JECT. 2003;35:143–151
The Journal of The American Society of Extra-Corporeal Technology

Quantification of the Effect of Altering Hematocrit and Temperature on Blood Viscosity

Alfred H. Stammers, MSA, CCP; See N. Vang, BS, CCP; Brian L. Mejak, BS, CCP; Eric D. Rauch, BS, CCP

Division of Clinical Perfusion Education, School of Allied Health Professions, University of Nebraska Medical Center, Omaha, Nebraska

Presented at the 40th International Conference of the American Society of Extra-Corporeal Technology, New Orleans, Louisiana, March 21–24, 2002.

Abstract: Rheological changes occurring with the conduct of cardiopulmonary bypass affect the distribution of blood throughout the cardiovascular system. The purpose of this study was to evaluate the effects of changing physical characteristics of fluid on the dynamics of blood flow in an in vitro model. An extracorporeal model simulating coronary vessel constriction was designed that consisted of tubing with varying internal diameters. Tubing sizes were selected as percentage reductions (11, 33, 56, and 78%) of a normal sized (3.6 mm) coronary artery. Flow rates were randomly varied between 150 and 300 mL min^{-1} temperatures of 6 and 37°C, and hematocrits of 0, 20, and 38%. Endpoints included viscosity, pressure drop, and volume distribution. As temperature fell from 37 to 6°C, viscosity increased with hematocrit as follows: 192% at 0%, 225% at 20%, and 249% at 38%, $p < .001$. Pressure drop increased significantly across each tubing size ranging from 173–351%, $p < .01$, as fluid was cooled from 37 to 6°C. However, intraconduit statistical differences in volumetric distribution of flow were not achieved. Although the induced hypothermia resulted in increases in resistance, statistical significance was only seen in the smallest lumen conduit. In conclusion, the effects of changing temperature has profound influence on fluid distribution secondary to changing blood viscosity in an in vitro model for fluid distribution. Knowledge of such flow alterations may aid in determining optimal perfusion strategies where vessel constrictions are encountered. **Keywords:** myocardial protection, cardioplegia distribution, viscosity, coronary artery stenosis. *JECT. 2003;35:143–151*

During cardiopulmonary bypass (CPB), all myocardial protective strategies are focused on the limitation and prevention of ischemic and reperfusion injury. Despite advances, myocardial protection through cardioplegic arrest remains imperfect, and inadequate myocardial protection is still a primary causative factor of cardiac mechanical failure (1,2). Clearly, the success of any cardioplegic formulation depends on the completeness of delivery. Inadequate regional delivery has been well documented in the setting of critical coronary stenoses (3–5). The coronary microvasculature plays a central role in the regulation of myocardial perfusion (6). Failure to protect the microvasculature may lead to derangements in coronary flow and potential alterations in postoperative ventricular function. Retrograde cardioplegia administration offers an important adjunct to antegrade infusion, although the protective capacity of retrograde blood cardioplegia remains controversial (7–9). Despite improvements in the instrumentation of cardioplegia solution delivery, the optimum hematocrit, temperature, route of administration, and infusion pressure for optimal cardioplegia distribution remains unknown.

Fluid profiles for cardioplegia delivery have been based on the application of Poisuille's law, with the general assumption that blood behaves as a single-phase Newtonian fluid. However, direct application of Poisuille's law to blood flow in the vascular system is frustrated by a number of complex physiologic influences. Regional and global distribution of cardioplegia to the diastolically arrested heart involves interactions between coronary perfusion pressure, oxygen content, regional vascular resistance, and rheologic properties determined by hematocrit and temperature. Several studies have demonstrated superior myocardial preservation by blood-based cardioplegia over crystalloid solutions when administered at temperatures as low as 15°C (10–14). However, concerns are raised when one considers using blood-based solutions with more extreme reductions of cardioplegia infusion temperature. The effect of temperature on blood viscosity suggests that cold blood cardioplegia may be less well distributed when compared to crystalloid solutions. For any given level of flow across a coronary stenosis, the pressure gradient required to maintain flow increases as the viscosity of the blood increases (15,16). Hypothermia is reported

