CARDIOPULMONARY BYPASS, MYOCARDIAL MANAGEMENT, AND SUPPORT TECHNIQUES

RETROGRADE CARDIOPLEGIA DOES NOT ADEQUATELY PERFUSE THE RIGHT VENTRICLE

Surgeons often rely primarily on retrograde cardioplegia for myocardial protection, because it provides adequate left ventricular perfusion even in the presence of coronary artery disease. Clinically, however, adequate right ventricular perfusion by retrograde delivery has not been demonstrated. Using intraoperative transesophageal echocardiography, we examined retrograde delivery of cardioplegic solutions by contrast echocardiography, which directly assesses myocardial perfusion. In 15 patients (seven having coronary bypass and eight having valve operations), 4 ml of sonicated Isovuc medium was injected retrograde via a coronary sinus catheter. Myocardial perfusion was assessed quantitatively by visual inspection and background-subtracted videodensitometric analysis. In five patients undergoing aortic valve replacement, right and left coronary ostial drainage was estimated during retrograde infusion. Before the aortic crossclamp was removed, myocardial oxygen extraction was calculated in all 15 patients by first delivering warm blood cardioplegic solution for 2 minutes in a retrograde fashion and then taking samples from the cardioplegia line and aortic root. This determined the oxygen extraction ratio across the myocardium at the end of retrograde delivery. Warm blood cardioplegic solution was next given antegrade, and 15 seconds later samples were taken from the cardioplegia line and a right ventricular (acute marginal) vein to determine the oxygen extraction ratio across the right ventricle. As assessed by contrast echocardiography, retrograde infusion resulted in almost four times more perfusion to the left ventricular free wall and septum than to the right ventricular free wall (74 ± 2 versus 69 ± 2 versus 20 ± 2 , $p < 0.05$). In those five patients with an aortotomy the right ostial drainage was less than 5 ml/min whereas left ostial drainage was estimated at 80 ml/min during retrograde administration. Oxygen extraction across the myocardium supplied by retrograde infusion was low after 2 minutes. Conversely, when antegrade cardioplegia was started, right ventricular oxygen extraction rose fourfold ($42\% \pm 5\%$ versus $11\% \pm 1\%$, $p < 0.05$), demonstrating that retrograde cardioplegia had not adequately perfused the right ventricular myocardium. **Conclusions:** 1. Retrograde cardioplegia provides poor right ventricular myocardial perfusion as assessed by contrast echocardiography and coronary ostial drainage. (2) This poor perfusion is inadequate to meet myocardial demands as

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Read at the Seventy-fourth Annual Meeting of The American Association for Thoracic Surgery, New York, N.Y., April 24-27, 1994.

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J THORAC CARDIOVASC SURG 1995;109:1116-26

Modern cardioplegic solutions afford surgeons the ability to provide improved myocardial protection.^{1,2} However, to be effective, they must be adequately distributed to all areas of the heart.^{1,3,4} The assurance of adequate cardioplegic distribution

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0022-5223/95 \$3.00 + 0 12/6/63006

demonstrated by the high right ventricular oxygen extraction after a prolonged retrograde infusion. (3) Therefore surgeons must not rely solely on retrograde cardioplegia for right ventricular myocardial protection. This concept is especially important if continuous warm blood cardioplegia is used, because myocardial requirements are then higher. (J THORAC CARDIOVASC SURG 1995;109:1116-26)

is especially important in patients with coronary disease, because maldistribution of flow is the reason for the operation. Studies show it is safer to clamp the aorta for 4 hours with good cardioplegic distribution than for as little as 30 minutes when the same cardioplegic solution is given without attempts to deliver it beyond coronary stenosis.⁴ This problem of maldistribution of cardioplegic solutions is particularly evident with antegrade delivery, because nonhomogenous distribution of cardioplegic solution is known to occur in the presence of coronary stenosis.³⁻⁵ This has resulted in surgeons pursuing alternative methods of cardioplegic administration to ensure adequate perfusion to all areas of the myocardium.

Several studies have demonstrated the distribution advantages of retrograde administration in the settings of left coronary stenosis and aortic valve regurgitation and when internal mammary artery grafts are used.⁵⁻⁷ Partington and associates^{7,8} studied the distribution of retrograde perfusion in dogs by mixing radioactive microspheres with a blood cardioplegic solution and administering it via the coronary sinus. Despite coronary stenosis, they observed good left ventricular perfusion, although the right ventricle received inconsistent and sometimes scant flow.^{7,8} However, the clinical significance of this poor right ventricular perfusion has been questioned because of differences in coronary venous anatomy between animals and human beings. Similarly, most clinical studies have also focused primarily on the ability of retrograde delivery to provide cardioplegic solution to the left ventricle,^{5,9,10} leaving the question of right ventricular perfusion unanswered. However, inadequate right ventricular protection may lead to an unexpectedly low postoperative cardiac output despite good preservation of left ventricular function.^{11,12} Although the patient usually recovers, this complication may prolong the postoperative period, increasing hospital costs. In addition, as more surgeons begin to rely primarily on retrograde delivery for cardioplegic distribution, the question of right ventricular perfusion assumes increasing importance.

