ASSESSMENT OF RETROGRADE CARDIOPLEGIA WITH MAGNETIC RESONANCE IMAGING AND LOCALIZED ^{31}P SPECTROSCOPY IN ISOLATED PIG HEARTS

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Objective: This study was done to determine whether retrograde delivery of cardioplegic solution provides uniform blood flow to the myocardium supplied by an occluded coronary artery and whether it maintains myocardial energy levels beyond the coronary occlusion. **Methods:** Isolated pig hearts were used. A hydraulic occluder was placed at the origin of the left anterior descending coronary artery. The perfusion pressure for retrograde delivery of cardioplegic solution was controlled at 40 to 50 mm Hg. Magnetic resonance imaging and localized ^{31}P magnetic resonance spectroscopy were used to assess myocardial perfusion and energy metabolism, respectively. **Results:** Magnetic resonance perfusion images ($n = 7$) showed that the perfusion defect that occurred during antegrade delivery of cardioplegic solution (as a result of the occlusion of the left anterior descending coronary artery) resolved during retrograde delivery of cardioplegic solution. Retrograde perfusion delivered similar amounts of flow to the jeopardized myocardium as it did to other areas of the myocardium. However, the distribution of cardioplegic solution by the retrograde route was heterogeneous (cloudlike) across both ventricular walls. ^{31}P magnetic resonance spectra showed that the ischemic changes induced by occlusion of the left anterior descending artery during antegrade perfusion were greatly alleviated by retrograde perfusion; however, it took longer for retrograde cardioplegia ($n = 7$, 17.08 minutes) to restore the levels of inorganic phosphate/phosphocreatine relative to the effect of releasing the left anterior descending artery occluder during antegrade delivery of cardioplegic solution ($n = 7$, 5.3 minutes). **Conclusions:** First, retrograde delivery of cardioplegic solution provides sufficient flow to the myocardium beyond a coronary occlusion to maintain near normal levels of energy metabolites, and second, the efficacy of the retrograde route of cardioplegic solution delivery (in terms of distribution of the solution and rate of myocardial energy recovery) is significantly lower than that of the antegrade route. (J Thorac Cardiovasc Surg 1997;114:109-16)

Antegrade cardioplegia has been extensively used to protect the heart during cardiac operations.¹⁻³ In the presence of coronary arterial narrowing or occlusion, antegrade delivery of cardioplegic solu-

tion is compromised, leading to ischemic injury in the myocardium beyond the occluded coronary arteries.⁴⁻⁶ Retrograde cardioplegia (with delivery of cardioplegic solution through the coronary sinus or the right atrium) has been used as an alternative to protect the jeopardized myocardium because coronary atherosclerosis (the most common cause of coronary arterial narrowing or occlusion) does not occur in the coronary venous system.⁷⁻¹⁰ On the basis of the structure of the coronary system, the coronary arterial system is not necessarily the only outlet for retrograde perfusion.¹¹⁻¹⁶ Retrograde perfusion is expected to deliver media to the intramuscular venous plexus and the capillaries in the myocardium supplied by an occluded coronary

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artery.¹¹⁻¹⁶ At present, it is not clear whether retrograde cardioplegic solution delivery provides sufficient flow to meet the energy requirements of the arrested myocardium nor is it known whether the distribution of solution by the retrograde method is homogeneous across the ventricular walls.¹⁷⁻¹⁹ The present study was performed to assess the efficacy of retrograde delivery of cardioplegic solution to perfuse the jeopardized myocardium and maintain myocardial energy levels.

Myocardial perfusion during antegrade and retrograde delivery of cardioplegic solution was assessed with the use of magnetic resonance (MR) perfusion imaging in conjunction with an extracellular MR contrast agent (gadolinium-diethylenetriamine pentaacetic acid [Gd-DTPA]). With use of this technique, myocardial perfusion was visualized immediately after injection of the contrast agent with relatively higher spatial and temporal resolutions compared to those obtained with conventional techniques, such as radioactive microspheres. The changes in cellular energetic metabolites (inorganic phosphate [Pi] and phosphocreatine [PCr]) during antegrade and retrograde cardioplegia in the myocardium beyond the arterial occlusion were monitored with localized ³¹P MR spectroscopy.

Material and methods

Isolated pig heart preparation. The pig was chosen as the animal model because the venous valves and the venous anastomoses in the pig heart are more similar to those of the human heart than those of the dog heart.²⁰⁻²² All animals received humane care in compliance with the "Guide to the Care and Use of Experimental Animals" (first edition) formulated by the Canadian Council on Animal Care. The protocols used in this study were approved by the Institute for Biodiagnostics Animal Care Committee.