Address correspondence to: Alfred H. Stammers, MSA, CCP, Geisinger Medical Center, 100 North Academy Ave., Danville, PA 17822-2015. E-mail: ahstammers@geisinger.edu
Received March 15, 2002; Accepted January 12, 2003.

to be associated with several potentially deleterious effects, and perfusion of blood-based cardioplegia solutions may be impeded at very low temperatures (4–8°C) microvasular sludging and rouleaux formation (1). Therefore, during cardioplegia administration, an increase in blood viscosity could be rheologically injurious to myocardial tissue perfusion.

The effect of hematocrit, temperature and vessel diameter on the rheology of blood complicates the formulation of effective strategies of improved cardioplegia distribution. The purpose of this research was to quantify the effects of fluid viscosity on cardioplegia delivery using an in vitro model simulating coronary vessels with various degrees of stenosis. We propose that variations in cardioplegia delivery parameters, including temperature, flow-rate, and blood:crystalloid ratio, may be manipulated to improve the resultant volume distal to simulated stenotic vessels.

MATERIALS AND METHODS

Test Circuit

A test circuit (Figure 1) was constructed to include a 3-L cardiotomy (BCR 3000; Bentley Laboratories, Irvine, CA), which served as a blood reservoir. Quarter-inch polyvinyl chloride (PVC) tubing was connected to the outlet of the reservoir and placed through the raceway of a just-occlusive twin roller pump (7400 MDX; Terumo-Sarns, Ann Arbor, MI). Distal to the roller pump, a heat exchanger (D1079E; Medtronic Cardiopulmonary, Minneapolis, MN) was inserted to regulate the temperature of the reservoir blood volume, and a 40-micron arterial line filter (Healthdyne Cardiovascular, Inc., Marietta, GA) placed distal to the heat exchanger. A 1/4-inch Y-connector was inserted distal to the arterial line filter to allow return blood delivery to the reservoir through a recirculation line. The other outlet of the Y-connector allowed flow through the inlet of the conduit bridge. The conduit bridge (Figure 2) consisted of four 14-cm sections of PVC tubing (Tygon® R-3603; Cole-Parmer Instrument Company, Vernon Hills, IL) with the following internal diameters (ID): 3.2, 2.4, 1.6, and 0.8 mm. These conduit sizes were chosen to represent approximate left anterior descending coronary artery lumen reductions of 12, 34, 56, and 78%, respectively (17). Quarter-inch straight connectors with Luer ports were placed proximal and distal to each of the four conduit segments. A T-connector was cut into the center of each conduit size, which had an ID that corresponded to the individual conduit ID. Attached to the vertical outlet of each T-connector was a 12-cm piece of tubing with an ID consistent with the T-connector. The vertical tubing segments of the four conduit sizes were directed into separate graduated cylinders, and remained clamped until volumetric determinations were performed. All Luer ports in the conduit bridge were connected to pressure transducers linked to a calibrated multichannel pressure amplifier (V2203A; Electromedics for Medicine, Inc., Pleasantville, NY). A calibrated thermistor (Model 4000 A; YSI Co., Inc., Yellow Springs, OH) was inserted 6 cm proximal to the inlet of the conduit bridge to monitor perfusate temperature. A Hoffman clamp was placed on the tubing distal to the conduit bridge and was used to regulate system pressure.

Outdated packed red blood cells (pRBCs) and fresh frozen plasma (FFP) were obtained from the local blood bank. The packed cells were washed with saline (0.9% NaCl) with an autotransfusion device (STAT-P; COBE Cardiovascular, Arvada, CO), and the resultant packed red cell volume was adjusted with plasma to achieve a starting hematocrit of 38 ± 2%. Viscosity measurements were made at Hct of 20 ± 2%, the average intraoperative Hct of the cardioplegic solution in a patient with 25% Hct blood mixed 4:1 with cardioplegic solution. A balanced physiologic saline solution was used as the asangunieous CP.