We therefore studied right ventricular myocardial perfusion in patients during retrograde cardioplegic delivery using (1) contrast echocardiography, a safe reliable method of assessing transmural and segmental blood flow distribution patterns in myocardium, (2) observations of coronary ostial effluent, and (3) metabolic analysis of right and left ventricular oxygen uptake.

Methods

Institutional approval and informed written consent were obtained in 15 patients (eight men, seven women; aged 27 through 79 years, mean age 54 years). From this group eight patients underwent valve operations (five mitral valve repair, two aortic valve replacement, and one mitral and aortic valve replacement), four underwent coronary artery bypass grafting (CABG), and three CABG and valve operations. Two-dimensional transesophageal echocardiography was used during the entire surgical procedure in all patients.

After systemic heparinization, cardiopulmonary bypass was established by means of an aortic cannula and either single right atrial (coronary bypass or aortic valve procedures) or bicaval cannulation (mitral valves). In all patients an antegrade cannula (DLP, Ann Arbor, Mich.) was placed in the aortic root and a retrograde cannula (Retropolegia; Research Medical, Salt Lake City, Utah) was positioned via the coronary sinus in the midportion of the great cardiac vein as previously described.⁵ Patients were cooled to 28° C, and the heart was arrested with either warm (patients in unstable condition) or cold blood cardioplegic solution by means of methods reported previously.^{5,13,14}

Retrograde contrast injections were performed during the initial cold blood cardioplegic infusion in all 15 patients. In five patients without coronary heart disease (mitral valve repair only) an antegrade contrast infusion was also performed. Sonicated Isovue medium (E. R. Squibb & Sons, Inc., Princeton, N.J.) was used as the contrast agent. Sonication of the solution was performed according to the methods first introduced by Feinstein and associates.¹⁵ A commercial sonicator (Heat Systems, Ultrasonics, Plainfield, N.J.) was used to sonicate 8 ml of Isovue medium and produced a medium for contrast enhancement, which was kept sterile in a 10 ml syringe and passed to the surgeon by pouring the sonicated contents into a sterile basin. The surgeon then aspirated the contents into another sterile syringe and manually injected 4 ml of contrast agent into the retrograde cannula via a stopcock. The contrast medium was flushed into the muscle by the blood cardioplegic solution, which was

given at a rate of 200 to 250 ml/min (pressure < 50 mm Hg). A similar method was used for the antegrade injections.

Transesophageal images of the right ventricular free wall, interventricular septum, and left ventricular free wall were obtained with a 5.0 MHz transducer by means of a commercial ultrasound scanner (Acuson, Mountainview, Calif.). Venous return was partially occluded to slightly distend the right ventricle for improved ultrasonic visualization. Images were recorded on half-inch videotape before and for approximately 2 minutes after each contrast injection. Optimal power and gain settings were obtained for each patient and were kept constant throughout the rest of the study. In some cases, contrast injections were repeated. Contrast enhancement was immediately noted by the surgeon, but recorded images were analyzed off-line by videodensitometric analysis.

An ultrasonic video acquisition system was used to measure pixel intensity in a given region of interest. Video data from the half-inch videotape was analyzed by a framegrabber computer. The computer system used a series 151 image processor (ITEX-150; Imaging Technology, Inc., Bedford, Mass.), which converts the video image into a pixel matrix (512 by 512 pixels per frame), making it possible to quantify the pixel intensity in gray levels of a predetermined region of interest. These intensities were generated within the region of interest in real time at a rate of 30 frames per second. Time versus intensity curves were generated for each region. In this study, regions of interest were placed in the right ventricular wall, the interventricular septum, and the left ventricular free wall. Background-subtracted analysis was performed; peak pixel intensity in gray levels was obtained during contrast injections and was subtracted from baseline (before injection) intensity, and the difference in pixel intensity was reported.

