REGIONAL CEREBRAL TISSUE BLOOD FLOW MEASURED BY THE COLORED MICROSPHERE METHOD DURING RETROGRADE CEREBRAL PERFUSION

Brain tissue blood flow was measured precisely by the colored microsphere method during retrograde cerebral perfusion in 10 normothermic mongrel dogs. The average tissue blood flow rates to the cerebral cortex, cerebral medulla, brain stem, cerebellum, and spinal cord during retrograde cerebral perfusion at 25 mm Hg of external jugular venous pressure were 10.5 ± 10.3, 4.2 ± 4.6, 11.1 ± 9.8, 12.3 ± 8.6, and 9.1 ± 5.8 ml/min per 100 gm, respectively. The brain was perfused wholly by retrograde cerebral perfusion without lateralization. Total cerebral blood flow was calculated as the sum total rates of blood flow to each area. Total cerebral blood flow during retrograde cerebral perfusion at 25 mm Hg was 7.8 ± 4.4 ml/min, which represented 3.5% ± 1.9% of whole body blood flow and one third of the total cerebral blood flow (28.0 ± 4.2 ml/min) during cardiopulmonary bypass at a flow rate of 1000 ml/min. Oxygen consumption and carbon dioxide elimination by the total cerebrum during retrograde cerebral perfusion at 25 mm Hg were 0.54 ± 0.23 ml/min and 34 ± 15 μmol/min, respectively, or 8.6% ± 3.6% and 7.0% ± 3.1% of the corresponding whole body value and represented about one third of that measured during cardiopulmonary bypass (1.21 ± 0.39 ml/min and 96 ± 15 μmol/min). Total cerebral blood flow, total cerebral oxygen consumption, and carbon dioxide elimination increased as the external jugular venous pressure increased from 15 to 25 mm Hg; however, no further increase occurred once the external jugular venous pressure exceeded 25 mm Hg. (J THORAC CARDIOVASC SURG 1995;109:772-9)

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Retrograde cerebral perfusion (RCP) via the superior vena cava is a new and simple technique used to protect the brain against interruption of cerebral circulation during aortic arch operations. As shown in our previous study,[1-4] RCP can provide sufficient blood flow and oxygen to the brain to maintain adenosine triphosphate levels in the brain. RCP can minimize further the ischemic damage during interruption of the circulation and may extend the duration of safe cerebral circulatory interruption.[1-4] However, regional blood flow and oxygen metabolism in the brain during RCP are not well understood. In the present study, we used the colored microsphere method to estimate regional cerebral blood flow and cerebral oxygen metabolism during RCP.

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Material and methods

All animals received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources and published by the National Institutes of Health (NIH Publication No. 86-23, revised 1985).

Preparation of the animal and RCP method. Ten mongrel dogs weighing 13.0 ± 1.1 kg (11.5 to 15.0 kg) were used. Anesthesia was induced with ketamine hydrochloride, 10 mg/kg, given intramuscularly and thiopental sodium, 5 mg/kg, given intravenously. After endotracheal intubation, each animal's lungs were ventilated mechanically with 100% oxygen. The ventilator rate and tidal volume were adjusted to maintain the arterial carbon dioxide tension at approximately 35 mm Hg. Anesthesia was maintained with intravenous ketamine hydrochloride, 2 mg/kg per hour, and pancuronium bromide, 0.1 mg/kg. Catheters were placed in the internal carotid artery, right external jugular vein, and right femoral vein to measure blood pressures and to withdrawn blood samples. A perfusion cannula (8F) for RCP was placed in both internal maxillary veins. Temperature was recorded from

a thermistor placed in the nasopharyngeal cavity. Cerebral tissue blood flow was measured by both the colored microsphere method and the hydrogen clearance method. Hydrogen electrodes were inserted into the mid-central parietal cortex through a burr hole in the skull and in the liver parenchyma and renal cortex through abdominal incisions.