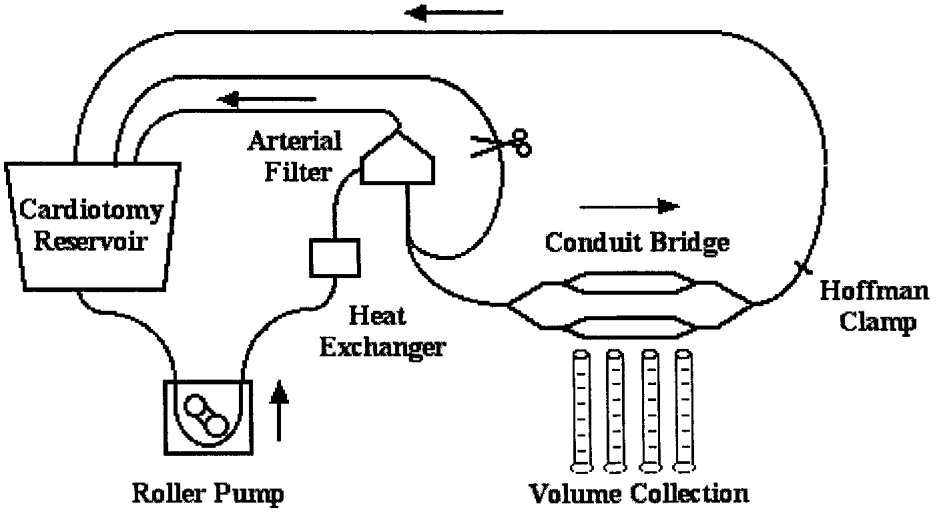

Figure 1. Circuit design.

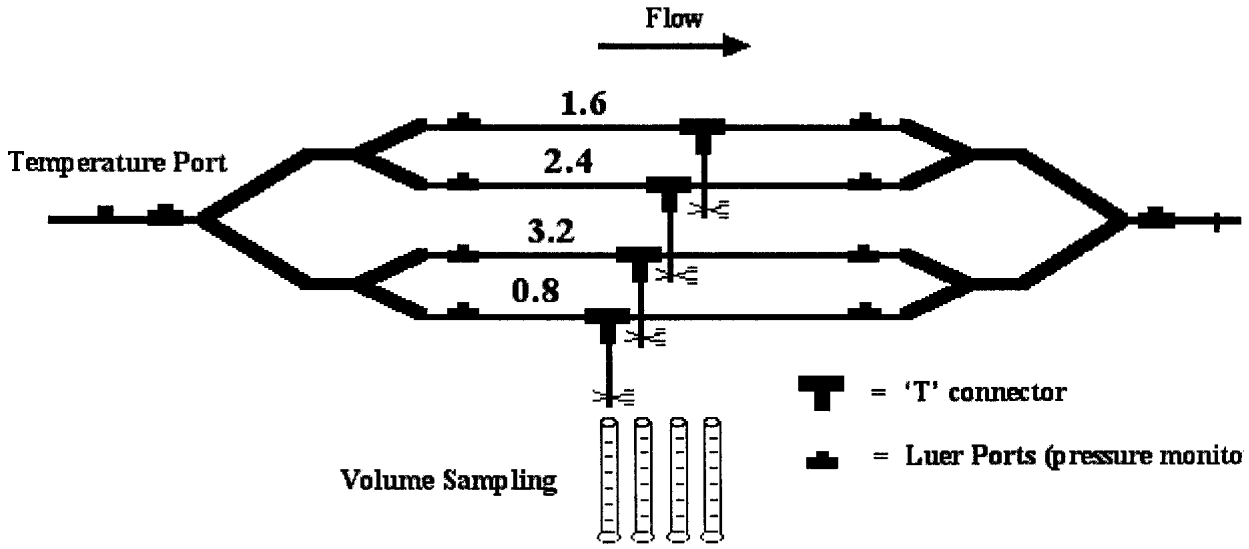

Figure 2. Conduit bridge design.