The operation was then conducted according to a cardioplegic strategy described previously.^{5, 13, 14} The details will only be summarized here to illustrate a slight variation in cardioplegic administration to that previously reported. All patients received cold blood cardioplegic solution for 4 minutes (2 minutes antegrade and 2 minutes retrograde) either as an induction dose or, in patients in unstable condition, after warm induction.^{14, 16} In patients undergoing CABG each distal anastomosis was performed during cold ischemic arrest. Next, the proximal anastomosis was constructed with the use of a *continuous* retrograde infusion of cold (4° C) blood cardioplegic solution. After completion of the proximal aortic anastomosis, a 1-minute infusion of cold blood cardioplegic solution was given antegradely before the next distal anastomosis. This procedure was repeated for each graft, with the internal mammary artery graft being done last to allow the infusion of a warm blood cardioplegic reperfusionate ("hot shot") after this anastomosis. In patients with valve disease cold (4°) blood cardioplegic solution was *continuously* infused (150 to 200 ml/min) in a retrograde fashion for almost the entire operation. The only time retrograde administration was stopped was during placement of the posterior leaflet (mitral) or left commissure sutures (aortic) or for intermittent (approximately every 20 to 30 minutes) cold antegrade blood cardioplegic

infusions. In the five patients having aortic valve operations the amount of blood draining from the right and left coronary ostia during retrograde infusion was noted.

After the last coronary anastomosis (CABG), aortotomy closure (aortic valve), or left atrial closure (mitral), an infusion of warm (37° C) substrate-enriched blood cardioplegic solution (200 to 250 ml/min) was given retrogradely for 2 minutes (pressure < 50 mm Hg). At the end of 2 minutes, 5 ml of blood was taken simultaneously from the aortic root and cardioplegia line to determine the oxygen uptake across the myocardium supplied by retrograde delivery. Antegrade cardioplegia was then started at a rate of 200 ml/min and 15 seconds later a sample was obtained from the cardioplegia line and a coronary vein (1 to 2 ml) on the surface of the right ventricle (acute marginal vein). This determined the oxygen uptake across the right ventricle. The warm antegrade infusion was then continued for a total of 2 minutes. The crossclamp was removed, and the operation was finished. Samples were analyzed for hemoglobin and oxygen by the use of an IL Co-Oximeter analyzer (Instrumentation Laboratories, Lexington, Mass.) and Radiometer blood gas analyzer (Radiometer A/S, Copenhagen, Denmark). Oxygen content was calculated as follows:

$$\text{O}_2 \text{ content} = 1.36 \text{ ml O}_2/\text{gm} \times \text{Hgb} \times \text{O}_2 \text{ saturation} \\ + (0.003 \times \text{Po}_2)$$

where Hgb is hemoglobin and Po_2 is oxygen tension. Oxygen extraction ratio across the myocardium was calculated as follows:

O_2 extraction ratio

$$= \frac{\text{O}_2 \text{ content (cardioplegia)} - \text{O}_2 \text{ (distal sample)}}{\text{O}_2 \text{ contents (cardioplegia)}}$$

where the distal sample was the aortic root when retrograde cardioplegia was in effect and the acute marginal (right ventricle) coronary vein when antegrade cardioplegia was in effect.

Statistics. Statistical analysis was done with the aid of the Statistical Analysis Systems (Cary, N.C.). Data are expressed as mean $\pm$ the standard error of the mean. Group data were compared by Student's *t* test. Significant differences were defined as a probability for each test of $p < 0.05$.

Results

All patients survived the procedure and none had major postoperative complications.

Echocardiographic observations. Perfusion was immediately assessed by observing the ultrasound monitor. This assessment alone clearly demonstrated better distribution of cardioplegic solution to the septum and left ventricular free wall than to the right ventricle. In one patient a retrograde contrast injection did not produce any myocardial enhance-

Fig. 1. Myocardial perfusion (assessed by contrast echocardiography) of the left ventricle, septum, and right ventricle during retrograde delivery of cardioplegic solution in 12 patients. Perfusion of the left ventricle and septum is three to four times greater than that of the right ventricle (mean $\pm$ standard error). * $p < 0.05$.

ment. After the retrograde cannula had been repositioned, a second contrast injection did produce enhancement, confirming that the catheter originally had been malpositioned. In three patients, complete analysis was not possible because of sub-optimal images of the left ventricular free wall.

Background-subtracted pixel intensity was measured in the right ventricular free wall, septum, and left ventricular free wall in 12 patients. In the 12 cases analyzed, perfusion to the left ventricular free wall and septum was three to four times greater than perfusion to the right ventricular free wall (74 ± 2 versus 69 ± 2 versus 21 ± 2 , $p < 0.05$) (Fig. 1).

In five patients with no coronary disease undergoing mitral valve repair, an antegrade contrast injection was performed through the aortic root immediately after the retrograde injection. In all five patients, antegrade injection of cardioplegic solution perfused all regions (left ventricle, right ventricle, and septum) equally (Fig. 2). Conversely, in these same five patients retrograde administration demonstrated poor perfusion of the right ventricular free wall when compared with the septum and left ventricular free wall ($p < 0.05$) (Fig. 3). Pixel intensities for the left ventricular free wall, the septum, and the right ventricular free wall were 76 ± 2 , 71 ± 3 , and 21 ± 3 , respectively. These

values were not statistically different from those in patients with coronary disease who had retrograde perfusion (see Figs. 1 and 3).

