CEREBRAL PROTECTION DURING MODERATE HYPOTHERMIC CIRCULATORY ARREST: HISTOPATHOLOGY AND MAGNETIC RESONANCE SPECTROSCOPY OF BRAIN ENERGETICS AND INTRACELLULAR pH IN PIGS

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Objective: We evaluated the effect of antegrade and retrograde brain perfusion during moderate hypothermic circulatory arrest at 28° C. **Methods:** Phosphorus 31-magnetic resonance spectroscopy was used to follow brain energy metabolites and intracellular pH in pigs during 2 hours of ischemia and 1 hour of reperfusion. Histopathologic analysis of brain tissue fixed at the end of the experimental protocol was performed. Fourteen pigs were divided into two experimental groups subjected to antegrade ($n = 6$) or retrograde ($n = 8$) brain perfusion. Anesthesia ($n = 8$) and hypothermic cardiopulmonary bypass groups (15° C, $n = 8$) served as control subjects. In the antegrade and retrograde brain perfusion groups, the initial bypass flow rate was 60 to 100 ml · kg⁻¹ · min⁻¹. In the antegrade group, the brain was perfused through the carotid arteries at a flow rate of 180 to 210 ml · min⁻¹ during circulatory arrest at 28° C. In the retrograde group, the brain was perfused through the superior vena cava at a flow rate of 300 to 500 ml · min⁻¹ during circulatory arrest at 28° C. **Results:** The intracellular pH was 7.1 ± 0.1 and 7.2 ± 0.1 in the anesthesia and hypothermic bypass groups, respectively. Brain intracellular pH and high-energy metabolites (adenosine triphosphate, phosphocreatine) did not change during the course of the 3.5-hour study. In the antegrade group, adenosine triphosphate and intracellular pH were unchanged throughout the protocol. In the retrograde perfusion group, the intracellular pH level decreased to 6.4 ± 0.1 , and adenosine triphosphate and phosphocreatine levels decreased within the first 30 minutes of circulatory arrest and remained at low levels until the end of reperfusion. High-energy phosphates did not return to their initial levels during reperfusion. Histopathologic analysis of nine regions of the brain showed good preservation of cell structure in the anesthesia, hypothermic bypass, and antegrade perfusion groups. The retrograde perfusion group showed changes in all the regions examined. **Conclusions:** The study shows that moderate hypothermic circulatory arrest at 28° C with antegrade brain perfusion during circulatory arrest protects the brain but that retrograde cerebral perfusion at 28° C does not protect the brain. (J Thorac Cardiovasc Surg 1996;112:1073-80)

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The brain is the organ most sensitive to ischemia.¹ Under normothermic conditions, obstruction of the cerebral circulation produces irreversible lesions in 5 minutes. Hypothermia is the most effective method of brain protection in use.² It decreases metabolism and preserves intracellular high-energy phosphates.³ The brain can be preserved for 45 minutes with deep hypothermic circulatory arrest.^{4,5} During the last two decades, clinical and experimental efforts have aimed at improving brain protection for the surgical treatment of aortic arch aneurysms and complex congenital heart diseases by the use of deep hypothermia.⁶ Antegrade and retrograde brain perfusion performed in conjunction with circulatory arrest have improved brain protection and increased

the safe time of circulatory arrest.^{7,8} Deep hypothermia, although effective in reducing metabolism, is associated with several disadvantages,⁹⁻¹¹ and consequently, the mortality and morbidity remain high for these procedures. Is it safe to increase the temperature of the cerebral perfusate during circulatory arrest?

The current study evaluates the effect of moderate hypothermia on the brain subjected to circulatory arrest and antegrade or retrograde cerebral perfusion. Phosphorus 31-magnetic resonance (³¹P-MR) spectroscopy was used to measure brain high-energy metabolites and intracellular pH in pigs undergoing 2 hours of circulatory arrest at 28° C and 1 hour of reperfusion. The results are correlated with histopathologic data.