Volumetric Analysis

During cardioplegia administration, the resultant volumes of solution flowing through each conduit size were collected and measured. Experimental variables included temperature, flow rate, and blood:crystalloid ratio. Cardioplegia solutions were delivered at temperatures of 37 and 6°C (±1°C) and at flow rates of 150 and 300 mL min^{-1} (±2 mL min^{-1}) within each trial. Solutions tested were blood, 4:1 blood:crystalloid, and all-crystalloid. At each temperature–flow paring, eight replications were taken for each solution tested. Volume samples were collected by clamping the four tubing segments of the bridge distal to each T-connector, while simultaneously unclamping the four tubing segments of the vertical T-connector. Volume samples were taken in 30-sec collection periods.

Pressure-Drop Analysis

During cardioplegia administration, pressure-drop determinations were conducted by comparing the pressure measured proximal and distal to each conduit size, and across the entire conduit bridge. At flow rates of 150 and 300 mL min^{-1} (±2 mL min^{-1}), and at both 75 and 150 mmHg (±5 mmHg) infusion pressures, this study consisted of a trial of four replications for each solution tested. The cardioplegia solutions tested were all-blood, 4:1 blood:crystalloid, and all-crystalloid. Cardioplegia was delivered at 37 and 6°C (±1°C) within each trial. System pressure was monitored and regulated with a Hoffman resistor clamp to maintain constant 75 and 150 mmHg (± 5 mmHg) infusion pressures.

Measured Fluid Viscosity

Kinematic viscosity measurements of blood (Hct 38 ± 2%), 4:1 blood:crystalloid (Hct 20 ± 2%), and all-crystalloid (Hct 0%) cardioplegia solutions were taken in quadruplicate at 37, 25, and 6°C (±1°C) using a cross arm viscometer (Zeitfuchs Cross-Arm; Technical Glass Products, Inc., Dover, NJ). Solution samples were taken from the circuit and pipetted into the sample tube of the viscometer. A water bath was used to establish the equilibrium of the desired temperature. A flow time was obtained for each sample by syphoning the fluid through the viscometer. Kinematic viscosity was calculated in centistokes by mulitiplying the flow time in seconds by the viscometer constant (18).

Statistics

All data were recorded in a spreadsheet format on a personal computer and were expressed as mean ± standard deviation of the mean. Statistical analysis was performed using a one-way analysis of variance (SuperANOVA; Abacus Concepts, Berkley, CA). When significant values were achieved, a post hoc test (Fisher's least significant difference) was performed. Statistical significance was accepted at the $p \leq .05$ level.

RESULTS

Blood viscosity increased by 249% as temperature was reduced from 37°C to 6°C; 225% for 4:1 blood:crystalloid solution; and 192% in crystalloid solution (Figure 3, Table 1). The effect of temperature on the volume of cardioplegia solution delivered through each lumen size of the conduit bridge is represented in Table 2. There were no differences between any of the tested solutions at the lower temperatures (Table 2). The mean volume distributions are shown in Figure 4. Again, there were no differences seen in flow distribution when temperature was lowered with decreasing lumen size.