Ostial observations. In all five patients undergoing aortic valve replacement, flow emanating from the right coronary ostium was less than 5 ml/min during retrograde cardioplegic infusion. In two patients the ostial effluent was essentially zero. Conversely, all five patients had abundant flow from the left coronary ostium which was measured in two patients and found to be 74 and 82 ml/min.

Metabolic observations. Fourteen patients were available for metabolic studies during the terminal warm infusion ("hot shot"); in one patient an adequate right coronary vein was not identified. At the end of the 2-minute retrograde infusion of warm cardioplegic solution, the oxygen extraction was $11\% \pm 1\%$ across the myocardium supplied by retrograde administration. Conversely, when antegrade delivery of cardioplegic solution was begun immediately after this infusion, oxygen extraction by the right ventricle increased fourfold ($42\% \pm 5\%$, $p < 0.05$) (Fig. 4).

Discussion

This study confirms animal experimental evidence^{7, 8, 17} and demonstrates that retrograde car-

Fig. 2. Myocardial perfusion (assessed by contrast echocardiography) of the left ventricle, septum, and right ventricle during antegrade cardioplegic delivery in five patients without coronary disease. All areas of the myocardium are perfused equally (mean $\pm$ standard error).

Fig. 3. Myocardial perfusion (assessed by contrast echocardiography) of the left ventricle, septum, and right ventricle during retrograde cardioplegic delivery in five patients without coronary artery disease. The right ventricle receives one third to one fourth the perfusion of the septum and left ventricular free wall despite the absence of coronary disease (mean $\pm$ standard error). * $p < 0.05$.

dioplegic administration provides inadequate and poor right ventricular perfusion in the clinical setting. The inability of retrograde delivery to provide substantial right ventricular myocardial perfusion is

demonstrated by (1) contrast echocardiography (see Figs. 1 and 3), (2) the lack of right coronary ostial effluent during retrograde infusion, and (3) the high oxygen uptake by the right ventricle when antegrade

Fig. 4. Oxygen extraction across the myocardium supplied by retrograde administration at the end of 2 minutes of warm blood cardioplegic infusion (*stippled bar*) and by the right ventricular myocardium when antegrade cardioplegia was started immediately after this retrograde infusion (*solid bar*). Note the fourfold increase in myocardial oxygen extraction by the right ventricle when antegrade infusion is started, demonstrating the lack of adequate right ventricular perfusion with retrograde delivery. See text for details (mean $\pm$ standard error). * $p < 0.05$.

delivery was given after a prolonged retrograde infusion had repaid the energy debt to its distribution (see Fig. 4).

Intraoperative contrast echocardiography has been shown to be a safe, reliable method of assessing myocardial perfusion.^{9,10} Sonicated contrast agents (i.e., Isovue medium) produce small, highly reflective microbubbles that, unlike microspheres, are capable of crossing the capillary microcirculation, making it possible to directly assess myocardial perfusion.¹⁵ Recently, Aronson and colleagues⁹ used contrast echocardiography to evaluate myocardial distribution of cardioplegic solution delivered in an antegrade or retrograde manner in human hearts. This study confirmed previous laboratory experimentation^{7,8,17,18} and concluded that retrograde cardioplegia provides perfusion to all left ventricular myocardial regions, regardless of coronary stenosis. However, assessment of right ventricular myocardium was not possible because of inadequate echocardiographic images.

The present study differed in that we primarily used contrast echocardiography to examine right ventricular perfusion by slightly distending the right ventricle to obtain good images. As shown in Fig. 1, contrast echocardiography shows poor right ventric-

ular myocardial perfusion with retrograde cardioplegic administration. Because retrograde delivery will perfuse left ventricular myocardium in the presence of this coronary stenosis,^{5,7-9} one would expect a similar phenomenon in the right ventricle. However, to discount this as the reason for poor right ventricular perfusion, we examined five patients without coronary artery disease undergoing only mitral valve repair. These same five patients also had an antegrade contrast injection performed to validate our method of imaging the right ventricle. As expected, in the absence of coronary artery disease, antegrade administration results in homogeneous distribution of cardioplegic solution to all areas of the heart (see Fig. 2), confirming antegrade perfusion of the right ventricle and our method of imaging. Conversely, despite the absence of coronary disease, right ventricular perfusion was poor with retrograde delivery in all five of these patients (see Fig. 3). Indeed, right ventricular perfusion was identical to that seen in patients with coronary disease (see Figs. 1 and 3), indicating that coronary stenosis does not play a role in distribution of cardioplegic solution to the right ventricle via retrograde infusion.