Materials and methods

Animal preparation. All animals (juvenile pigs weighing 20 to 40 kg) received humane care in compliance with the guidelines of the Canadian Council on Animal Care.¹² Preanesthesia was induced with xylazine (2.2 mg/kg intramuscularly), ketamine (20 mg/kg intramuscularly), and atropine (0.03 mg/kg intramuscularly). Anesthesia was maintained after endotracheal intubation with intravenous pentobarbital (20 mg/kg per hour) and inhalation of 1.5% isoflurane with 60% oxygen and 38.5% compressed air. Pancuronium (0.05 mg/kg) was given every hour for muscle relaxation. A temperature probe was placed in the esophagus to monitor the core temperature. The right carotid artery and right external jugular vein were dissected and cannulated without occlusion of the artery or vein for arterial and venous pressure monitoring. A catheter was inserted into the bladder to measure urine output. The chest was opened with a median sternotomy. Heparin (500 IU/kg) was administered intravenously before cannulation. A 21F cannula was inserted into the ascending aorta to provide arterial input during cardiopulmonary bypass. Venous return to the bypass circuit was achieved with 24F and 28F cannulas inserted into the superior and inferior venae cavae. A 16F cannula was inserted into the innominate artery to provide antegrade perfusion of the brain. The left ventricle was vented through the left atrium. The lungs were not inflated during bypass or circulatory arrest. The cardiopulmonary bypass circuit consisted of a Cobe roller pump (model C22.2, Cobe Hospital Products Div., Lakewood, Colo.), cardiotomy reservoir (Cobe), arterial filter (Cobe Sentry), water bath (Lauda MGW type RMSG, VWR, London, Ontario, Canada), and a membrane oxygenator (Cobe CML) with integral heat exchanger. The circuit was primed with Ringer's lactate solution (1.5 L), mannitol (50 gm), and heparin (10,000 IU). Arterial blood gases and electrolytes were measured with STAT6 and STAT7 analyzers (Nova Biomedical Corporation, Waltham, Mass.). Blood gases were measured at 37° C, and no correction was made for the temperature during hypothermia. The alpha-stat approach was used. The bypass

circuit was designed to allow elective changes between antegrade or retrograde brain perfusion and normal bypass. The hematocrit value was kept between 15% and 23%; the normal pig hematocrit value is about 30%. Homologous blood transfusions were used to maintain the hematocrit value within these parameters. Additional heparin was used on the basis of activated clotting times (ACT II, Medtronic Hemotec Inc., Englewood, Colo.).

Groups and protocol. For MR spectroscopy studies, 14 pigs were divided into two experimental groups that were subjected to antegrade ($n = 6$) or retrograde ($n = 8$) brain perfusion during circulatory arrest. Anesthesia ($n = 8$) and bypass groups ($n = 8$) served as controls. The animals in the anesthesia group received anesthesia alone (37° C) for the entire duration of the protocol (3.5 hours). The pigs in the bypass group received deep hypothermic cardiopulmonary bypass (HCPB) at 15° C for 2 hours, followed by rewarming to 37° C for 1 hour. The arterial blood flow was maintained at 60 to 100 ml · kg⁻¹ · min⁻¹, and the arterial pressure was kept between 60 and 100 mm Hg.

Pigs in the antegrade group underwent normothermic cardiopulmonary bypass for a period of 30 minutes before hypothermic circulatory arrest and antegrade brain perfusion. The perfusate was cooled to achieve systemic hypothermia at 28° C, body circulation was stopped, and the animals were exsanguinated by unclamping the venous return line. The brain was perfused with blood at 28° C through the innominate and carotid arteries during 2 hours of circulatory arrest. The right carotid pressure was monitored continuously and was maintained at 65 to 85 mm Hg, with a blood flow of 180 to 210 ml · min⁻¹. After 2 hours, bypass was reestablished, and the animals were rewarmed to 37° C. Bypass was continued for 1 additional hour of reperfusion.

In the retrograde group, the pigs were subjected to normothermic cardiopulmonary bypass for a period of 30 minutes before hypothermic circulatory arrest and retrograde brain perfusion. The perfusate was cooled to achieve systemic hypothermia at 28° C, circulation was stopped, and the animals were exsanguinated. The brain was perfused with blood at 28° C through the superior vena cava during 2 hours of circulatory arrest. The right internal jugular venous pressure was monitored continuously and was maintained at 35 mm Hg, with a concomitant blood flow of 300 to 500 ml · min⁻¹. During reperfusion, management of the pig was the same as for the antegrade group. Minimal doses of homologous blood products and crystalloid infusion were used to maintain the systemic pressure above 60 mm Hg during reperfusion of the animals subjected to antegrade and retrograde perfusion.

MR methods. The MR data were acquired with a Bruker Biospec spectrometer (Bruker Medical Instruments, Inc., Billerica, Mass.) equipped with a Magnex 7T/40 cm magnet and actively shielded gradients with a clear bore of 30 cm. The ¹H-RF coil was a semicylindrical, inductively coupled surface coil fix tuned to the ¹H frequency (300.1 MHz). The ³¹P-RF coil was a flat, circular, inductively coupled surface coil fix tuned to ³¹P frequency (121.5 MHz).

