In doing so, we further reduced the potential for complement activation (15).

Despite these additional perfusion considerations, the introduction of low-dose heparin bypass with the Carmeda<sup>®</sup> cir-

cuitry has facilitated difficult neurosurgical repairs with an increased level of safety not possible with conventional bypass techniques.

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