A thoracotomy was made through the right fourth intercostal space. Heparin, 300 U/kg, was given intravenously. The ascending aorta was cannulated with a 16F metal-tipped perfusion catheter, the right atrium was cannulated with two separate venous cannulas (28F), and vena caval tapes were applied before the azygos vein was clamped. Cardiopulmonary bypass (CPB) was established at a flow rate of 1000 ml/min with pure oxygen administered at a rate of 0.5 L/min. Mechanical ventilation was discontinued, a crossclamp was applied to the ascending aorta, the heart was arrested, and intermittent cold crystalloid cardioplegic solution was applied. The nasopharyngeal temperature was maintained around 37° C with intermittent core heating. Then RCP was established by perfusing blood through both internal maxillary vein cannulas by means of the Y-shaped connector and another small peristaltic pump to maintain a nasopharyngeal core temperature of approximately 37° C with intermittent heating of the inflow blood. The aortic cannula was opened and directed by gravity to the cardiotomy reservoir while the caval cannula was clamped bilaterally. The pump circuit consisted of a membranous oxygenator (D705 MIDIFLO, Dideco, Italy) with a cardiotomy reservoir (3L CARDF PLUS; Shiley, Inc., Irvine, Calif.) primed with electrolyte solution and 500 ml of blood obtained from another dog to prevent hemodilution. No intervention was made to control blood pressure during this study.

Experimental protocol. CPB was established at a flow rate of 1000 ml/min at normothermia (37° C). Ten minutes after aortic crossclamping, when the vital signs had been stabilized, perfusion was switched to RCP while the external jugular venous pressure was being monitored. During RCP, the external jugular venous pressure was varied from 15 (RCP15 model) to 25 (RCP25 model) or 35 (RCP35 model) mm Hg during 10-minute intervals. During each interval, the external jugular venous pressure was maintained at a certain pressure while perfusion flow rate was varied. At the end of each period, colored microspheres were injected via the cannulas placed in each internal maxillary vein and the blood pressure in each catheter was recorded. Blood samples were withdrawn from each catheter and from the inflow and outflow cannulas. Return blood flow from the aorta was measured directly. Tissue blood flow was measured simultaneously by the hydrogen clearance method.

Another eight mongrel dogs weighing 13.0 ± 1.1 kg (range 12.0 to 14.0 kg) were used to estimate tissue blood flow in each organ during normograde CPB. CPB was established at a rate of 1000 ml/min during normothermia (37° C nasopharyngeal temperature). The same measurements were made in the RCP group and were compared with the values measured during RCP.

Analysis. Blood pressure was measured with a blood pressure monitor (HP7835, Hewlett-Packard Company, Andover, Mass.) with disposable transducers (SCK7178, Viggo-Spectramed Co. Ltd., Singapore). The zero pressure level was set at the level of the operating table. Perfusion flow was calculated from the pump rotation rate, which was calibrated for each pump circuit after each procedure. The blood samples were drawn into heparinized syringes, placed immediately on ice, and analyzed at 37° C for pH, oxygen tension, carbon dioxide tension, oxygen saturation, oxygen content, total carbon dioxide tension, oxygen saturation, oxygen content, total carbon dioxide, and hemoglobin with the ABL-300 analyzer (Radiometer A/S, Copenhagen, Denmark). Cerebral, hepatic, and renal tissue blood flow was measured with the RBF-2 device (Biomedical Science, Inc., Kanazawa, Japan) by the hydrogen clearance method.[5, 6] Cerebral tissue blood flow was calculated by subtracting the baseline value measured during total circulatory arrest. Tissue blood flow was also measured with the colored microsphere method.

Colored microsphere method. In the colored microsphere method, tissue blood flow was calculated form the number of microspheres trapped in the capillaries.[7] Nonradioactive colored microspheres (E-Z Trac, Los Angeles, Calif.), made of a polystyrene-divinylbenzene bridging complex and labeled with special chemically stable dyes, were used for the present study.[7] Microspheres were of several sizes and colors. A 10 ml dose of saline solution containing 200,000 microspheres, 50 μm in diameter, of each color were injected at a constant rate for 1 minute at the end of each study period (RCP15, RCP25, and RCP35) via the cannulas placed in the internal maxillary veins. Blood pressure measurement and blood sampling from each catheter were performed simultaneously. Every animal was put to death at the end of the study. The skull was opened and blood was perfused via each internal maxillary vein to confirm that there was no interference by any venous valve. The whole brain, upper and lower parts of the spinal cord, tongue tip, part of the right lobe of the liver, right kidney, and part of the stomach and small intestine were dissected for analysis. The cerebrum was dissected into six parts: frontal, parietal, and occipital lobe of each side and the cerebral cortex and medulla. The brain stem was dissected into the thalamus, putamen, pons, and medulla oblongata. From each specimen, a 2 to 3 gm sample was separated and weighed precisely. It was processed by chemical digestion and centrifugation. The number of microspheres in each sample was counted with a hemocytometer.