In the five patients undergoing aortic valve re-

placement, coronary ostial flow was measured during retrograde cardioplegic delivery. No effluent from the right coronary ostium was apparent in two patients, and in the other three drainage was less than 5 ml/min. This lack of flow from the right coronary ostium during retrograde infusion has been documented experimentally^{17,19} and is consistent with the poor right ventricular perfusion demonstrated by contrast echocardiography. Conversely, all patients had abundant flow emanating from the left coronary ostium. Flow was measured in two and found to be approximately 80 ml/min, confirming good retrograde catheter placement and left ventricular perfusion.

Although contrast echocardiography and the lack of right coronary ostial effluent both demonstrate poor right ventricular perfusion, they cannot predict whether this small amount of right ventricular flow is sufficient to meet the demands of the arrested heart. To address this question, we performed metabolic studies. At the end of each operation a 2-minute infusion of warm (37° C) substrate-enriched blood cardioplegic solution was infused retrograde via the coronary sinus (200 ml/min, pressure < 50 mm Hg). Samples taken from the cardioplegia line and aortic root at the end of this 2-minute infusion demonstrated low oxygen extraction (11%) across the myocardium supplied by retrograde administration. Indeed, the amount of oxygen extraction in this sample was equivalent to what we¹⁶ previously reported to represent basal metabolic demands of the warm arrested heart. This indicates that the left ventricle is sufficiently perfused by retrograde cardioplegia to allow all the cellular processes that were damaged or depleted during ischemia to be repaired. Conversely, when antegrade cardioplegia was started immediately after this 2-minute infusion, samples taken from a right coronary vein 15 seconds later demonstrated almost a fourfold increase in oxygen extraction by the right ventricular myocardium (see Fig. 4). This high oxygen uptake is consistent with what has been shown to occur when reversible ischemic myocardium is reperfused and indicates that the right ventricular myocardium was insufficiently perfused by retrograde cardioplegia^{1,20,21} to allow the same cellular process to be repaid. In addition, this right ventricular energy debt occurred despite a cardioplegic strategy that used prolonged periods of continuous cold (4° C) retrograde cardioplegic perfusion and intermittent antegrade infusions.

Our use of cold cardioplegia may have lessened

this right ventricular energy debt inasmuch as some retrograde flow drains into the right ventricle via thebesian veins.^{7,17,19,22} Indeed, we did see (by contrast echocardiography) some drainage into the right ventricle, but we were unsure whether it was coming from thebesian veins or simply cardioplegic solution that escaped the coronary sinus and traversed the tricuspid valve. This thebesian drainage helps cool the right ventricle, thereby reducing its energy demands and limiting ischemic damage.^{5,7} However, it cannot repay the energy debt, inasmuch as it is nonnutritive,^{5,7} reaching the thebesian veins only through venovenous collaterals. Therefore, we would have expected the energy debt incurred by the right ventricle to be even greater had these patients received continuous warm retrograde cardioplegia, because the metabolic demands are increased at 37° C, making this nonnutritive flow less important.^{1,8,17,22}

Cardiac venous anatomy plays a key role in understanding our results. According to a postmortem study of 280 hearts by Ludinghausen,²³ only 21% to 25% of all hearts have a small cardiac vein. This vein courses in the sulcus between the right atrium and the right ventricle and drains to the dorsal wall of the right ventricle, entering the coronary sinus at its origin. Thus it is difficult to perfuse this vein with a balloon-tipped catheter. When the small cardiac vein is missing (75% of all cases), drainage of the right ventricle is limited to thebesian veins, which drain directly into the ventricle.^{7,17,23} Therefore, in the majority of patients, retrograde perfusion to the right ventricular free wall may be technically impossible to accomplish via any type of coronary sinus cannula.

Antegrade delivery avoids right ventricular ischemia and limits cardioplegic volume by producing prompt myocardial arrest.^{1,5} However, the solution is distributed poorly in the presence of severe coronary artery disease, especially in patients who receive arterial (internal mammary artery) grafts.^{5,7,8} Other limitations of antegrade cardioplegia included inadequate distribution with aortic regurgitation, the need to interrupt mitral valve procedures to remove retractors, and ostial damage during cardioplegic infusions in aortic valve operations.⁵ Retrograde (coronary sinus) cardioplegia offsets some of these problems and has been associated with a lower risk of myocardial damage and improved postoperative performance.^{1,5,24} Retrograde cardioplegia also avoids trauma to the coronary arteries and interferes minimally with the surgical procedures. However, this study demon-

strates that only antegrade delivery provides adequate nutritional right ventricular perfusion. Therefore both routes of administration are required to maximize the advantages while limiting the inherent inadequacies each method possesses. We believe adapting a rigid approach of using only one method of cardioplegia delivery is unwarranted and potentially harmful, because it does not ensure distribution to all areas of the heart. In addition, because only antegrade delivery adequately perfuses the right ventricle, we currently recommend that the right coronary artery be grafted first in patients with total occlusion so that cardioplegic solution can be distributed via the graft.

