Optimal Management of Cardiopulmonary Bypass for the High Risk Patient

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CNS Outcomes Related to CPB

In a prospective clinical trial evaluating 2108 patients undergoing coronary artery bypass (CAB) surgery at 24 U.S. institutions, adverse cerebral outcomes consisting of focal injury, stupor or coma; or seizures, memory deficit or deterioration in intellectual function, occurred overall in 6.1% of patients. Age, proximal aortic atherosclerosis, and history of neurological disease were all strongly correlated with these adverse neurological outcomes.[1] In our own series assessing postoperative neurobehavioural sequelae in over 300 CAB patients, the stroke rate was 2.5%, while 33% of all CAB patients demonstrated cognitive dysfunction and a further 18% demonstrated abnormal neurological signs two months postoperatively.[2] In a preliminary report of three year follow-up in 97 of these same patients, 22% suffered cognitive impairment and a further 18% again demonstrated abnormal neurological signs.[3] Newman et al evaluated long-term cognitive outcomes in 261 patients who underwent CAB using neurocognitive tests performed preoperatively, before discharge, and six weeks, six months, and five years after CAB surgery.[4] They demonstrated that the incidence of cognitive decline was 53 percent at discharge, 36 percent at six weeks, 24 percent at six months, and rising to 42 percent at five years. Cognitive function at discharge was shown to be a significant predictor of long-term cognitive function. It must be borne in mind however, that none of these studies involoved a non-operated control group, and that up to 10% of patients undergoing total hip arthroplasty (THA) can be demonstrated to have postoperative cognitive dysfunction.[5] However, THA patients are also a group in whom cerebral lipid macroemboli and microemboli have been identified.[6] It thus remains unclear how much of this cognitive decline is due to progression of concomitant disease, how much to 'stress' of major operative procedures, and how much is due to specific events during CAB surgery

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Atheroemboli

Increasingly, aortic atheromatosis is being recognised as a significant cause of stroke independent of cardiac surgery, with non-calcific plaque representing the greatest risk.[7] Of concern, this is exactly the type of lesion that is least likely to be identified by intraoperative surgical palpation of the aorta, despite this being the *de facto* standard of care in North America and elsewhere. It is apparent that atheroemboli, due to disruption of aortic atherosclerotic plaque within the ascending aorta and aortic arch, account for a large portion of the central nervous system (CNS) injury occuring in patients undergoing CAB surgery. In most centres, however, aortic cannulation is preceded by manual palpation of the aorta to determine suitable sites for cannulation and placement of aortic clamps and vascular anastamoses. This is currently the standard of care in many cardiac centers in North America and Europe.

In a series of 1200 patients in whom intraoperative epiaortic ultrasound scanning (EAS) was employed, moderate (3 to 5 mm thick) or severe (>5 mm, or ulcerations, circumferential aortic involvement, mobile atheroma) ascending aortic atherosclerotic disease was found in 231 (19.3%) patients.[8] In 27 patients with severe atherosclerotic disease, the ascending aorta was replaced, with no strokes occurring in this group. In a series of 168 patients with less extensive aortic disease, technical modifications included the use of femoral or distal aortic arch cannulation sites, no aortic clamping or more proximal placement of aortic clamps, delivery of cardioplegia retrograde through the coronary sinus or hypothermic fibrillatory arrest, and more proximal placement of proximal anastamoses or use of skip grafts without proximal aortic anastamoses, again with good outcomes.[9]

In a series of 10 patients undergoing CAB surgery, St Amand and colleagues reported that epiaortic scanning resulted in a change in cannulation site in 2 patients, one after detection of unrecognised atheroma,

