CARDIOPULMONARY BYPASS, MYOCARDIAL MANAGMENT, AND SUPPORT TECHNIQUES

SYSTEMIC HYPOTHERMIA AND CIRCULATORY ARREST COMBINED WITH ARTERIAL PERFUSION OF THE SUPERIOR VENA CAVA

Effective intraoperative cerebral protection

We have used retrograde arterial perfusion of the superior vena cava as an adjunct to deep hypothermia and systemic circulatory arrest for intraoperative cerebral protection in 43 adult patients (18 of whom were 70 years old or older). The indications for the use of circulatory arrest were thoracic aortic operations (37 patients) and atherosclerosis or calcification of the ascending aorta (6 patients) in patients needing aortic valve or coronary operations. In all patients systemic hypothermia (16° to 18° C) was achieved with cardiopulmonary bypass and the systemic arterial circulation was arrested. Retrograde arterial perfusion of the superior vena cava was established through a wire-reinforced venous cannula (with a superior vena cava tourniquet) at a temperature of 15° C. In 36 patients a separate roller pump system was used for the retrograde cerebral perfusion. Central venous pressure was monitored at 25 to 30 mm Hg; mean flow rate was 250 ml/min. Periods of circulatory arrest and retrograde cerebral perfusion ranged from 4 to 110 minutes (mean 38 minutes), and for seven patients the period of circulatory arrest was longer than 60 minutes. Four postoperative deaths occurred, one related to stroke in a patient who had an aortic dissection during coronary surgery and the others related to noncerebral complications. Three nonfatal cerebral complications occurred, although all had completely resolved by late follow-up. Advantages of retrograde cerebral perfusion are (1) simplicity of use and avoidance of vascular trauma, (2) excellent exposure, (3) retrograde flow that minimizes embolization of air and atherosclerotic debris, and (4) effective cerebral oxygen delivery. Retrograde cerebral perfusion appears to be an important adjunct to hypothermia and circulatory arrest not only for patients undergoing operation for ascending aorta and aortic arch disease but also for patients with diffuse aortic atherosclerosis undergoing coronary or valve operations. (*J THORAC CARDIOVASC SURG* 1995;109:738-43)

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Deep hypothermia with circulatory arrest is now commonly used to achieve operative exposure and cerebral protection during operations for aneurysms or dissections of the ascending aorta, aortic arch, and proximal descending aorta.¹⁻³ In general, this strategy has been successful. However, the

cerebral protection produced by hypothermia alone has limits. Analysis of a large series of adult patients undergoing aortic arch operations demonstrated an increased risk of cerebral complications with more than 40 minutes of hypothermic circulatory arrest, and Griep and colleagues⁴ noted that evidence of diffuse cerebral injury increased in frequency as the time of circulatory arrest approached 60 minutes. At this point our ability to protect the brain during circulatory arrest has not kept pace with our ability to protect the myocardium.

Recently, perfusion of the superior vena cava (SVC) with arterial blood during systemic circulatory arrest has been used in attempts to advance intraoperative cerebral protection beyond that

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achieved with hypothermia and circulatory arrest alone. Retrograde cerebral perfusion (RCP) was initially described by Mills and Ochsner⁵ as a treatment for air embolization during cardiopulmonary bypass. Intermittent SVC perfusion was subsequently used by Lemole and associates⁶ for cerebral protection during aortic arch operations in 1982. Ueda and colleagues⁷ used continuous RCP during aortic arch operations in 1987, a strategy that is now being evaluated by many surgical groups.^{8,9} We began the use of continuous hypothermic retrograde SVC perfusion associated with systemic hypothermia and circulatory arrest during 1992 for cerebral protection during aortic arch operations and have extended the use of this technique for some patients undergoing valve or coronary bypass operations who also have severe aortic atherosclerosis.

Methods and patients

Technique. All operations in this series were performed through a median sternotomy. Heparinization was monitored with activated clotting times, and acid-base management during hypothermia was via an alpha-stat approach. Before hypothermic circulatory arrest, steroids were given routinely and the head was packed in ice to maintain cerebral hypothermia.