After completion of the operation, the animal was placed in the supine position in a polyvinylchloride cradle with its head secured to a ^1H -RF coil attached to the cradle. The pig was then positioned with its head at the magnet isocenter, and a transverse scout MR image was acquired (spin echo, TR = 1000 msec, TE = 20 msec, 5 mm thick, field of view = 16 cm). From this scout image, a 2 cm thick coronal slice through the posterior part of the brain was selected and imaged (same parameters). Shimming was then performed to improve magnetic field (B_0) homogeneity over the entire 2 cm thick coronal slice. Linear and higher-order shims were used to obtain a water line width of 20 to 30 Hz.

The pig was then partially removed from the magnet to allow exchange of RF coils to the ^{31}P -RF coil. Care was taken to position the cradle at the same position (± 2 mm) on reinserting to the isocenter. Calibration of RF power was then performed by collecting the ^{31}P signal from the entire 2 cm thick coronal slice previously selected and adjusting the power to maximize the high-energy phosphate signal. A two-dimensional spectroscopic image dataset was acquired with a gradient echo sequence (TE = 1.5 msec, TR = 1500 msec, field of view = 16 cm), with two phase-encoding gradients applied in-plane with the selected slice (with eight increments along each axis for a nominal voxel size of 8 cm^3), spectral width = 10 kHz, 2048 acquisition points, 1 msec gradient pulses with a 0.5 msec rise-time, and 1 msec slice-selective Gaussian RF pulse for a total acquisition time of 25.6 minutes. A similar dataset was then acquired every 30 minutes during bypass, before arrest, during circulatory arrest, and during reperfusion.^{13, 14}

Processing of the spectroscopic dataset, performed with product data processing software (UXNMR, Bruker), included exponential line broadening of 50 Hz along the spectral dimension and Gaussian filtering along the two spatial dimensions, resulting in broadening of the nominal voxel size to $2.7 \times 2.7\text{ cm}^2$. Three-dimensional Fourier transformation resulted in a grid of 64 spectra from which the spectrum from the central voxel, corresponding to the central region of the porcine brain as verified by the coronal localizer image, was extracted for further analysis and quantification. This spectrum was phase corrected (zero and first-order phasing) and baseline adjusted with the use of a cubic spline algorithm, with baseline points selected manually. This spectrum was used for display purposes but not for quantification purposes because of the subjective nature of the manual baseline correction algorithm.

For quantification of peak areas, the unphased complex spectra were fitted with the use of in-house software (ALLFIT).¹⁵ This software uses an iterative complex lorentzian fitting procedure and prior information to fit a series of spectral peaks. Prior information used in this analysis included the spectral peak positions as measured from the phased spectra (determined using UXNMR peak-picking routines) and the number of missing data points, which were used to estimate the phase as a function of peak position (15 data points were missing from the gradient echo acquisition). These data were used as initial values for the subsequent fitting, which was free to shift peak positions or alter peak phases. The optimi-

zation iterative procedure converged to minimal and stable χ^2 values within five to seven iterations.

Fitted metabolite peak areas and chemical shifts were tabulated in spreadsheet form, and total adenosine triphosphate ($\alpha\text{-ATP} + \beta\text{ATP} + \gamma\text{ATP}$ peaks), phosphocreatine (PCr), and inorganic phosphate (P_i) levels were determined. Intracellular pH was calculated from the chemical shift difference between P_i and PCr, taking into account the variation in temperature throughout the experiment.¹⁶

Histopathologic analysis. At the end of each experiment, the pig brain was perfused under anesthesia with 4 L of heparinized saline solution through the carotid arteries to wash blood from the brain. This procedure was followed by perfusion with 10% buffered formaldehyde solution. The brain was then removed for further fixation by immersion in the same formaldehyde solution at 4°C .

After 2 weeks of immersion fixation, the brain was separated into anatomic areas of interest. The tissue blocks were further cut into approximately $1 \times 1 \times 0.5\text{ cm}$ samples that were then prepared by means of standard frozen-section procedures.¹⁷ The prepared sections were cut into 5, 10, 15, and $20\text{ }\mu\text{m}$ thick slices with a cryostat at a temperature of -25° to -28°C . Hematoxylin and eosin staining was performed on every tenth section. Quantification of ischemic neuronal injury was obtained in the areas of the caudate nucleus, putamen, cortex (cingulate and temporal regions), thalamus, cerebellum, pons, mesencephalic gray matter, and hippocampus. Injury was graded (0 to 4) by the number of damaged neurons in eight slices that came from the same area¹⁷: 0 ($<10\%$), 1 (between 11% and 25%), 2 (between 26% and 50%), 3 (between 51% and 75%), and 4 ($>75\%$).