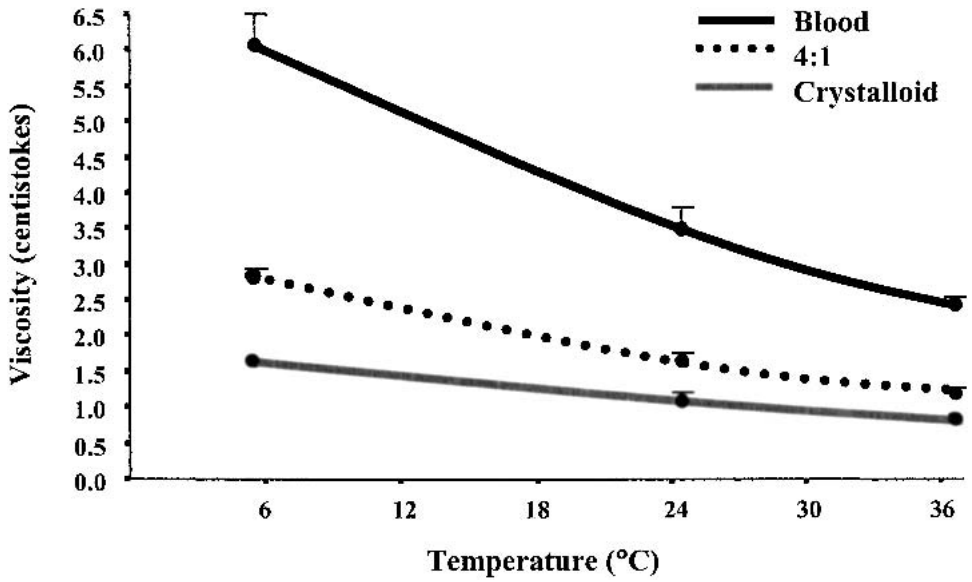

Figure 3. Relationship between viscosity, temperature, and changing solution composition. Zeitfuchs Cross-Arm viscometer. Blood (Hct 38 ± 2%), 4:1 (Hct 20 ± 2%), and physiologic saline solution (crystalloid). Temperatures were set at 37 ± 1°C, 25 ± 1°C, and 6 ± 1°C.

Table 1. Mean Viscosity (Centistokes) of Blood and Crystalloid Cardioplegia Solutions with Varying Temperature.

	37°C	*p*	25°C	*p*	6°C
Blood	2.44 ± 0.09	.0023	3.50 ± 0.29	.0001	6.07 ± 0.42
			.0001		
4:1	1.26 ± 0.02	.0002	1.65 ± 0.10	.0001	2.83 ± 0.11
			.0001		
Crystalloid	0.85 ± 0.03	.0033	1.10 ± 0.11	.0001	1.63 ± 0.03
			.0001		

Zeitfuchs Cross-Arm viscometer. Blood (Hct 38 ± 2%), 4:1 (Hct 20 ± 2%), and physiologic saline solution (crystalloid). Temperatures were recorded at 37 ± 1°C, 25 ± 1°C and 6 ± 1°C.

Pressure drop across the entire circuit significantly increased when temperature was dropped from 37 to 6°C, $p < .0078$ (Table 3). The greatest increase was seen in the smallest lumen (0.8 mm) when compared to all other conduit sizes (Figure 5).

DISCUSSION

Numerous formulations of cardioplegic solutions are currently in use, and the identification of an optimum cardioplegic formula, which decreases energy requirements, minimizes the sequelae of energy loss during arrest, and provides energy sources during ischemia, remains elusive. Regardless of the arresting agent composition, adequate regional distribution of cardioplegia solution is critical for optimal myocardial protection. Inadequate protection is still a significant cause of post-operative morbidity and mortality in technically successful cardiac operations (1,19). The lack of homogeneous cardioplegia distribution is believed to be a significant contributing factor to reperfusion injury with current methods of myocardial protection (2,3).

Models examining the maldistribution of coronary blood flow are based upon coronary distribution patterns that use varying degrees of vascular stenosis. The risk of intraoperative ischemic injury is greatest in poststenotic regional myocardium, because these areas paradoxically receive the least uniform distribution of cardioplegia solutions, resulting in delayed arrest and large myocardial temperature gradients (20). A significant number of perioperative infarctions occur distal to bypassed stenotic arteries and are frequently found in the presence of patent coronary bypass grafts (4). The functional consequences of impaired delivery of cardioplegia beyond stenoses have been documented by Grondin, Hilton, and their associates (4,5). Their segmental wall-motion studies showed persistent hypokinesia in areas supplied by stenotic coronary vessels.