and the other after ultrasonic identification of a section of disease free aorta in a patient in whom diffuse aortic atherosclerosis had been determined by palpation.[10] None of these patients suffered a postoperative stroke. Similarly, Nicolosi and colleagues compared the sensitivity of intraoperative epiaortic scanning and manual palpation of the aorta for detection of atherosclerotic disease in 89 cardiac surgical patients.[11] Operative techniques were modified to avoid plaque detected on scanning in 11.2% of patients. The sensitivity of palpation compared with scanning was 0.46. There were two strokes in this group, one in a patient with minimal aortic atherosclerotic disease, the other having extensive aortic calcification. In a much larger series, EAS of the ascending aorta was performed in 500 of a consecutive series of 540 patients 50 years of age or older (mean 68 years) who underwent a variety of cardiac operations.[12] Eighty-nine percent required bypass grafting. Sixty-eight patients (13.6% of the total) with a mean age of 72 years (range 55 to 85 years) had significant atheromatous disease in the ascending aorta and were considered to be at increased risk for embolisation. It is of note that palpation identified atheromatous disease in only 26 (38%) of these patients and underestimated its severity. A total of 168 modifications to the standard techniques for cannulation and clamping of the aorta were implemented in the 68 patients (mean 2.5 per patient) and included alterations in the sites of aortic cannulation (50 patients), aortic clamping (54 patients), attachment of the vein grafts (35 patients), and cannulation for infusion of cardioplegic solution (29 patients). Ten patients with severe diffuse atheromatous disease underwent graft replacement of the ascending aorta with hypothermic circulatory arrest without aortic clamping. Permanent neurologic deficits occurred in five (1.0%) of the patients in the entire group but in none of the 68 patients with significant atheromatous disease in whom modifications in technique were used.

It should also be commented that while use of a long arterial arch cannula placed beyond the orifice of the left subclavian artery has been recommended for patients with extensive aortic atheromatosis, in clinical practice this often translates in cannulation of the ascending aorta with a long cannula, the tip of which is directed distal to the left subclavian artery. While this may avoid perfusion related cerebral embolisation, the risk of plaque fracture and embolisation engendered by passage of the cannula through the potentially diseased aortic arch cannot be overlooked. Nevertheless, this is often what is done in such high risk patients in the mistaken belief that it minimises risk of stroke. As has recently been shown using EAS after aortic cannulation and clamping, the presence of aortic atheromatosis significantly increases the chance of plaque fracture and intimal flap formation after aortic instrumentation.[13] The potential for subsequent embolisation of either plaque or secondary thrombus is thus high and in all likelihood accounts for many of the otherwise unexplained strokes seen on day 2 and 3 postoperatively

Emboli: Capture of Diversion

Based on the high incidence of aortic atheroma and the associated risk of embolisation, two new devices have been introduced. The Embol-X intraaortic filter is a 150 µm net that is inserted through a side port of a modified aortic cannula. It is deployed prior to release of the aortic cross-clamp and partial occlusion clamp. To date, it has been used in several hundred cardiac surgical patients in Europe[14] and it is currrently undergoing large scale prospective randomised trials in North America. In a similar fashion, the Cardion 'cobra' is a modified double-lumen aortic cannula with an inflatable shield that acts to divert emboli away from the great vessels of the aortic arch. One lumen can be used to perfuse the body while the other perfuses the aortic arch vessels. This enables differential perfusion of the head and body to be undertaken, enabling differential cooling of the head while maintaining normothermic perfusion of the body.[15] This device has now entered clinical trials, though results are not yet available.

Microemboli

Whether from data obtained using fluoroscein retinal angiography, histological brain sections or transcranial Doppler, it is apparent that there is evidence from multiple diverse sources for cerebral emboli associated with CPB. A paper from Pugsley et al, the relationship between the magnitude of the embolic load and postoperative cognitive performance was assessed using pre and postoperative neuropsychological testing.[16] These investigators were able to show that patients having the lowest numbers of emboli as detected using transcranial Doppler evidenced a relatively low (<10%) incidence of neurobehavioural dysfunction on postoperative psychometric testing. However, as the embolic load increased, over 40% of patients who had greater than 1,000 emboli detected intraoperatively demonstrated postoperative cognitive impairment. Accordingly, they showed a direct relationship between embolic load and postoperative outcome, and since they were employing arterial line filters to reduce the embolic counts, they found that employment of an arterial line filter decreased embolic load and therefore resulted in an improved outcome postoperatively. This data helps further confirm the association between intraoperative

cerebral embolisation and postoperative neurobehavioural outcome, and demonstrates the positive role judicious equipment modifications can make to postoperative outcome.

Hypoperfusion

In the context of cardiac surgery, it is apparent that cerebral embolisation and / or ischaemic hypoperfusion are the mechanisms most likely etiologic in the genesis of neurocognitive injury. Gold et al have reported on the lower incidence of morbidity including CVA in patients in whom mean arterial pressure (MAP) was maintained at greater than 80 mmHg.[17] While this may imply a requirement for higher MAP to better optimise cerebral well-being during CPB, it is also apparent that during CPB, cerebral venous hypertension may be another unrecognised, yet equally devastating contributor.