Domestic pigs weighing 45 to 60 kg were sedated with an intramuscular injection of diazepam (5 to 10 mg) and ketamine (25 mg). Anesthesia was maintained with 1% to 2% isoflurane in a mixture of oxygen and nitrous oxide. The respiratory rate and volume were adjusted to keep the arterial blood gas values within the normal physiologic range. The brachiocephalic artery was cannulated at the level of the common carotid artery for arterial pressure monitoring, blood sampling, and infusion of cardioplegic solution. A sternotomy was performed. The brachiocephalic and subclavian arteries were dissected. The pericardium was opened longitudinally along the midline. The ascending aorta and the main pulmonary artery were isolated by threading umbilical tape around the origin of the descending aorta. Anticoagulation was provided by injection of heparin (3000 IU) into the superior venae cavae. A cannula was inserted centrally in the brachiocephalic artery. The brachiocephalic artery, subclavian ar-

tery, descending aorta, and superior and inferior venae cavae were then clamped in succession. Heparinized cold (about 4° C) cardioplegic solution was infused into the aortic root (10 ml/kg body weight). The right and left atria were cut to allow drainage of the cardioplegic solution and to prevent warm blood in the lungs from returning to the heart.

The heart was then excised. The brachiocephalic artery was joined to a cannula to be connected to a Langendorff perfusion apparatus. The subclavian artery was cannulated for measurement of antegrade perfusion pressure and drainage of blood cardioplegic solution during retrograde perfusion. A hydraulic occluder was placed at the origin of the left anterior descending coronary artery (LAD). A retrograde cannula was positioned in the coronary sinus with a purse-string suture and over-and-over sutures to prevent solution leakage. With use of this technique we found that the posterior descending vein was well inflated or extended during retrograde cardioplegic solution delivery, which indicated good perfusion of this vessel. The hearts were then placed in the MR magnet and perfused in the Langendorff apparatus.

Perfusion solutions. Pig hearts were arrested with a crystalloid cardioplegic solution containing (in millimoles per liter) NaCl 100, KCl 16, MgCl₂ 16, ethylenediaminetetraacetic acid 0.5, glucose 11, NaHCO₃ 25, and CaCl₂ 1.75 with bovine serum albumin 0.5%. The concentration of free calcium in this solution was 1.1 to 1.2 mmol/L.

For MR imaging studies, complete washout of the contrast agent before subsequent injection of agent is a prerequisite for accurate measurement of tissue perfusion. The amount of blood obtained from one pig was not sufficient to perform an imaging study. Thus the oxygenated crystalloid cardioplegic solution was used as the perfusion medium for the MR imaging study.

For the transmural localized ³¹P MR spectroscopy studies, the pig hearts were perfused with a mixture of autogenous blood and the crystalloid cardioplegic solution (1:1, vol/vol) such that the hematocrit level was 12% to 15% (the normal pig hematocrit is about 30%).

All perfusion media were oxygenated and their pH was maintained at 7.4 to 7.5 (pH unit). The temperature of the heart was maintained at 36.5° to 37° C throughout the protocol.

MR perfusion imaging. T1-weighted MR imaging was performed with a 7 tesla 40 cm horizontal-bore magnet and a Helmholtz probe surrounding the whole heart. T1-weighted images were acquired with an inversion-recovery gradient-echo sequence with a short repetition time (TR = 10 msec) and short echo time (TE = 4 msec). The inversion time (TI) and flip angle of the pulse were 250 msec and 10 degrees, respectively. Each image covered a 15 cm² field of view with 128 × 128 matrix size. Thus the size of each pixel was 1.17 mm². The perfusion images were acquired along the short axis of the heart. This orientation of the images provides the best view of myocardial perfusion throughout the heart with a single slice. Gd-DTPA (0.05 ml/kg body weight, Berlex Canada, Montreal, Canada) was used as the MR contrast agent.

Time courses of the signal intensity of the perfusion images were generated by averaging the signal intensities

measured from the areas covering the LAD and the left circumflex perfusion beds.