Surgical techniques to improve the uniform distribution of cardioplegia solutions are standard in clinical practice, and these include retrograde delivery through the coronary sinus and infusion through the graft. The coronary venous system is relatively uninvolved by atherosclerotic obstruction (21), and although retrograde delivery notably improves perfusion to poststenotic myocardium, it is not a panacea to the problems of cardioplegia distribution. Recent studies have suggested that the right ventricular myocardium is suboptimally perfused with retrograde infusion (7,8). In their analysis of warm retrograde distribution, Gates et al. demonstrated that all regions of the left and right ventricles, as well as the intraventricular septum, are perfused by retrograde technique (9). However, their results also indicate that the nutritive blood flow to the myocardium of the right ventricle is minimal because approximately 70% of retrograde cardioplegia is shunted through

Table 2. The Effect of Temperature on the Volume of Cardioplegia Delivered across Simulated Restrictions of Coronary Artery Lumen Diameter.

6° Delivery Temperature

	150 mL min^{-1}			300 mL min^{-1}		
	Blood	4:1	Crystalloid	Blood	4:1	Crystalloid
mm						
3.2	98.8 ± 3.8	97.5 ± 3.3	103.3 ± 1.5	182.0 ± 6.6	178.5 ± 4.5	169.3 ± 9.2
2.4	36.0 ± 1.1	36.8 ± 3.1	39.0 ± 2.6	83.0 ± 4.0	86.5 ± 2.8	90.9 ± 4.6
1.6	10.1 ± 0.4	11.1 ± 0.5	11.9 ± 1.1	25.4 ± 2.1	29.5 ± 1.2	29.0 ± 1.7
0.8	1.2 ± 0.4	2.0 ± 0.1	1.8 ± 0.2	2.5 ± 0.1	3.2 ± 0.2	3.5 ± 0.4

37° Delivery Temperature

	150 mL min^{-1}			300 mL min^{-1}		
	Blood	4:1	Crystalloid	Blood	4:1	Crystalloid
mm						
3.2	101.5 ± 4.9	98.8 ± 3.7	103.8 ± 4.3	183.0 ± 7.5	178.5 ± 6.4	170.0 ± 12.2
2.4	39.0 ± 1.4	41.3 ± 3.4	39.0 ± 5.0	84.0 ± 3.4	87.8 ± 4.2	92.6 ± 3.4
1.6	11.1 ± 0.8	13.3 ± 0.8	12.8 ± 1.7	25.6 ± 1.1	30.4 ± 1.4	29.8 ± 4.4
0.8	0.8 ± 0.4	1.6 ± 0.4	1.7 ± 0.2	2.5 ± 0.3	3.6 ± 0.2	3.8 ± 0.9

Volume delivery at 150 ± 2 mL min^{-1} and 300 ± 2 mL min^{-1}. Blood (Hct 38 ± 2%), 4:1 (Hct 20 ± 2%), and physiologic saline solution (crystalloid). Temperatures were recorded at 37 ± 1°C and 6 ± 1°C.

the thebesian veins, thereby bypassing the microvasculature. Conversely, it has been shown that 90% of antegrade perfusion nourishes the myocardium and ensures right ventricular perfusion if the right coronary artery is unoccluded (22). For these reasons, an integrated technique, using both antegrade and retrograde delivery, is preferred in surgical practice (23). Although infusion pressure is a key determinant of the completeness of cardioplegia distribution (24,25), an optimal flow rate to improve myocardial perfusion when using integrated cardioplegia has not been determined (26,27).