Statistical analysis. The data are expressed as the mean $\pm$ standard deviation of the mean. Statistics were performed using statistical software (Statistica/W, StatSoftOE, Tulsa, Okla.). Comparisons of brain intracellular pH between the groups throughout the protocol were carried out by analysis of variance, with further use of the Kruskal-Wallis test and the Tukey test. Comparisons of brain intracellular pH obtained before and after circulatory arrest within each group were performed using the Student's t and Wilcoxon matched pair tests. A statistically significant difference was said to exist at a probability value of less than 0.05 ($p < 0.05$).

Results

The average intracellular pH values measured in pig brain tissue at intervals of 30 minutes during bypass, circulatory arrest, and reperfusion are listed in Fig. 1. In the control anesthesia and HCPB groups, the intracellular pH levels were 7.1 ± 0.1 and 7.2 ± 0.1 , respectively, during the entire experiment. In the animals subjected to circulatory arrest with antegrade perfusion of the brain, the intracellular pH was 7.1 ± 0.1 before, during, and after circulatory arrest. In the pigs subjected to circulatory arrest with retrograde brain perfusion the intracellular pH was 7.1 ± 0.1 before circulatory

Fig. 1. Intracellular pH measured from localized ^{31}P -MR spectra of the pig brains. $^+p < 0.05$ compared with the anesthesia and HCPB groups at the same stage of the experiment. During the entire course of the experiment (210 minutes), the anesthesia (37°C) group maintained a brain intracellular pH of 7.1 ± 0.1 , and the HCPB group (15°C) maintained an intracellular pH of 7.2 ± 0.1 . $^{\#}p < 0.05$ compared with bypass before circulatory arrest within the same group. Time (min) indicates the midpoint of each spectral acquisition. CA, Circulatory arrest; R, reperfusion; R15, spectrum taken during the first 30 minutes of reperfusion.

arrest, 6.4 ± 0.1 during the arrest period ($p < 0.05$ compared with control groups and the prearrest value in this group), and 6.4 ± 0.1 during the reperfusion period ($p < 0.05$ compared with control groups and the prearrest value in this group).

Representative ^{31}P -MR spectra from the four groups in this study are shown in Fig. 2. In the group subjected to circulatory arrest with antegrade brain perfusion at 28°C , the ATP peaks remained at control values during the entire experiment. PCr and P_i levels did not change during circulatory arrest. In the group that underwent circulatory arrest with retrograde brain perfusion at 28°C , the P_i increased and the ATP and PCr decreased to very low levels during circulatory arrest and did not recover during reperfusion. The time course of ATP, PCr, and P_i levels measured by MR in the brains of the pigs in the antegrade and retrograde groups are shown in Fig. 3.

Table I shows the histopathologic results for the anesthesia (37°C), HCPB (15°C), and antegrade and retrograde groups at 28°C . For comparison, Table I also includes data for circulatory arrest and antegrade and retrograde perfusion at 15°C .¹⁷ Histologic analysis showed preservation of brain anat-

omy in the anesthesia, HCPB, and antegrade groups and diffuse damage over the entire brain of pigs subjected to retrograde perfusion during circulatory arrest at 28°C .

Discussion

The safe time of deep hypothermic circulatory arrest is limited to 45 to 60 minutes.¹⁸ Brain protection during circulatory arrest at 15°C can be improved with antegrade or retrograde brain perfusion.¹⁴ However, many disadvantages of deep hypothermia have been reported,⁹⁻¹¹ including prolonged cardiopulmonary bypass time, which is a good predictor of postoperative death and stroke; prolonged rewarming, which increases the risk of microembolism; disturbances of acid-base balance and the coagulation system; an increase of blood viscosity; and a decrease of oxygen dissociation. Neuropsychologic tests after cardiac operations have shown better results for patients who were subjected to normothermic cardiopulmonary bypass.¹⁹

We studied brain energy metabolites and intracellular pH during 120 minutes of circulatory arrest with selective brain perfusion at 28°C . This ap-

Fig. 2. Representative MR spectra from the four study groups: *Top left*, Anesthesia; *top right*, HCPB; *bottom left*, antegrade perfusion during circulatory arrest; *bottom right*, retrograde perfusion during circulatory arrest.