Arterial cannulation was through the aorta ($n = 3$), the femoral artery ($n = 28$), the axillary artery ($n = 11$), or the innominate artery ($n = 1$). We have used axillary artery cannulation in situations in which we wished to avoid retrograde arterial perfusion through the femoral artery because of concerns of retrograde embolization of clot or atheromatous debris or when the femoral arteries were compromised by dissections. All patients underwent separate cannulation of the SVC and inferior vena cava. The SVC was usually cannulated with a wire-reinforced cannula inserted via the right atrial appendage. Cannulation of the inferior vena cava has been either through a right atrial pursestring suture or through the femoral vein.

In all cases but two, hypothermic circulatory arrest was a planned procedure and once cardiopulmonary bypass was established systemic cooling was initiated immediately. During systemic cooling and rewarming, the perfusionist has monitored the pump arterial and venous blood temperatures and maintained a difference of no more than 10° C between the two. The patient's temperatures that were monitored included nasopharyngeal, esophageal, and bladder temperatures.

We have considered systemic cooling to be adequate for hypothermic circulatory arrest when the bladder temperature has reached 18° C, the arterial-venous temperature difference is 3° C or less, and the arterial inflow temperature is approximately 12° C. The mean period of cooling for these patients was 36 minutes. When we are ready to arrest the circulation, the systemic flow is decreased to 200 ml/min, a tourniquet around the SVC is tightened, and perfusion of arterial blood through the SVC is initiated at a flow rate of 200 ml/min. The table is tilted so that the

patient's head is down and the systemic arterial flow is then totally arrested.

The RCP flow rate is then adjusted to maintain a central venous pressure of 25 to 30 mm Hg. The resulting rate of RCP flow is usually between 150 and 400 ml/min, and the mean flow rate for the 43 patients was 250 ml/min.

Two different perfusion circuits have been used for RCP at our institution. Most commonly (36 patients), separate roller pumps have been used for systemic arterial flow and SVC perfusion with arterial blood so that independent perfusion of the SVC and systemic arterial circulation is possible (Fig. 1). Perfusion through both circuits is controlled at the level of the pump. With this system it is possible to perfuse both the systemic arterial circulation and the SVC at the same time and to switch back and forth between the two routes of perfusion. For the other seven patients a circuit incorporating a single arterial line that is divided and inserted into the SVC cannula was used.

Once RCP is established the aorta is opened. As oxygenated blood is perfused into the SVC, desaturated blood flows back into the aortic arch from the cerebral vessels and is removed from the aorta by a sump sucker and returned to the pump. This provides excellent exposure of the aortic arch and proximal descending aorta. For procedures on the distal arch and on the descending aorta, the retrograde flow from the carotid arteries does occasionally obscure the operative field. Under those circumstances we will sometimes reduce the flow to 100 ml/min for a few minutes. We do not ever completely interrupt flow, because constant positive pressure prevents air from getting into the system. Once circulatory arrest has been initiated we maintain myocardial protection with intermittent antegrade and retrograde cardioplegia.

When that portion of the procedure requiring circulatory arrest is completed, we remove the sump sucker from the aorta and allow the aorta to fill with desaturated blood. The head is shaken by the anesthesiologist to dislodge any trapped air and the systemic perfusion is restarted. At this point the graft or the aorta is clamped and rewarming is begun, usually while an aortic root portion of the procedure is completed. If aortic clamping is not possible, the aorta is closed completely. Then systemic arterial flow is restarted and rewarming is initiated. The time for rewarming averaged 62 minutes for these patients.

Patient population. The mean age of the 43 patients (15 women) was 64.3 years (range 20 to 80 years); 18 patients were 70 years old or older. Nine patients (21%) had undergone previous cardiac or thoracic aortic surgery, and 20 operations (46%) were done on an emergency basis.

For 35 patients the intended operation involved a procedure on the thoracic aorta. Twenty-four patients underwent operations for dissections. In 13 of these patients (54%) part or all of the aortic arch was resected, and in the remainder circulatory arrest and RCP was used to avoid aortic clamping, allow construction of an open distal anastomosis, and allow inspection of the aortic arch. Four patients with dissections were undergoing a reoperation, six received concomitant coronary artery bypass grafts, two had total aortic root replacements, and two

Fig. 1. The RCP circuit includes an open membrane oxygenator and separate roller pumps for the systemic arterial, SVC, and cardioplegia delivery systems. During RCP we monitor central venous pressure in the distal SVC and the pressure in the SVC arterial line.

underwent aortic valve replacement. Nine patients underwent operations for aneurysmal disease, replacement of the aortic arch or the descending aorta (or both) being performed in eight. Three patients with aneurysms were undergoing reoperation and four had concomitant bypass grafting. In two cases the aortic arch operation was combined with composite graft replacement of the aortic root.