Within the past decade, microprocessor technology has improved the design of cardioplegia delivery systems and has made the achievement of better myocardial protection more accessible (28). Despite improvements in the instrumentation of cardioplegia solution delivery, the hematocrit, temperature, route of administration, and infusion pressure for optimal cardioplegia distribution remain controversial.

Surprisingly, little attention has been given to blood rheology as opposed to studies of its static properties. The study of blood flow and its relation to the vessel in which it is contained has been termed 'hemorheology' and considers blood viscosity and the liquid–surface interface reactions that regulate normal hemostasis. The movement of blood within the circulation is difficult to characterize and does not directly conform to conventional Newtonian or Poiseuille mechanics, which complicates the calculation of flow distribution. The salient features of Poiseuille's law are the critical influence of vascular geometry (lumen radius) and blood viscosity on the resistance to flow. Direct application of Poiseuille's law to blood flow in living vascular beds is complicated by a number of physiologic influences (29). It is accurate for only nonpulsatile, laminar flow of Newtonian fluids, and microvessels are not the straight, constant diameter, cylindrical tubes upon which Poiseuille's law is based. Whole blood has a nonlinear pressure–flow relationship, and as a result, does not possess a unique coefficient of viscosity. The viscosity of blood is shear rate-dependent—as flow velocity falls, blood viscosity markedly increases, a characteristically non-Newtonian behavior. However, at high flow rates observed in larger vessels, blood behaves largely as a Newtonian fluid with almost constant viscosity. At high shear rates ($\geq$100 sec^{-1}), the viscosity of blood is independent of sheer rate and is primarily a function of hematocrit and fibrinogen concentration (30,31). It is now well recognized that blood can no longer be treated as a single-phase Newtonian fluid when the diameter of the blood vessel is smaller than 1 mm (32,33).

In addition, in the capillary vasculature, blood demonstrates a phenomenon known as the Fahraeus–Lindquist effect. At lumen diameters of approximately $\leq$300 μm, both the hematocrit and the regional viscosity of blood traversing the tube decrease with diminishing tube diameter (32,34). This behavior is caused by channeling of the relatively heavy and rigid red cells into the axis of flow, creating a cell-poor plasma layer along the wall of the vessel and a core of packed red cells at the axial center (35). The viscous properties of the plasma and the plasma layer in determining vessel wall shear stress are particularly significant in the microcirculation caused by this migration of red cells to the centerline of the vessel (36).