Tissue blood flow (TBF) in each sample was calculated by the following formula: $TBF = A \times (Mo/Mi) \times (Q/W)$ (ml/min per 100 gm), where A is a constant, 2381, Mo is the number of observed microspheres, Mi is the number of injected microspheres, Q is the perfused flow rate + 10 (ml/min), and W is the weight of the tissue sample (gm). Total cerebral blood flow (TCBF) was calculated as the sum total of blood flow in each specimen.

Calculations. Total vascular resistance (R) was calculated by the formula: $R = 79{,}920 \times (Pi - Po)/Q$(dynes·sec·cm^{-5}), where Pi is the external jugular venous pressure, Po is internal carotid arterial pressure, and Q is blood flow (ml/min) returned via the aortic cannula during RCP or Pi is

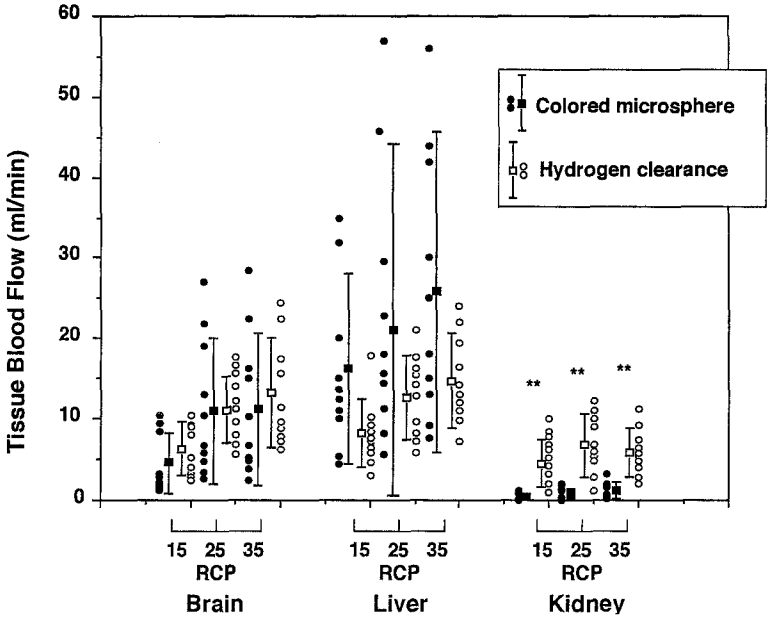

Fig. 1. Scattergram of cerebral, hepatic, and renal tissue blood flow rates using both hydrogen clearance and colored microsphere methods. *Closed dots* represent tissue blood flow according to the hydrogen clearance method. *Open dots* represent tissue blood flow using the colored microsphere method. *Bars* indicate 1 standard deviation. **Any $p < 0.01$ represents a significant difference between methods.

internal carotid arterial pressure, Po is the central venous pressure, and Q is the perfusion flow rate during CPB.

Whole body oxygen consumption (Vo_2) was calculated from the equation: $Vo_2 = (Cao_2 - Cvo_2) \times Q/100$ (ml/min) where Cao_2 is the oxygen content of the perfusate blood, Cvo_2 is the oxygen content of returned blood, and Q is the blood flow (ml/min) returned via the aortic cannula at RCP or perfusion flow rate during CPB.

Whole body excretion of carbon dioxide ($Exco_2$) was calculated by the formula: $Exco_2 = (tco_2v - tco_2a) \times Q$ (μmol/min), where tco_2a is the carbon dioxide content of the perfusate blood, $tco_2v$is the carbon dioxide content of returned blood, and Q is the blood flow (ml/min) returning via the aortic cannula at RCP or the perfusion flow rate during CPB.