In summary, retrograde cardioplegia provides inadequate protection of the right ventricular myocardium as shown by contrast echocardiography, observations of poor right coronary ostial effluent, and metabolic analysis. Therefore surgeons must not rely solely on this method of myocardial protection if they are to assure optimal myocardial protection.

We thank Greg Mork, Jim Murray, and Nancy Bourtsos for technical support and Felicia Mitchell for organizational assistance.

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Discussion

Dr. John M. Kratz (*Charleston, S.C.*). Your comments regarding warm continuous cardioplegia are well taken, and I agree that retrograde infusion may not deliver an adequate flow to the right ventricle. However, most of us are practicing intermittent cold retrograde perfusion to the right ventricle. Although we all know from our simple fingertip thermistors that are used every day in the operating room that it takes a little longer to cool the right side of the heart than the left, we know the right side does cool.

I would like to remind you of a study that my colleagues and I presented before the Southern Thoracic Surgical Association and published in *The Annals of Thoracic Surgery* in 1992. This study evaluated right ventricular ejection fractions during use of retrograde versus antegrade cold intermittent blood cardioplegia.

We demonstrated that right ventricular ejection fraction falls mildly over the first hour or so after separation from bypass with both antegrade and retrograde cardioplegia. With retrograde cardioplegia right ventricular ejection fractions were just as good and at some points slightly better than when antegrade cardioplegia alone was used. I think that although the flow to the right ventricle is slower, that problem can be overcome with just a bit more volume of cardioplegic solution being given, and one can rely on intermittent cold retrograde cardioplegia alone to protect the right ventricle.

Dr. Allen. In general, Dr. Kratz, I would agree. We recently studied continuous retrograde cardioplegia at various flow rates and examined recovery of right ventricular function after 2 hours of aortic crossclamping. In animals protected with continuous warm retrograde cardioplegia, right ventricular function was depressed despite flow rates up to 400 ml/min. Conversely, when we used continuous cold retrograde blood cardioplegia, even at much lower flow rates, right ventricular stroke work index was well maintained. We therefore concluded that although the right ventricle is poorly perfused by the retrograde cardioplegia technique, if the metabolic demands are kept low by cooling the myocardium, function

can be preserved despite the absence of substantial nutritive perfusion. However, we still believe all patients should be given antegrade cardioplegia for two reasons. First, a terminal warm reperfusate ("hot shot") has been shown to lower operative mortality and improve postoperative function by counteracting any deficiencies in myocardial protection and preventing a reperfusion injury. As demonstrated by this study, only antegrade administration provides the right ventricle with sufficient flow to benefit from this infusion. Second, antegrade cardioplegia results in quicker myocardial arrest, thereby limiting cardioplegic volumes and right ventricular ischemia during cardioplegic induction.

Dr. Lawrence I. Bonchek (*Lancaster, Pa.*). Since the early days of cold cardioplegia in the 1970s, we have been concerned about right ventricular protection, particularly in patients with pulmonary hypertension. Our concern was heightened in those days by two patients who died after double valve replacement with clear-cut right ventricular failure despite the use of topical saline hypothermia. We therefore devised a cooling jacket now known as the DLP Lancaster cooling jacket, which surrounds and cools the entire heart and eliminates many of the difficulties of topical hypothermia and the need for frequent or antegrade perfusion.

I realize your preference may be for warm cardioplegia. Have your findings in this study affected your clinical practice? What is your current clinical practice? That is of interest, particularly for patients who require prolonged procedures such as replacement of the ascending aorta.

Dr. Allen. Yes, this study has changed our clinical practice. We now believe that the right ventricle is relatively underperfused by retrograde cardioplegia and so always use antegrade administration to ensure adequate perfusion. The only time that we allow more than 20 minutes to elapse without an antegrade infusion is if we are using continuous cold retrograde perfusion, because this probably provides enough protection for the right ventricle by maintaining hypothermia. However, we always try to deliver some cardioplegic solution antegradely, especially during the terminal warm reperfusion period ("hot shot"), because this study has shown that retrograde administration does not adequately repay the right ventricular energy debt that develops despite good hypothermic cardioplegic protection. As demonstrated in Fig. 4, even though all of our patients received prolonged continuous cold retrograde and intermittent antegrade infusions of cardioplegic solution, we still saw a right ventricular energy debt at the end of the operation, which was repaid only during antegrade administration. This energy debt probably occurred because (1) even though we used prolonged periods of continuous cold retrograde cardioplegia that cooled the myocardium, it still did not provide much nutritive flow, and (2) we still had some short intervals of cold ischemic arrest when optimal visualization was needed. Regarding topical hypothermia, we published several years ago the detrimental effects of topical ice on the phrenic nerve. In addition, this same study demonstrated no improvement in myocardial protection when topical cooling was added to combined antegrade/retrograde cardioplegic protection. We therefore believe topical cooling is necessary only when the