Two patients underwent an operation that was intended to be coronary bypass grafting (one patient also received an aortic valve replacement), but ascending aortic dissections developed during the operations. The aortic cannula was shifted to the femoral artery, and hypothermic circulatory arrest and RCP were used during repair of the dissection.

Two patients had unusual aortic abnormalities. One underwent an emergency operation for a perforation of the proximal descending aorta that occurred during cardiac catheterization and created a large mediastinal hematoma that could not be controlled with conventional means. In another patient an infected distal aortic arch and descending aortic graft was removed and replaced with an ascending aorta-supradiaphragmatic aortic graft.

For six patients undergoing operation for aortic valve replacement or coronary bypass grafting, hypothermic circulatory arrest and RCP were used in the management

of severe ascending aortic atherosclerosis or calcification. For two patients undergoing aortic valve replacement the entire valve replacement was completed without aortic clamping; in the other, aortic endarterectomy was performed, the aorta then clamped, and systemic perfusion restarted. For the three patients undergoing isolated coronary artery bypass grafting, RCP was used to allow removal of atherosclerotic debris from the aorta and construction of proximal anastomoses, in one case via a bovine pericardial patch that was used to replace the anterior aortic wall. It was also our hope that RCP might remove atherosclerotic debris from the cerebral arterial circulation.

Results

The mean duration of RCP was 38 minutes (range 4 to 110 minutes). Fig. 2 shows the numbers of patients receiving RCP for selected time intervals.

There were four in-hospital deaths. Two patients who underwent aneurysm operations died after regaining full consciousness with no apparent neurologic deficit, one of pulmonary failure and one of chronic myocardial failure. A third patient died early after operation for an aortic arch dissection of

coagulopathy and bleeding, and assessment of the neurologic status was not possible. The fourth death occurred because of a stroke in a patient who had an aortic dissection while undergoing coronary bypass grafting. At postmortem examination, dissection was evident in both carotid arteries.

Three patients had nonfatal postoperative neurologic complications that resolved without residual deficits. One patient undergoing bypass grafting and aortic endarterectomy for severe aortic atherosclerosis had a short period of RCP (11 minutes) and had a small temporary focal motor deficit ipsilateral to a significant carotid stenosis. The two other patients underwent extensive aortic procedures (one for dissection, one for aneurysm) and received prolonged periods of RCP (90 and 105 minutes). They had generalized cerebral depression early after the operation, but recovered. In all the patients who had postoperative neurologic deficits, fatal and nonfatal, the perfusion circuit requiring division and separation of the arterial line was used and systemic arterial cannulation was via the femoral artery.

Discussion

The use of hypothermia and circulatory arrest has become a valuable adjunct in adult cardiac surgery and has usually been used for achieving both operative exposure and cerebral protection for patients undergoing operations involving the ascending aorta and aortic arch. Circulatory arrest does provide excellent exposure, but the cerebral protection associated with hypothermic circulatory arrest is not perfect, particularly when the time of circulatory arrest approaches 60 minutes. In an enlightening clinical study of the determinants of cerebral complications in patients undergoing circulatory arrest, Svensson and associates³ noted that the length of circulatory arrest and age were univariate predictors of risk.

Cerebral hypoxia is a factor limiting the period during which circulatory arrest is safe, even at hypothermic temperatures. Working with patients undergoing systemic circulatory arrest for the surgical treatment of complex cerebrovascular disease, Ausman and colleagues¹⁰ used infrared spectroscopy to measure cerebral oxygen saturation. Their data indicate that even at 18° C (tympanic temperature) progressive desaturation of cerebral hemoglobin occurs, and during long periods of circulatory arrest (45 to 65 minutes) there was dramatic desaturation of cerebral hemoglobin, a situation that was associated with a poor neurologic outcome. Even though both clinical and experimental data indicate

Fig. 2. Patients grouped according to the length of RCP. The largest number of patients had relatively short RCP times (<30 minutes), but seven did receive RCP for more than 60 minutes.

that cerebral oxygen consumption decreases during hypothermia, it is not eliminated and there is still a discrepancy between cerebral oxygen delivery and oxygen consumption.