Cerebral vascular resistance (R) was calculated by the formula: $Cerebral\ R = 79920 \times ([Pa - Pv]/TCBF) \times (100/W)$ (dynes · sec · cm^{-5}/100 gm), where Pa is the external jugular venous pressure and Pv is the internal carotid arterial pressure at RCP, Pa is the internal arterial pressure, Pv is the external jugular venous pressure during CPB, TCBF is total cerebral blood flow, and W is the weight of the whole brain.

Cerebral oxygen consumption was calculated by the equation: $Cerebral\ Vo_2 = (Cao_2 - Cvo_2) \times TCBF/100$ (ml/min), where Cao_2 is the oxygen content of perfused blood, Cvo_2 is the oxygen content of perfused blood, Cvo_2 is the oxygen content of the blood in the internal carotid artery at RCP and in the external jugular vein during CPB, and TCBF is total cerebral blood flow.

Cerebral carbon dioxide excretion was calculated by the formula: $Cerebral\ Exco_2 = (tCO_2v - tCO_2a) \times TCBF$ (μmol/min), where tCO_2a is the carbon dioxide content of the perfusate, tCO_2v is the carbon dioxide content of the blood in the internal carotid artery at RCP and in the external jugular vein during CPB, and TCBF is total cerebral blood flow.

Results are expressed as the mean ± standard deviation and statistical significance was determined by the paired *t* test (lateralization and localization in the cerebrum and RCP15 or RCP35 versus RCP25) or nonpaired *t* test (localization in the brain except the cerebrum and RCP25 versus CPB).

Results

Perfusion flow rates and blood pressure. Perfusion flow rates during RCP were 112 ± 24 ml/min (RCP15), 206 ± 42 ml/min (RCP25), and 350 ± 62 ml/min (RCP35). Blood pressures in the internal carotid artery and femoral vein were 6.2 ± 2.1 and 12.8 ± 2.6 mm Hg (RCP15), 8.2 ± 1.6 and 16.8 ± 3.2 mm Hg (RCP25), and 9.2 ± 3.6 and 20.2 ± 4.2 mm Hg (RCP35), respectively.

Comparison between the colored microsphere method and hydrogen clearance method. Fig. 1 is a scattergram of tissue blood flow in the right parietal cerebral cortex, liver, and right renal cortex determined by both the colored microsphere and hydrogen clearance methods during RCP. No significant difference was noted in the tissue blood flow in the

Table I. *Regional tissue blood flow (ml/min per 100 gm) measured by the colored microsphere method*