Transmural localized ^{31}P MR spectroscopy. Transmural localized ^{31}P MR spectroscopy was performed with the same magnet mentioned previously. For maximum sensitivity, a 2.5 cm diameter surface coil was placed on the anterior surface of the heart over the region perfused by the LAD. The magnetization was excited with use of an adiabatic pulse. This pulse can excite and invert the magnetization in the presence of large heterogeneity in the radio-frequency magnetic field and, therefore, is particularly suitable for use with a surface coil. A two-dimensional column perpendicular to the plane of the coil was selected with ISIS (image-selected in vivo spectroscopy) with an adiabatic inversion pulse. Localization in the third dimension along the two-dimensional column was achieved with the FLAX (Fourier-series-window, longitudinally modulated, and using adiabatic excitation) technique.

The observed phosphorus compounds in the ^{31}P spectrum included Pi, phosphocreatine (PCr), and three peaks of adenosine triphosphate (ATP) (α , β , and γ peaks). The signal intensity of these peaks is dependent on the distance between the layer of the myocardium and the surface coil, and on the amount of the components in the layer examined. The signal intensity decreases as the distance between the myocardium from which the signal is acquired and the coil increases. It is not possible to compare the absolute value of the signal intensity between the various layers of the myocardium.

In addition, the adiabatic pulse has a finite length and limited bandwidth. The transmitter frequency was set between the PCr peak and the Pi peak to achieve the maximum excitation of these two components. The β -ATP peak is at approximately 18 ppm, or more than 2 KHz (in a 7 tesla magnet) from the peak of PCr. The excitation of β -ATP, therefore, was attenuated significantly. The amplitude of the β -ATP peak in these experiments was considerably smaller than that observed when the β -ATP is fully excited. Consequently, the actual changes in ATP levels may not be accurately measured by the changes in the β -ATP peaks. Therefore, we did not use the β -ATP peak to assess retrograde cardioplegia although all three peaks can be observed in the ^{31}P spectra. On the other hand, because the Pi/PCr ratio is sensitive to ischemic insult and directly related to the cellular phosphorylation potential, this ratio was used to assess the effect of retrograde cardioplegia on myocardial energy metabolism.

Because of the small percentage of the vascular space relative to the total tissue volume (approximately 5%) and the use of diluted blood, the 2,3-diphosphoglycerate peak is negligible when a spectrum is acquired from the myocardium. Therefore, the presence of 2,3-diphosphoglycerate did not significantly affect our measurement of Pi.

Experimental protocol. The experimental protocols are summarized schematically in Fig. 1.

MR imaging study. Pig hearts with intact LADs ($n = 7$) were perfused antegradely through the aorta for 30 minutes with the oxygenated crystalloid cardioplegic solution, followed by 15 minutes of LAD occlusion with antegrade cardioplegia. The hearts were then subjected to retro-

Fig. 1. Schematic summary of the experimental protocols.

grade cardioplegia for 30 minutes with the LAD occluded. The perfusion pressure for antegrade cardioplegic solution administration was controlled at about 30 mm Hg to minimize myocardial edema. The coronary flow rate at this perfusion pressure was approximately 200 ml/min. It has been shown that the rate of myocardial oxygen consumption during arrest is approximately 1 ml/min per 100 gm tissue. The average size of the pig hearts used in this study was 250 gm. The total oxygen demand of the hearts was about 2.5 ml/min per heart. The oxygen content in the blood cardioplegic solution (a mixture of blood and crystalloid solution in a ratio of 1:1) after full oxygenation was about 7.2 ml/100 ml (about 5.4 ml oxygen carried by about 4 gm hemoglobin contained in the mixture and about 1.8 ml oxygen physically dissolved in the mixture). According to this calculation, the coronary flow at 30 mm Hg perfusion pressure was expected to deliver more oxygen than required by the heart. In addition, it has been shown that a pressure of 25 to 30 mm Hg during antegrade cardioplegic solution delivery is sufficient to maintain normal myocardial homeostasis.²³

Coronary flow was reduced slightly after occlusion of the LAD to maintain a constant perfusion pressure. The perfusion pressure for retrograde delivery of cardioplegic solution was kept at 40 to 50 mm Hg according to recommendations in the literature.⁷ MR perfusion imaging was performed during the three stages of the protocol.

Transmural localized ^{31}P MR spectroscopy study. Pig hearts ($n = 14$) with a patent LAD were perfused antegradely for 20 minutes. The LAD was then occluded for 25 minutes to induce reversible myocardial ischemia. Again, the rate of coronary flow was reduced slightly (by 10% to 20% of the previous levels) during occlusion of the LAD to maintain the perfusion pressure (30 mm Hg). After ischemia, seven hearts were subjected to retrograde perfusion at a perfusion pressure of 40 to 50 mm Hg with an occluded LAD and the other seven were maintained under antegrade perfusion and the occlusion was re-

Fig. 2. Representative T1-weighted MR images obtained during antegrade (*top panel*) and retrograde (*bottom panel*) delivery of cardioplegic solution from a pig heart subjected to occlusion of the LAD.

leased. The levels of energy metabolites in the region supplied by the LAD were monitored throughout the protocol.