Fig. 3. Comparison of changes in intensity of MR signals arising from ATP (A), PCr (B), and P_i (C) in the retrograde and antegrade perfusions during initial bypass, circulatory arrest, and reperfusion. Error bars represent standard errors. + $p < 0.05$ versus the initial bypass value in the same group; # $p < 0.05$ versus retrograde; *Arbitrary intensity units. Time (min) indicates the midpoint of each spectral acquisition. CA, Circulatory arrest; R, reperfusion; CA15, spectrum taken during the first 30 minutes of circulatory arrest.

proach was chosen to alleviate the negative effects of deep hypothermia while increasing the availability of oxygen to the brain (relative to the amount available from perfusion at 15° C) as a result of the increased dissociation of oxygen from hemoglobin at the higher temperature. We did not find any significant differences when we compared the antegrade perfusion group with the control anesthesia and HCPB groups. During the ischemic time, the intracellular pH and the signals arising from ATP, PCr, and P_i remained at their initial, normal values. The histologic study showed preservation of brain anatomy across the entire brain (see Table I).

In the group subjected to circulatory arrest and retrograde brain perfusion at 28° C, P_i increased during the first 30 minutes of circulatory arrest; ATP and PCr decreased to very low levels; and the intracellular pH became acidic. This metabolic alteration was maintained during the 2 hours of circulatory arrest, and there was very little recovery during reperfusion. The histologic study showed diffuse lesions in all the regions examined (see Table I). Our previous MR spectroscopy study¹⁴ of pigs subjected to circulatory arrest at 15° C with retrograde brain perfusion showed that intracellular pH, ATP, and PCr levels decreased during circulatory arrest and recovered fully during reperfusion.

This study shows that moderate hypothermia provides less protection than deep hypothermia when retrograde brain perfusion is used in conjunction with circulatory arrest. This suggests that low brain temperature, rather than the supply of oxygen to the brain, is the major determinant of brain protection during retrograde cerebral perfusion. Hypothermia may protect the brain by attenuating the generation of reactive oxygen species.²⁰ Removal of toxic metabolites and the provision of metabolic substrates may also contribute to brain protection during retrograde cerebral perfusion. Antegrade brain perfusion associated with circulatory arrest at 28° C provides excellent protection of brain ATP and intracellular pH, as does antegrade brain perfusion during hypothermic circulatory arrest at 15° C.¹⁴ Crittenden and colleagues²¹ also demonstrated that during prolonged hypothermic circulatory arrest antegrade cerebral perfusion offered better brain protection than retrograde cerebral perfusion in sheep.

Comparison of histopathologic data obtained from the study of pigs subjected to antegrade perfusion at 15° C and 28° C shows that both temperatures preserve cell structure equally well and that the results are not statistically different from those

Table I. Histopathologic damage grading in nine brain areas

	Anesthesia 37 (n = 5)	Bypass 15 (n = 6)	Antegrade 28 (n = 6)	Antegrade 15 (n = 5)	Retrograde 28 (n = 8)	Retrograde 15 (n = 7)	CA 15 (n = 6)
Caudate nucleus	0.2 ± 0.2*	0.3 ± 0.2	0.7 ± 0.5	0.6 ± 0.2	4.2 ± 0.3†	3.9 ± 0.3†	3.8 ± 0.4†
Putamen	0	0.3 ± 0.3	0.2 ± 0.2	0	1.8 ± 0.4	2.0 ± 0.5	3.2 ± 0.4†
Cortex (cingulate)	0	0	0.3 ± 0.3	0.8 ± 0.2	1.7 ± 0.5	2.3 ± 0.7§	3.2 ± 0.6†
Cortex (temporal)	0	0.2 ± 0.2	0.8 ± 0.5	0.4 ± 0.2	1.7 ± 0.6	2.7 ± 0.6#	3.2 ± 0.6†
Thalamus	0.2 ± 0.2	0.2 ± 0.2	0.3 ± 0.2	0.6 ± 0.4	2.9 ± 0.5†	1.4 ± 0.5	2.5 ± 0.6§
Cerebellum (PC)	0.4 ± 0.2	0	0.3 ± 0.2	0.4 ± 0.2	2.1 ± 0.6‡	1.0 ± 0.4	2.6 ± 0.5†
Pons	0.2 ± 0.2	0	0.2 ± 0.2	0.4 ± 0.2	2.1 ± 0.5‡	0.9 ± 0.6	2.5 ± 0.6†
Mesencephalic gray	0.2 ± 0.2	0	0	0	2.2 ± 0.6†	0.4 ± 0.3¶	1.8 ± 0.4**
Hippocampus CA1	0	0	0.2 ± 0.2	0.4 ± 0.2	0.9 ± 0.6	0.7 ± 0.5	1.7 ± 0.7§