	RCP15	*RCP25*	*RCP35*	*CPB*
Cerebral cortex				
Frontal				
Left	6.3 ± 5.3	10.2 ± 9.6	4.7 ± 4.6	49.9 ± 19.1
Right	2.8 ± 2.2	11.5 ± 9.9	9.7 ± 7.0	38.9 ± 20.4
Parietal				
Left	6.7 ± 5.0	13.9 ± 10.4	11.2 ± 9.7	30.7 ± 10.3
Right	4.4 ± 3.7	11.0 ± 8.5	11.2 ± 8.4	26.0 ± 19.3
Occipital				
Left	4.8 ± 3.3	9.9 ± 8.1	6.4 ± 5.0	54.3 ± 22.9
Right	3.0 ± 2.2	6.5 ± 5.1	6.9 ± 5.3	39.7 ± 14.8
Total	4.7 ± 3.6*	10.5 ± 10.3	8.4 ± 6.7	39.9 ± 17.1*
Cerebral medulla				
frontal				
Left	2.4 ± 1.8	4.6 ± 4.0	10.1 ± 8.9	34.4 ± 14.2
Right	1.4 ± 1.1	4.1 ± 2.7	2.9 ± 2.2	36.0 ± 12.1
Parietal				
Left	2.0 ± 1.2	5.1 ± 4.4	4.8 ± 3.4	24.1 ± 10.8
Right	1.5 ± 0.8	7.5 ± 6.0	6.0 ± 5.4	21.6 ± 12.4
Occipital				
Left	2.2 ± 1.2	2.2 ± 1.3	1.7 ± 1.1	19.4 ± 9.4
Right	1.4 ± 1.0	1.8 ± 1.2	1.7 ± 1.4	23.8 ± 12.3
Total	1.8 ± 1.2*	4.2 ± 4.6	4.5 ± 3.7	26.5 ± 11.9*
Brain stem				
Thalamus	10.9 ± 7.2	23.9 ± 16.5	16.4 ± 12.2	50.0 ± 10.5
Putamen	6.3 ± 4.8	10.2 ± 8.4	8.7 ± 7.6	34.6 ± 17.1
Pons	7.0 ± 4.3	6.7 ± 5.0	5.1 ± 3.2	59.3 ± 14.3
Medulla oblongata	3.0 ± 1.7	3.7 ± 2.5	6.2 ± 4.2	40.2 ± 22.1
Total	6.8 ± 4.5†	11.1 ± 9.8	9.1 ± 6.8	46.0 ± 16.0*
Cerebellum				
Left	4.9 ± 2.0	10.0 ± 6.3	6.8 ± 2.7	42.9 ± 13.6
Right	5.3 ± 1.7	14.5 ± 10.2	16.2 ± 8.5	38.0 ± 8.9
Total	5.1 ± 1.8*	12.3 ± 8.6	11.5 ± 5.6	40.4 ± 11.2*
Spinal cord				
Upper	5.7 ± 2.7	8.2 ± 4.7	5.3 ± 1.2	45.7 ± 16.8
Lower	5.2 ± 3.5	10.0 ± 6.9	9.2 ± 3.2	38.6 ± 16.3
Total	5.4 ± 3.1†	9.1 ± 5.8	7.2 ± 2.2	42.1 ± 16.6*
Tongue	3.2 ± 4.1	8.1 ± 7.5	22.4 ± 13.7*	30.1 ± 6.7*
Liver	16.2 ± 10.8	21.0 ± 22.1	25.8 ± 16.1	44.3 ± 10.7*
GI tract				
Stomach	1.1 ± 0.9†	5.1 ± 6.4	3.6 ± 2.6	38.8 ± 24.5*
Small bowel	0.5 ± 1.0	1.5 ± 2.1	1.0 ± 2.1	38.6 ± 25.2*
Kidney				
Renal cortex	0.5 ± 0.4	0.6 ± 0.8	1.2 ± 1.0	19.0 ± 4.4*
Renal medulla	0.0 ± 0.0	0.4 ± 0.4	0.0 ± 0.0	11.2 ± 4.6*

*$p < 0.01$ compared with RCP25.
†$p = 0.05$.

cerebral cortex and liver between methods; however, renal tissue blood flow was significantly higher as measured by the hydrogen clearance method.

Distribution of the tissue blood flow according to the colored microsphere method. The average rates of blood flow to the cerebral cortex, cerebral medulla, brain stem, cerebellum, and spinal cord at RCP25 were 10.5 ± 10.3, 4.2 ± 4.6, 11.1 ± 9.8, 12.3 ± 8.6, and 9.1 ± 5.8 ml/min per 100 gm, respectively, or 28.7%, 16.6%, 24.4%, 30.8%, and 22.0%, respectively, of the values measured during CPB (Table I). These values increased significantly as the external jugular venous pressure increased from 15 to 25 mm Hg, but they did not change as the external jugular venous pressure increased from 25 to 35 mm Hg (Table I). There was no lateralization of tissue blood flow in the cerebral cortex, cerebral medulla, or cerebellum. There was also no significant difference

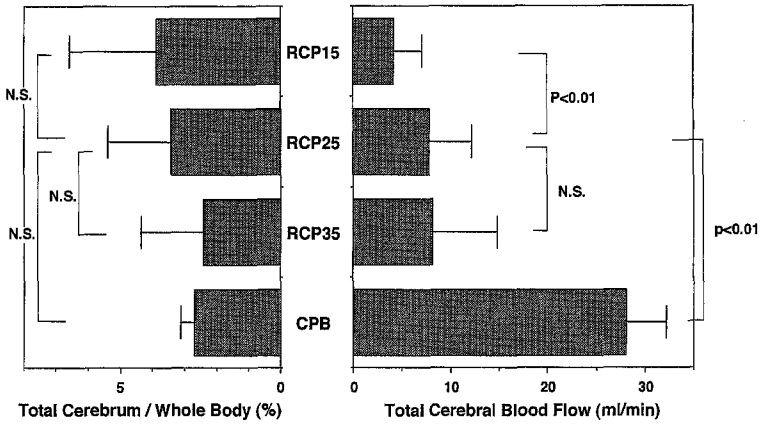

Fig. 2. Total cerebral blood flow and its ratio to whole body blood flow at RCP and normograde CPB. *RCP15, RCP25,* and *RCP35* mean RCP at 15, 25, and 35 mm Hg of the external jugular venous pressure. *CPB* indicates normograde cardiopulmonary bypass at 1000 ml/min of perfusion flow rate. *N.S.,* Not significant.

among frontal, parietal, and occipital lobes in the cerebral cortex and medulla. The cerebral medulla had lower tissue blood flow than did the cerebral cortex, cerebellum, and brain stem.