Statistical analyses. Statistical analyses were performed with STATISTICA software (STATSOFT Inc., Tulsa, Okla.). For ^{31}P MR spectra, the peak areas were integrated to measure myocardial energy metabolites. Comparisons of Pi/PCr values between various layers of the myocardium were performed by a one-way analysis of variance. A significant change in the Pi/PCr levels induced by occlusion of the LAD and retrograde cardioplegia was determined by one-way analysis of variance. Comparison of the time courses of signal intensities of MR images obtained from the LAD region and the left ventricular free wall was performed by one-way analysis of variance with repeated measurements.

Results

Effect of retrograde cardioplegia on the perfusion deficit. The perfusion deficit induced by occlusion of the LAD during antegrade cardioplegia was reversed with retrograde cardioplegia. Fig. 2 shows representative MR images obtained during antegrade (*top panel*) and retrograde (*bottom panel*) delivery of cardioplegic solution with an occluded LAD. During antegrade delivery of cardioplegic solution, the region of the myocardium supplied by the occluded LAD exhibited a perfusion deficit that was reversed during retrograde cardioplegic solution delivery in all seven hearts (7/7). Moreover, the distribution of myocardial perfusion was heterogeneous (cloudlike) during retrograde delivery of cardioplegic solution in all hearts (7/7). The distribution of solution by retrograde perfusion in the various regions of the myocardium varied significantly from heart to heart. Moreover, there was no clear-cut edge between the high-intensity areas (perfused areas) and "cold" spots (nonperfused areas) of the myocardium during retrograde cardioplegic solution delivery.

Fig. 3 shows time courses of signal intensity obtained during antegrade (*top panel*) and retrograde (*bottom panel*) delivery of cardioplegic solution with occlusion of the LAD. During antegrade delivery of cardioplegic solution, the signal from the LAD region remained unchanged throughout the perfusion, which indicated essentially no perfusion to this area of the myocardium ($p = 0.000$). When retrograde delivery of cardioplegic solution was used, the myocardium supplied by the occluded LAD was perfused at the same flow rate relative to that in other regions of the left ventricular free wall ($p = 0.252$). Equal, but uneven, perfusion of solution by the retrograde method in the myocardium supplied by the occluded LAD and other areas of the left ventricular wall was observed in all seven hearts.

Effect of retrograde cardioplegia on myocardial energy metabolism. Fig. 4 shows the ratio of Pi/PCr obtained during antegrade perfusion with the LAD open and occluded and during retrograde perfusion with the LAD occluded. The ratio of Pi/PCr during antegrade delivery of cardioplegic solution with an open LAD was 0.159 ± 0.003 ($n = 14$). Occlusion of the LAD during antegrade cardioplegic solution delivery resulted in a significant increase in Pi/PCr (2.29 ± 0.12 , $n = 14$). The Pi/PCr ratios were not significantly different ($p = 0.937$) among the four layers of the myocardium during antegrade car-

Fig. 3. Time course of signal intensity of T1-weighted MR images from the left ventricular (LV) free wall and the regions supplied by the LAD during antegrade (top panel) and retrograde (bottom panel) delivery of cardioplegic solution ($n = 7$).

dioplegic solution delivery with the LAD open or occluded. Retrograde cardioplegic solution delivery with the LAD occluded resulted in a near complete return of Pi/PCr (0.23 ± 0.006 , $n = 7$) to preocclusion values. Although statistically significant ($p = 0.018$), the differences in Pi/PCr between the corresponding layers of the myocardium during antegrade perfusion with an open LAD and retrograde perfusion with an occluded LAD were small. However, with retrograde delivery of cardioplegic solution it took much longer ($p = 0.000$) for Pi/PCr values to return to normal than it did when the LAD occluder was released during antegrade delivery of cardioplegic solution (Fig. 5). Recovery of Pi/PCr values induced by release of the LAD occluder was usually complete

Fig. 4. Effect of retrograde cardioplegic solution delivery on myocardial energy levels. Measurements were obtained from the region supplied by the LAD. AO (antegrade open), antegrade delivery of cardioplegic solution with intact LAD; AC (antegrade closed), antegrade cardioplegic solution delivery with an occluded LAD; RC (retrograde closed), retrograde cardioplegic solution delivery with an occluded LAD. The differences in Pi/PCr values between corresponding layers of the myocardium during the three stages of the protocol were statistically significant ($p = 0.00$ for antegrade open vs. antegrade closed and for antegrade closed vs. retrograde closed; $p = 0.0186$ for antegrade open vs. retrograde closed).

and occurred within the period of the first MR spectrum (5.3 minutes).