patient does not have an open right coronary artery because at other times it is very easy to cool the right ventricle via the antegrade route. We therefore use topical cooling (1) when we are unable to use antegrade cardioplegia (i.e., severe aortic insufficiency) or (2) in patients with total occlusion of the right coronary artery, and then only until we have constructed a vein graft, at which point we use this new graft to distribute our antegrade cardioplegic solution.

Dr. William D. Spotnitz (*Charlottesville, Va.*). I congratulate Dr. Allen and his coauthors for their clinical use of the emerging technology of contrast echocardiography. At the University of Virginia, we have demonstrated in a dog model of retrograde coronary sinus cardioplegia that the interventricular septum is underperfused as measured by a gold standard of radiolabeled microspheres, as well as by contrast echocardiography. This work confirmed the ability of contrast echocardiography to qualitatively evaluate the retrograde delivery of cardioplegic solution.

Use of radiolabeled microspheres, at our institution, to quantitatively evaluate microvascular flow has confirmed that all cardioplegic solution delivered antegradely reaches the microvasculature. However, significant decreases in microvascular flow were noted with retrograde delivery of cardioplegic solution. In fact, using extraction fraction of thallium and technetium as markers of tissue perfusion revealed even larger reductions of cellular flow with retrograde cardioplegia. This occurs as a result of thebesian veins.

Although retrograde perfusion results in decreased microvascular and cellular flow, measurements of myocardial temperature revealed similarly excellent cooling by retrograde and antegrade techniques.

Thus my question concerns the excellent clinical results obtained with retrograde cardioplegia. Is this improvement the result of good cooling of the right ventricle or some other phenomenon that allows adequate right ventricular protection despite the decreased perfusion of contrast material you have demonstrated?

Dr. Allen. Dr. Spotnitz, I believe that one must examine the distribution of retrograde cardioplegic solution to the right and left ventricles separately. Most experimental and clinical studies demonstrate that in the presence of coronary stenosis, retrograde administration provides good perfusion of the left ventricle. Therefore, since surgeons are performing an increasing number of arterial grafts in which antegrade cardioplegic solution cannot be distributed down the new graft, we believe retrograde cardioplegia is warranted in most cases.

The question is how well retrograde administration protects the right ventricle and why some surgeons are reporting good clinical results with continuous warm retrograde cardioplegia. First, although this was not a functional study, we did examine right ventricular function by having an independent cardiologist review the echocardiograms postoperatively in all patients. Right ventricular wall motion was then graded from zero (normal) to four (dyskinesis) before CABG and immediately after bypass was discontinued. The results demonstrated improvement in right ventricular wall motion after bypass. Therefore we can conclude that a cardioplegic strategy that combines both antegrade and retrograde delivery results in com-

plete preservation of right ventricular function. Second, most studies of continuous warm retrograde cardioplegia have examined primarily determinants of left ventricular function (i.e., use of intraaortic balloon pump, postoperative cardiac output, inotropic agents). However, many surgeons have seen high central venous pressures in the range of 12 to 14 cm H₂O after continuous cardioplegic protection has been used. This indicates that although the right ventricle is functioning, it is not functioning normally and is probably shifted to a point further out on its Starling function curve. We believe that this poor right ventricular protection is totally avoidable by simply using the antegrade route to infuse cardioplegic solution intermittently and as a terminal warm infusion. We do not understand why surgeons continue to take the adversarial approach of using *only* antegrade or retrograde delivery. Each method of administration has advantages and disadvantages and only by using both methods can the advantages of each be maximized. Therefore, we use retrograde delivery to distribute cardioplegic solution beyond coronary stenoses, especially with arterial grafts, and antegrade cardioplegia to assure perfusion of the right ventricle, obtain rapid cardiac arrest, and avoid right ventricular ischemia during induction.

Dr. Robert A. Guyton (*Atlanta, Ga.*). I have a question about the oxygen extraction levels. The normal oxygen extraction in a normal beating heart is 60% to 65%. I contend that the 11% oxygen extraction that you obtained between the cardioplegia line and the aorta is a reflection of the presence of noncoronary collateral flow, mixing of blood that has come through the pulmonary vessels with cardioplegic blood. The oxygen extraction of 42% in the right ventricle gives us an indication that the protection of the right ventricle is quite adequate, because it is better than the extraction of the normal beating heart. Can you respond to that? I agree with you that the right ventricle is relatively underperfused, but your data support adequate metabolic flow in the right ventricle, not inadequate metabolic flow.