The hepatic blood flow at RCP25 was 21.0 ± 22.1 ml/min per 100 gm, which was 42.9% of the CPB and did not change with the external jugular venous pressure. Renal blood flows were 0.6 ± 0.8 ml/min per 100 gm in the cortex and 0.4 ± 0.4 ml/min per 100 gm in the medulla during RCP25. These values represent only 3% of the values measured during CPB. The tissue blood flow rates to the visceral organs were also small. These flow rates were 5.1 ± 6.4 ml/min per 100 gm to the stomach and 1.5 ± 2.1 ml/min per 100 gm to the small bowel and represented 13.1% and 3.9% of the values during CPB, respectively.

Total cerebral blood flow and whole body blood flow. Total cerebral blood flow rates during RCP were 4.2 ± 2.9 ml/min (RCP15), 7.8 ± 4.4 ml/min (RCP25), and 8.2 ± 6.6 ml/min (RCP35), which were 3.9% ± 2.7%, 3.5% ± 1.9%, and 2.4% ± 1.9%, respectively, of whole body blood flow. Total cerebral blood flow increased significantly from RCP15 to RCP25, but it did not differ significantly between RCP25 and RCP35, whereas whole body blood flow increased as the external jugular venous pressure increased.

CPB provided 28.0 ± 4.2 ml/min of total cerebral blood flow, which represented 2.7% ± 0.4% of whole body blood flow. The ratio of total cerebral blood flow to whole body blood flow did not differ significantly between RCP25 and CPB. RCP25 provided one third of the total cerebral blood flow provided by CPB (Fig. 2).

Total cerebral oxygen consumption and whole body oxygen consumption. CPB permitted 1.21 ± 0.39 ml/min of total cerebral oxygen consumption, which represented 7.3% ± 2.3% of whole body oxygen consumption. Total cerebral oxygen consumption during RCP was about one third of that during CPB. These values were 0.29 ± 0.21 ml/min (RCP15), 0.54 ± 0.23 ml/min (RCP25), and 0.44 ± 0.20 ml/min (RCP35) or 10.3% ± 7.4%, 8.6% ± 3.6% and 6.8% ± 3.1%, respectively, of whole body oxygen consumption. Total cerebral oxygen consumption and whole body oxygen consumption were significantly higher at RCP25 than at RCP15; however, there was no significant difference in oxygen consumption between RCP25 and RCP35. The ratio of total cerebral oxygen consumption to whole body oxygen consumption did not differ significantly between RCP and CPB conditions (Fig. 3).

Total cerebral and whole body carbon dioxide excretion. The total cerebral carbon dioxide excretion rates were 22 ± 14 μmol/min (RCP15), 34 ± 15 μmol/min (RCP25), 30 ± 12 μmol/min (RCP35), and 96 ± 15 μmol/min (CPB) or 7.5% ± 4.9%, 7.0% ± 3.1%, 5.2% ± 2.1%, and 10.2% ± 1.6%, respectively, of whole body carbon dioxide excretion. Cerebral carbon dioxide excretion during RCP25 was one third of that during CPB. The carbon dioxide excretion from the whole cerebrum and whole body was significantly higher at RCP25 than at RCP15, but there was no significant change between RCP25 and RCP35 (Fig. 4).