It has been observed that extradural pressure, measured via an intracranial catheter, is independent of central venous pressure, and frequently exceeds it.[18] This has also been observed by recording proximal superior vena cava (SVC) pressure as measured using the introducer port of a pulmonary artery access cannula.[19] As described, it is apparent that dislocation of the heart in the presence of a single, two-stage venous return cannula during CPB, may occlude the SVC giving rise to inadequate cerebral perfusion pressure (CPP) despite apparently adequate MAP, due to jugular venous hypertension. This results in both cerebral venous hypertension, and a proportional decrease in cerebral blood flow as measured using transcranial Doppler (TCD).[20] Repositioning the heart, or re-siting the venous cannula, readily rectifies the problem, provided it has been recognised.

That this type of injury may give rise to cerebral dysfunction can be inferred from the small series of Harris et al.[21] They described cerebral oedema in the immediate postoperative period in 6 of 6 adult patients undergoing uncomplicated CAB surgery using CPB. How much this can be ascribed to cerebral venous hypertension, how much to what has been described as the 'systemic inflammatory response', and how much to other as yet unknown mechanisms is still not clear. It is apparent, however, that CPB induces myriad changes that are to the detriment of the systemic as well as the cerebral milieu.

Systemic Inflammatory Response

In a post hoc analysis of 816 CABG patients from a recent multicenter study assessing aprotinin and graft patency,[22] patients were separated into those receiving more than 300 mL shed blood versus those receiving none, and analysed for perioperative CVA.[23] This analysis demonstrated a strong drug effect, with aprotinin administration being associated with a significantly ($p = 0.04$) lower overall incidence of stroke, 1.1% compared with an incidence in placebo-treated patients of 2.6%. Overall, in placebo patients, return of shed blood increased the risk of CVA more than three-fold (3.1% versus 0.0%) whereas aprotinin therapy was not associated with increased risk of CVA independent of retransfusion or not (1.1% versus 1.2%). Further, only 18% of aprotinin-treated patients had over 300 mL of shed blood returned, compared to 46% of the placebo group. This data thus further supports the premise that the return of shed blood has a negative effect on patient outcome, and that aprotinin both decreases the risk of receiving such shed blood and also appears to ameliorate the CNS effects of such transfusion, possibly related to its antinflammatory properties.[24,25]

Further support for this hypothesis comes from a recent meta-analysis[26] of 7 placebo controlled, randomised, double-blind studies of CABG patients receiving full dose aprotinin or placebo. The rationale for combining these data rests on the low percentage of patients who suffer stroke, rendering no single study large enough to detect differences between groups given the low occurrence of such a relatively rare event. Therefore, combining data across studies increases the ability to detect meaningful differences between groups. The meta-analysis contained data from 1867 placebo and full dose aprotinin patients.

A significantly lower incidence of stroke was found in aprotinin-treated patients in both this and a previous meta-analysis from this earlier database.[26,27] In the prior meta-analysis of Smith and Muhlbaier, 2.4% of the placebo group experienced stroke compared to only 1.0% in the treatment group.[27] The most recent study showed that 4.2% versus 0%, respectively, of the patients valid for safety analysis were identified as having a cerebrovascular accident as an adverse event.

Guidelines

Overall, it can be concluded that there are multiple sources of CNS injury that can give rise to perioperative stroke or cognitive impairment in patients undergoing coronary revascularisation. In addition to the standard considerations for management of patients undergoing coronary revascularisation, specific management of the patient at increased CNS risk should include:

1) epiaortic scanning to detect unrecognised ascending aortic atherosclerosis
2) monitoring of cerebral venous pressure via a proximal CVP catheter or the introducer port of a pulmonary artery catheter, and maintainance of

cerebral perfusion pressure in excess of 60 mmHg
3) full dose (6 m KIU) aprotinin administration
4) avoidance of cerebral hyperthermia during rewarming via monitoring nasopharyngeal temperatures
5) use of heparin bonded CPB circuitry incorporating membrane oxygenator and 40μ arterial line filter
6) avoidance of unprocessed cardiotomy suction blood

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