In addition, the coronary flow rate of retrograde cardioplegic solution delivery at a perfusion pressure of 40 to 50 mm Hg was 50 to 60 ml/min; generation of a similar perfusion pressure at the aorta during antegrade cardioplegic solution delivery requires a much higher coronary flow rate (>300 ml/min), which suggests that the impedance of the coronary system is significantly higher during retrograde perfusion than during antegrade perfusion.

Discussion

Perfusion of the heart through the coronary sinus was originally proposed by Pratt²⁴ in 1898. He used this approach to perfuse beating devascularized feline hearts and was able to maintain heart contraction for up to 10 minutes. His work suggested that blood in the coronary vascular system can be made to flow in a direction opposite to the physiologic direction. However, this unusual perfusion technique can maintain normal heart function for only a short period. In 1956, Lillehei and associ-

Fig. 5. Recovery time of Pi/PCr obtained either by releasing the LAD occluder during antegrade delivery of cardioplegic solution or by retrograde delivery of cardioplegic solution in the presence of LAD occlusion. The difference in the recovery time between the two groups was statistically significant ($p = 0.000$).

ates²⁵ first used the technique to protect the human heart during cardiac operation. They perfused hearts with oxygenated blood to prevent myocardial injury and found that retrograde perfusion could not provide sufficient flow in the beating heart to maintain normal myocardial energy metabolism.

It has been gradually realized that the distribution of cardioplegic solutions to all regions of the heart is a prerequisite for optimal cardiac protection during heart operations. The presence of coronary obstruction can disrupt the distribution of cardioplegic solution by the antegrade method. This leads to a significant reduction in the amount of cardioplegic solution that reaches the myocardium beyond the occluded coronary arteries. In aortic valve procedures, cardioplegic solutions are usually delivered by direct cannulation of both coronary ostia; however, it was found that this route may occasionally lead to acute dissection or late ostial stenosis.²⁶ Perfusion deficits in the jeopardized myocardium and during aortic root procedures and reoperative bypass procedures suggest that antegrade delivery of cardioplegic solution may not necessarily be the optimal strategy to protect the heart under all conditions. Because coronary atherosclerosis, which severely interrupts the even distribution of cardioplegic solution by the antegrade method, does not occur in the coronary venous system, retrograde perfusion was revived in the 1980s.^{9,11} Although there are a number of studies that have assessed retrograde cardioplegia, its efficacy in maintaining the normal myocardial energy state has not been fully established. This study was done to determine

whether retrograde cardioplegic solution delivery provides sufficient flow to the myocardium beyond a coronary arterial occlusion to prevent ischemia.

Under steady-state conditions, the reactions involving energy synthesis and consumption occur at the same rate. Although cardioplegic solution delivered retrogradely may meet the energy requirement of the arrested heart, perfusion through the coronary sinus for long periods is expected to cause tissue edema that may compromise the oxygen supply, resulting in partial myocardial ischemia or anoxia. Thus it is difficult to determine whether any ischemic changes that occur during retrograde cardioplegia are a result of direct insufficiency of retrograde cardioplegic solution delivery or its side effect (edema). In the present study, a short period of ischemia induced by occlusion of the LAD during antegrade perfusion of cardioplegic solution was applied before the introduction of retrograde perfusion. It was proposed that if retrograde cardioplegia was able to meet myocardial energy requirements under arrest conditions, the ischemic changes would be expected to be reversed within a short period. Because the levels of Pi and PCr are more sensitive to ischemia than are the levels of ATP and the ratio of Pi/PCr is directly associated with cellular phosphorylation potential,²⁷ the efficacy of retrograde cardioplegia was assessed using the ratio of Pi/PCr.