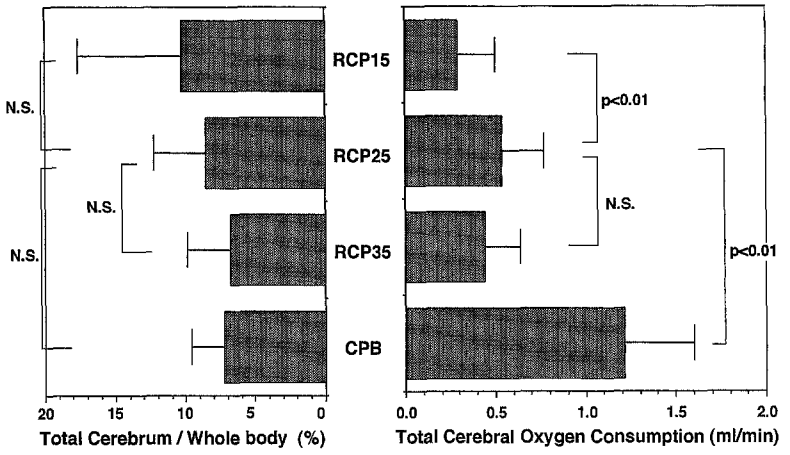

Fig. 3. Total cerebral oxygen consumption and its ratio to whole body oxygen consumption during RCP and normograde CPB. *RCP15, RCP25,* and *RCP35* signify RCP at 15, 25, and 35 mm Hg of the external jugular venous pressure. *CPB* is normograde CPB at 1000 ml/min of perfusion flow rate. *N.S.,* Not significant.

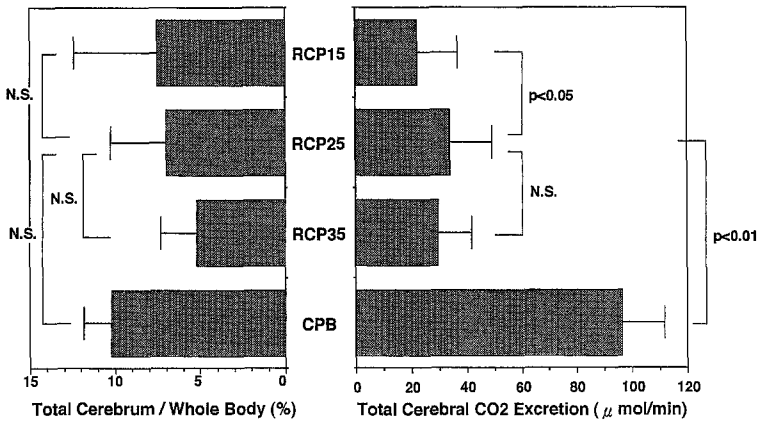

Fig. 4. Total cerebral and whole body carbon dioxide excretion during RCP and normograde CPB. *RCP15, RCP25,* and *RCP35* signify RCP at 15, 25, and 35 mm Hg of external jugular venous pressure. *CPB* is normograde CPB at 1000 ml/min of perfusion flow rate. *N.S.,* Not significant.

Vascular resistance of the total cerebrum. Total vascular resistance in the cerebrum was 186 ± 105 (RCP15), 174 ± 54 (RCP25), or 242 ± 104 × 10^3 dynes · sec · cm^{-5} (RCP35), respectively. These values were higher at RCP35, but no vascular resistance parameter differed significantly among the groups.

Discussion

During surgery of the aortic arch, it is important to protect the brain. Retrograde perfusion through a superior vena caval cannula is a new technique used to protect the brain during circulatory arrest. In previous studies we reported that RCP can provide blood and oxygen, which is not enough to maintain brain function, to both the brain and body.[1,2] RCP can minimize oxygen debt and ischemic damage to the brain and may extend the duration over which cerebral circulation can be safely interrupted.[3] The optimum venous pressure for RCP should be 25 mm Hg, which is the lowest pressure that provides effective cerebral blood flow and is the highest pressure at which brain edema does not result.[4] However, the distributions of regional blood and total cerebral oxygen metabolism during RCP have not been made clear.