*Values shown as grade and mean ± standard error of the mean. CA, Circulatory arrest; PC, Purkinje cells. Data in columns 2, 5, 7, and 8 from Ye J, Yang L, Del Bigio MR, Filgueiras CL, Ede M, Summers R, et al. Neuronal damage following hypothermic circulatory arrest and retrograde cerebral perfusion in the pig. *Ann Thorac Surg* 1996;61:1316–22.

†p < 0.05 versus anesthesia, bypass, antegrade 15 and 28.

‡p < 0.05 versus bypass.

§p < 0.05 versus anesthesia, bypass, and antegrade 28.

#p < 0.005 versus anesthesia, bypass, and antegrade 15.

||p = 0.07.

¶p < 0.05 versus retrograde 28.

**p < 0.05 versus bypass and antegrade 28.

obtained for the anesthesia and HCPB control groups (see Table I). A similar comparison for animals subjected to retrograde perfusion shows poorer preservation at 28° than 15° C in the mesencephalic gray area. Retrograde perfusion during circulatory arrest at 28° C also produces significantly more damage in the caudate nucleus, thalamus, and mesencephalic gray area than does antegrade perfusion, HCPB, or anesthesia (see Table I).

The safe pressure in the superior vena cava during retrograde perfusion may vary among species because of variations in the anatomy of the jugular vein system. Pigs do not have a valve or have an incomplete valve in the internal jugular veins, which is similar to those in human beings. Our experiments showed that a pressure in the superior vena cava of approximately 35 mm Hg would yield less than 20 mm Hg intracranial pressure (data not shown). Pressure in the superior vena cava, rather than intracranial pressure, was monitored during the experiments to minimize physiologic changes in the brain and avoid compromising procedures during the MR studies. However, no single pressure measured elsewhere exactly reflects intracranial pressure.

These studies have demonstrated significant advantages in terms of metabolic and histopathologic outcomes for antegrade brain perfusion during circulatory arrest. These conclusions must be extrapolated with caution to the treatment of human beings because of interspecies differences in anatomy. In

the pig, both carotid arteries arise from the brachiocephalic artery, and in our work, the brain was perfused through the three major arteries of the circle of Willis. In human beings, Kazui and associates²² used a cannula with a balloon inside the true lumen and cannulated the ostia of the brachiocephalic artery and the left carotid artery to perform antegrade brain perfusion. No complications were reported with this technique. Tabayashi and associates²³ cannulated the brachiocephalic, left carotid, and left subclavian arteries. Bachet and associates²⁴ reported data from 56 patients operated on with circulatory arrest and antegrade brain perfusion. They used deep hypothermia for brain perfusion (6° to 12° C) and maintained the body temperature at 28° C. The mortality rate was 13% (7/54), with only one death from neurologic complications and all other patients awaking within 8 hours after the operation.

Antegrade brain perfusion requires manipulation of the aortic branches for dissection and cannulation. Individual arterial cannulas could be cumbersome and interfere with the surgical field, but the technique has been used clinically with success. Kazui and associates²² reported a study of 80 patients with aortic arch aneurysms who underwent operations with selective cerebral perfusion to prevent cerebral ischemia during aortic arch repair. Severe stroke occurred after the operation in one patient (1.3%). The overall early mortality rate was 16.3%. This early mortality is relatively low for all

patients who undergo operations for aneurysms of the aortic arch.

The current study focused on brain protection for which antegrade and retrograde perfusion was used during prolonged circulatory arrest. Although antegrade cerebral perfusion provided adequate brain protection during prolonged circulatory arrest either at 15° C or at 28° C, questions remain concerning the tolerance of other organs to prolonged hypothermic circulatory arrest (2 hours) and are being investigated in our laboratory. The methods described in this article are not intended for clinical use.

This study of pig brain metabolism using MR spectroscopy and histologic techniques shows that retrograde brain perfusion with circulatory arrest does not protect the brain under moderate hypothermic conditions. Antegrade brain perfusion preserves brain metabolism and anatomy during 2 hours of circulatory arrest at 28° C. The protection offered by this technique may make it the best choice for patients who require long and difficult operations, but in the presence of vascular disease, its applicability may be limited.

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