This study demonstrated that the distribution of cardioplegic solution by retrograde perfusion is heterogeneous (cloudlike) across the ventricular wall compared with that of solution delivered by the antegrade route. Patches of the myocardium in the left and right ventricular walls appear to receive no perfusion during retrograde delivery of cardioplegic solution. Moreover, there is no clear-cut edge between well-perfused areas and nonperfused areas of the myocardium. Nevertheless, the perfusion deficit induced by occlusion of the LAD during antegrade delivery of cardioplegic solution (Fig. 2, *top panel*) disappeared during retrograde cardioplegic solution delivery. Moreover, the flow of cardioplegic solution delivered by the retrograde route to the occluded area was similar to that in the nonoccluded area of the myocardium (Fig. 3, *bottom panel*). Using an intravascular contrast agent (hydroxyethyl-starch-ferrioxamine), we found that the changes in signal intensity of T1-weighted images induced by the agent were small because of the small percentage (about 5%) of intravascular space in the total tissue volume.²⁸ Conversely, the extracellular contrast

agent Gd-DTPA (freely distributed between vascular and interstitial spaces) induced relatively large changes in signal intensity compared with those caused by hydroxyethyl-starch-ferrioxamine.²⁸ This greater increase in signal intensity induced by Gd-DTPA is expected to be mainly related to the contrast agent distributed in the interstitial space. In the present study, the myocardial perfusion images were obtained with use of T1-weighted imaging in conjunction with Gd-DTPA. The distribution and perfusion kinetics of cardioplegic solution delivered via the retrograde route that were observed should be highly related to nutritive flow.

In the present study, the efficacy of retrograde cardioplegia was further assessed using the Pi/PCr ratio. Occlusion of the LAD during antegrade delivery of cardioplegic solution resulted in a significant increase in Pi/PCr values (from about 0.159 to about 2.29). Retrograde delivery of cardioplegic solution at 40 to 50 mm Hg perfusion pressure caused Pi/PCr to return to its preocclusion value (Fig. 4). These results suggest that retrograde cardioplegic solution delivery provides sufficient flow to the myocardium beyond the occlusion of a coronary artery to maintain a near "normal" cellular energy state. We also found that it took much longer for retrograde cardioplegia to reestablish the preischemic value of Pi/PCr in the jeopardized myocardium than did releasing the LAD occluder during antegrade delivery of cardioplegic solution (Fig. 5), which suggests that the oxygen delivery capacity of retrograde cardioplegia is significantly lower than that of antegrade cardioplegia under similar perfusion pressures (40 to 50 mm Hg and 30 mm Hg for retrograde and antegrade perfusion, respectively). From an energetics point of view, the results suggest that retrograde cardioplegia, under our experimental conditions, allows energy production at a rate that is equal to or slightly greater than the rate of energy consumption. On the other hand, the energy supply with antegrade delivery of cardioplegic solution (with significantly higher coronary flow) seems considerably higher than that required by the heart. Therefore it took less time for antegrade cardioplegia to reestablish the preischemic Pi/PCr value than it did for retrograde cardioplegia. More important, the results of this study suggest that a small increase in myocardial energy consumption (such as by elevating heart temperature) may cause an imbalance in the energy supply/demand ratio and lead to ischemia. This relatively lower capacity of retrograde delivery of cardioplegic solution for myocar-

dial perfusion relative to antegrade perfusion is likely to be related to its lower coronary flow rate. The effects of equal coronary flow of cardioplegic solution by antegrade and retrograde delivery on myocardial energy metabolism are still under investigation in our laboratory.

In summary, the retrograde method of cardioplegic solution administration delivers solutions to the jeopardized myocardium. The patency of a coronary artery may not affect myocardial perfusion with retrograde delivery of the solution. Although its efficacy is significantly lower than that of antegrade delivery of cardioplegic solution, the retrograde method provides sufficient flow to prevent myocardial ischemia in arrested hearts. Because of its low efficacy of tissue perfusion and heterogeneous distribution, retrograde delivery of cardioplegic solution should be used only when antegrade delivery of cardioplegic solution cannot reach all regions of the myocardium and cannot be performed adequately.

One must realize that the period of ischemia in human beings may be longer than that in this study and that the delayed energy production resulting from retrograde perfusion may not be as useful as in this experiment. In addition, this experimental study dealt with acute coronary occlusion, which is rarely the case in human cardiac operations. Nevertheless, the combined benefits of antegrade/retrograde delivery of cardioplegic solution have been established and it seems therefore that the combined use of antegrade/retrograde delivery of cardioplegic solution (either sequentially or simultaneously) is warranted.²⁹ Future studies should address the effects of temperature on the adequacy of protection of myocardial energy metabolism and the flow distribution of solution delivered by the antegrade and retrograde methods. Ideally, such work would be performed in a long-term model of myocardial ischemia that would better simulate the clinical situation than do acute measurements.

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