It is in an attempt to deliver oxygen and thus to extend the period of safe circulatory arrest that RCP with oxygenated blood has been used.^{3, 7, 8, 9} Some evidence exists that RCP does, in fact, deliver oxygen. The oxygenated blood perfused into the SVC clearly desaturates before retrograde flow through the cerebral vessels. Ueda and associates⁷ measured a consistent difference in oxygen content between the SVC and aortic arch blood for up to 30 minutes of RCP. Deeb and coworkers⁹ used a technique similar to that established by Ausman and his colleagues¹⁰ in an attempt to monitor cerebral hemoglobin oxygenation saturation spectroscopically. They believed that they were able to maintain the hemoglobin saturation within 10% of normal with the use of RCP. Much more work concerning cerebral metabolism during RCP lies ahead, but it appears that oxygen delivery does occur.

It is likely that another aspect of the positive effect of RCP is maintenance of hypothermia. However, perfusion at 15° C still establishes a temperature at which substantial cerebral oxygen consumption does occur.

The clinical evaluation of techniques for intraoperative cerebral protection is complicated by the multiple causes of intraoperative cerebral injury. Embolization of air, thrombus, or atherosclerotic debris may cause intraoperative cerebral injury, and

the separation of the adverse effects of embolization and prolonged circulatory arrest may be difficult. However, we believe that the use of RCP helps to avoid and treat embolization. Mills and Ochsner⁵ first described RCP as a treatment for embolization, and it is of obvious benefit in preventing air embolization during operations on the aortic arch. The retrograde flow back through the cerebral vessels during the operation also aids in evacuating air from the aortic arch at the end of the procedure. In addition, we have frequently seen fragments of atherosclerotic debris being floated back out of the cerebral arteries by this retrograde flow.

Strategies for avoidance of cerebral embolization must be multifaceted. Ueda,⁷ Safi,⁸ and their associates reported cerebral embolization caused by retrograde aortic flow from femoral cannulation as a cause of an adverse cerebral outcome despite apparently adequate RCP. We are now frequently using axillary artery cannulation instead of femoral artery cannulation for patients with extensive atherosclerosis or aneurysmal disease of the aorta to avoid retrograde systemic arterial perfusion through these dangerous abnormalities.

We are early in our experience with RCP, and our series does not yet firmly establish that this technique clearly decreases the risk of cerebral complications during hypothermic circulatory arrest. Four patients did have neurologic complications, one of which was fatal, despite the use of RCP. For two of these patients the cause of stroke was clearly anatomic. One patient with a very short period of RCP had a focal deficit probably based on a very severely atherosclerotic ascending aorta. The patient who died of a fatal neurologic complication had an intraoperative aortic dissection and, therefore, had an unknown period of cerebral ischemia before RCP could be established. In addition, persistent carotid dissection was found at autopsy. Two other patients had generalized cerebral impairment after long periods of RCP and may have represented a failure of the technique. On the other hand, they did recover fully. There were also five patients who underwent hypothermic circulatory arrest and RCP for 60 minutes or longer with no cerebral complications, three of those patients being more than 70 years of age.

The success of RCP, however anecdotal, in providing cerebral protection for up to 110 minutes of circulatory arrest convinces us of its potential consistent efficacy. Establishing optimal RCP perfusate temperature and flow rates may increase the effec-

tiveness of RCP and increase the consistent safety limit of circulatory arrest. Although many aortic procedures can be completed within the time limits of hypothermic circulatory arrest alone, some cannot. Furthermore, effective cerebral protection will allow the use of circulatory arrest as a tool for the management of more extensive procedures, for example, total aortic replacement. Yasuura and colleagues¹¹ have already reported total body retrograde perfusion associated with operations for aortic dissection. We found circulatory arrest and RCP to be useful in the management of six patients with severe aortic atherosclerosis undergoing operations for nonaortic disease in this study and are extending its application further for these types of indications as our confidence in it grows. We believe that RCP will be an important aid to cardiac surgeons in the future.

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Discussion

Dr. Julie A. Swain (*Las Vegas, Nev.*). I congratulate Dr. Lytle and his group for an excellent clinical series with a mortality of 9% in a challenging series of patients. The authors have emphasized the importance of avoiding femoral cannulation (with the possible production of retrograde cerebral emboli) and of considering axillary cannulation in these patients. The authors importantly have pointed out the need to consider circulatory arrest for cases other than for aortic vascular surgery.