In the present study we measured regional blood flow using the colored microsphere method. The

present result clarified our understanding of blood flow distribution during RCP. The colored microsphere method measures tissue blood flow by counting the microspheres trapped in capillaries.[7] Therefore, if a microsphere runs through and is not be trapped by a capillary, tissue blood flow may be underestimated. Smaller microspheres tend to distribute more like red cells, but are subject to shunting, particularly when physiologic changes develop in vascular tone.[8-10] During normograde circulation, microspheres of 15 μm in diameter should be trapped in capillaries; however, it was easy to shunt capillary flow during RCP (unpublished data). Therefore, we used microspheres of 50 μm in diameter because they should be trapped in any capillary during retrograde circulation. Larger microspheres, however, are trapped preferentially in areas of higher flow because of their axial redistribution in the bloodstream.[8-10] We compared the colored microsphere and hydrogen clearance methods and found no significant difference between the methods in measurement of cerebral and hepatic tissue blood flow rates. However, renal tissue blood flow, as determined by the hydrogen clearance method, was significantly higher than that determined by the colored microsphere method. It is possible that the hydrogen clearance method overestimates renal tissue flow because hydrogen diffuses into the urine.

We measured precisely tissue blood flow in the brain and estimated the distribution of perfusate in the brain during RCP. RCP can perfuse the brain wholly with blood without lateralization of perfusion. At RCP25, one third of blood flow during CPB was delivered to the cerebral cortex, the brain stem, and the cerebellum. Blood flow to the cerebral medulla was a little lower than that to the cerebral cortex. The present study showed no significant area of inadequate cerebral perfusion, although some area may have been perfused insufficiently, particularly in the watershed area.

Blood perfused via the internal maxillary vein runs directly into the basal venous plexus; however, it spreads over the superior vena caval system. The superior vena caval system has rich connections to the inferior vena caval system. Therefore, blood perfusing via the internal maxillary vein can reach even visceral organs. Hepatic tissue blood flow during RCP was about one half of that during CPB. Hepatic vascular resistance should be low, because the liver is perfused mainly through the portal vein, which has a low pressure. Therefore, the liver can be perfused easily with a pressure even lower than that required during RCP. During RCP, tissue blood flow to visceral organs, as determined with colored microspheres, is probably underestimated because the visceral organs were perfused via the portal vein with blood that had already run through and become trapped in the liver. On the other hand, the kidney is hardly perfused during RCP. The kidney requires a high perfusion pressure even in normograde circulation.

Tissue blood flow to any part of the brain increased significantly as the external jugular venous pressure increased from 15 to 25 mm Hg. However, it did not increase as the external jugular venous pressure increased from 25 to 35 mm Hg. The main parameters that reflect cerebral tissue blood flow during RCP are considered to be venous pressure, arterial pressure, intracranial pressure, and cerebral vascular resistance. As venous pressure increases, cerebral tissue blood flow should increase.[3] However, high venous pressures are associated with high intracranial pressure, which restricts cerebral tissue blood flow. Therefore, cerebral tissue blood flow did not increase once the external jugular venous pressure exceeded 25 mm Hg.

For oxygen metabolism in the brain to be estimated, total cerebral blood flow should be measured. We measured each cerebral tissue blood flow in each cerebral area using the colored microsphere method and calculated total cerebral blood flow as the sum total of blood flow to each area. Total cerebral blood flow also did not increase once the external jugular venous pressure exceeded 25 mm Hg. The brain was perfused with only 3% of the total perfusate flow rate during RCP, but the ratio of total cerebral blood flow to whole body blood flow was the same as that with CPB.

The ratios of total cerebrum to whole body oxygen consumption and carbon dioxide excretion showed no significant change once the external jugular venous pressure exceeded 25 mm Hg. Therefore, any venous pressure exceeding 25 mm Hg cannot provide any effective blood flow or oxygen supply to the brain.

The dog is not a good model for RCP study because it has a small internal jugular vein and also has many cervical vein valves.[11] Human beings differ in that they have a large internal jugular vein and have few jugular vein valves.[12, 13] Venous valves interfere with retrograde perfusion. We observed both internal maxillary veins after each procedure to confirm that there was no interference by any ve-

nous valve. Nevertheless, this experimental study suggests that retrograde cerebral perfusion may be used in human beings.

RCP can provide about one third of the blood flow and oxygen possible during CPB to the whole brain. It can extend the duration of safe cerebral circulatory arrest. However, the duration of circulatory arrest is still limited. Venous pressure during RCP should be maintained below 25 mm Hg, because total cerebral blood flow and oxygen consumption did not increase once the external jugular venous pressure exceeded 25 mm Hg.

This study was prepared in consultation with a statistician, Nobuyuki Hamajima, MD.

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