Dr. Allen. Dr. Guyton, with regard to the oxygen extraction across the myocardium supplied by retrograde cardioplegia, we believe this represents primarily the metabolic demands of the left ventricle, because only the left coronary ostium had significant drainage during retrograde administration. As to the 11% oxygen extraction obtained during retrograde administration, these measurements were taken in the arrested flaccid heart, not the beating working heart, so one would expect the oxygen extraction to be approximately 11%. This is what we and others have shown represents basal metabolic demands of the warm arrested heart. Therefore, we believe that retrograde cardioplegia provides sufficient flow to the left ventricle to allow the depleted cellular processes to be repaired, so that now it requires only enough oxygen to meet its basal metabolic demands.

Oxygen extraction across the right ventricle was measured during antegrade cardioplegic administration immediately after the retrograde infusion, also in the arrested heart. Therefore, we once again did not expect the oxygen extraction to be 65%, but approximately the same 11% we saw at the end of the retrograde cardioplegic infusion. However, the fourfold increase in myocardial

oxygen extraction indicates that, unlike the left ventricle, the right ventricle still had an energy debt that had not been repaid, despite the prolonged retrograde infusion.

I should also mention that although we did not measure lactate levels, because of lack of sample, we did measure pH across the myocardium during the warm cardioplegia infusions ("hot shot"). At the end of the retrograde infusion, the pH was unchanged across the left ventricular myocardium and the oxygen extraction was at basal metabolic levels. Conversely, when antegrade cardioplegia was next begun there was an acidotic washout from the right ventricle and the oxygen extraction rose fourfold. This further supports our contention that the right ventricular myocardium was underperfused by retrograde administration and could only have its energy debt repaid by antegrade administration.

To make sure we were not having sampling errors from the aortic root (i.e., sampling pulmonary bronchial collaterals or noncoronary collateral flow), we analyzed hematocrit values for each sample. Because we used cardioplegic solution at a 4 to 1 ratio, the hematocrit value of cardioplegic blood was slightly lower than that of systemic blood. Therefore, if the hematocrit value was higher, indicating that we had some mixing, we discarded the sample.

Because of the possibility of this occurring, two samples were taken from the aorta root in each patient and were compared to make sure the results were similar. In addition, many of these patients had left ventricular vents (i.e., aortic valves) or the left atrium was still opened (mitral valves) during the retrograde infusion, which further prevented aortic sampling problems.

Dr. John L. Ochsner (*New Orleans, La.*). In these 15 patients, did you look at the pattern of the coronary anatomy? In the case of a diminutive right coronary artery and hyperdominant left, in which the left posterior descending artery branches off and the veins are always present, you would expect to have much better flow to the right side on retrograde perfusion than you would in patients with a large right coronary artery.

Dr. Allen. No, Dr. Ochsner, we did not look at variations in coronary anatomy. We originally started this study in patients with valve disease. As you saw, eight of the 15

patients underwent only a valve procedure. We did this because we wanted to exclude coronary stenosis as a problem. Later in the study we did include seven patients undergoing CABG, but we did not specifically examine each heart to see which had a small cardiac vein. However, as you have pointed out, those that have a small cardiac vein do tend to have fewer right ventricular acute marginal veins, as do patients with a small right coronary artery.

Dr. Randas J. V. Batista (*Curitiba, Brazil*). Our experience has been different from yours. We use retrograde continuous warm blood cardioplegia with a Foley catheter, and we routinely open the right atrium and place a purse-string suture around the ostium of the coronary sinus. We can see a posterior coronary vein and other right ventricular veins draining into the coronary sinus right at the mouth of the coronary sinus.

From your presentation, I believe you use balloon catheters. These catheters must be placed distally into the coronary sinus; otherwise these right ventricular veins are not perfused and the right ventricle is not protected.

Dr. Allen. Dr. Batista, I will answer your question in two different ways. First, Dr. Laks, Dr. Drinkwater, and the group from UCLA have done two studies in which they put a purse-string suture around the coronary sinus and perfused the heart in a retrograde fashion. Despite not using a balloon-tipped catheter, they still saw relatively poor perfusion of the right ventricle in human hearts.

Second, if you look at postmortem studies, only 21% to 25% of people have a small cardiac vein, in which case you are going to have to do what you are saying and cannulate a lot of right atrial veins separately. To me it seems very complicated to double cannulate, put a purse-string suture in the coronary sinus, look for multiple draining right atrial veins, and still worry about whether you have cannulated all of the important right ventricular drainage vessels. In contrast, it seems much simpler to give intermittent antegrade infusions. This approach is important not only for right ventricular protection, but for limiting cardioplegic volume and preventing right ventricular ischemia during cardioplegic induction.