A 9% incidence of cerebrovascular accidents was found in this series of 43 patients. Of most interest are the seven patients who had circulatory arrest times over 60 minutes. Two of the seven patients had global neurologic damage not explained by anatomic factors, and this gives a 29% incidence of damage. The question in this retrospective study is how sensitive the methods were to determine neurologic damage. In some series reported by surgeons, the gross neurologic injury rate has been as low as 2% for similar patients. Mr. Chris Lincoln in London last year led an international symposium in which careful prospective psychometric and motor studies were evaluated, and it showed a 50% to 100% incidence of neurologic damage after circulatory arrest with even shorter periods.

How were your patients studied to determine neurologic damage and what is the incidence of gross neurologic damage in patients who undergo circulatory arrest for longer than 60 minutes and who do *not* have retrograde cerebropoplegia?

Dr. Lytle. We do not know the answer to the second question and I am not going to find out.

We did not examine these patients with psychometric testing postoperatively. These types of studies and many other investigations need to be done concerning the technique of retrograde cerebral perfusion in the future, but they were not carried out for this series of patients.

I agree, and have pointed out in the manuscript, that the cerebral protection for the patients in this series was not perfect. The patients who had neurologic injury all received arterial perfusion via the femoral artery and all received retrograde cerebral perfusion via an alternative perfusion system where the arterial line was divided and connected directly to the SVC venous line. I think that it is possible that the neurologic complications that occurred may have been related to anatomic causes, perhaps air or atherosclerotic embolization, even though they were diffuse cerebral complications.

Looking at things the other way around, there were a number of patients with long arrest and retrograde cerebral perfusion times who should have been at extremely high risk for severe neurologic complications but who woke up early after operation fully alert. These patients were not tested psychometrically but they were extremely alert and bright postoperatively. I would compare the

observation of how well these patients did to watching Michael Jordan play basketball. It is so dramatically different from previous experience that the difference is obvious.

Dr. Swain. You mentioned the two techniques of RCP. One was the separate circuit and pump head (which is somewhat more costly and complex). The other was the division and separation of the arterial lines. It was implied in the manuscript that separate circuits were better and that simultaneous retrograde and systemic perfusion was important. Why not use a simple shunt that can be quickly clamped to change the direction of flow? Is there evidence that simultaneous antegrade and retrograde flow is beneficial?

Dr. Lytle. We used the more complex and costly system because it gives us the ability to simultaneously perfuse the systemic arterial and RCP system. That capability is helpful in preventing air from getting into the system. I am sure that improvements on our system are possible.

Dr. Jorge Wernly (*Albuquerque, N.M.*). I have a brief question. I found the paper very interesting and the technique very appealing. We have tried it on several occasions and got the same emotional evaluation of its result that you describe. We do not have any hard data.

It has been demonstrated that pH is important in regulating the metabolism of the cell and its several enzymatic pathways. What kind of pH management did you follow during the perfusion of brains that have been cooled to that significant degree?

Dr. Lytle. We use the alpha-stat pH management in which we do not adjust for the difference in temperature, so we do end up with a little alkalosis.

Dr. G. Frank O. Tyers (*Vancouver, B.C., Canada*). When I saw your axillary arterial cannulation, and we have done some innominate perfusions, I wondered whether you really need the retrograde perfusion. At least in some patients you could just snare the innominate and be perfusing the brainogradely.

Dr. Lytle. That is an excellent point. It is certainly possible to perfuse arterial blood antegrade using an axillary artery cannulation. The one patient in whom we were unable to use RCP was a patient with a persistent left SVC, and in that case we did what you suggested. Every now and then we would put a finger over the innominate artery—we could not clamp it because it was heavily atherosclerotic—and perfuse arterial blood via the axillary cannula. Cerebral protection was fine, and I think that is an advantage of axillary artery cannulation. However, that perfusion is not continuous and is more cumbersome than using RCP. In addition, retrograde perfusion helps remove air and particulate emboli.

We do not yet understand all the situations where the concept of retrograde perfusion is going to help. This technology is in its infancy. Cardiopulmonary bypass with antegrade perfusion through atherosclerotic arterial vessels has a fundamental problem associated with it, and that is the risk of atherosclerotic embolization. Retrograde perfusion is a way of decreasing that risk. Once we can reach a low temperature any cardiac operation can be performed with circulatory arrest, and retrograde perfusion will increase the length of circulatory arrest that is safe.