Hematocrit is the primary determinant of blood viscos-

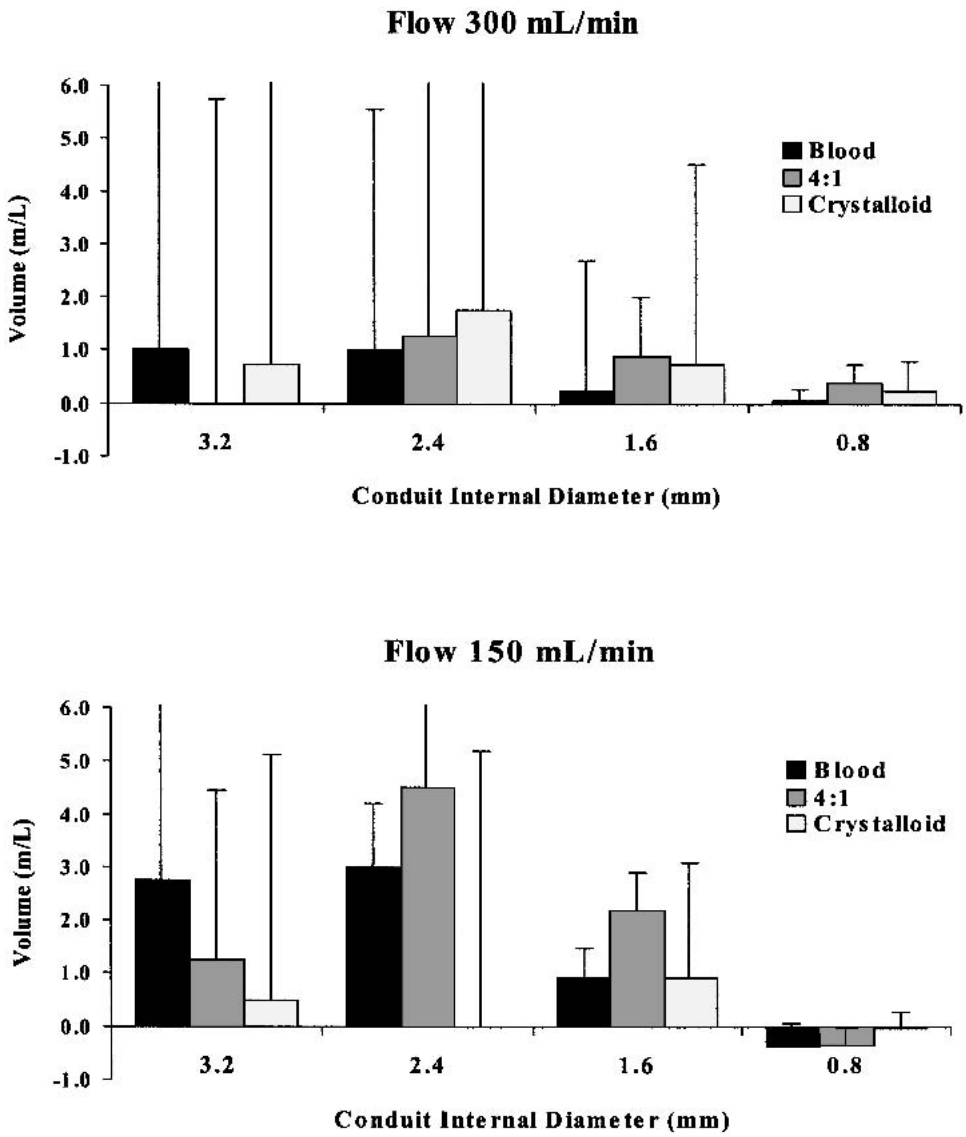

Figure 4. Mean difference in total volume collection as related to cardioplegia solution temperature. Values represent the mean difference in volume collected (37°C vs. 6°C) at flow rates of 300 ± 2 mL^{-1} min and 150 ± 2 mL min^{-1}. Blood (Hct 38 ± 2%), 4:1 (Hct 20 ± 2%), and physiologic saline solution (crystalloid). Temperatures were recorded at 37 ± 1°C and 6 ±°C.

Table 3. Pressure-Drop Analysis (mmHg).

	Total Circuit	1.6 mm	2.4 mm	3.2 mm	0.8 mm
37°C	4.9 ± 1.9	4.9 ± 2.7	5.4 ± 2.4	4.4 ± 2.3	1.9 ± 1.8
6°C	8.8 ± 4.1	8.9 ± 4.7	9.6 ± 3.6	7.4 ± 4.2	5.4 ± 4.1
p-value	.0078	.0182	.0026	.0391	.0235

Mean values for differences in pressure-drop across all conduit sizes, at all flow rates, CP solutions, and pressures. Temperatures were recorded at 37 ± 1°C and 6 ± 1°C.

ity (37,38). Although red cell deformity, plasma viscosity, and red cell aggregation influence overall blood viscosity, these effects are relatively insignificant when compared with red cell concentration. The two most important resistances in the coronary vasculature are the caliber of the blood vessels and the viscosity of the blood (39). Hemodilution works to offset the negative effects of CPB by significantly reducing blood viscosity during bypass. Reduced viscosity results in decreased resistance to blood flow through the capillaries, improving tissue perfusion to a degree that compensates for the reduction in red cell concentration. Therefore, it may be expected that crystalloid cardioplegia solutions would allow better distribution and tissue perfusion because of their decreased viscosity and lower microvascular resistances, as opposed to blood-based cardioplegia.

The practice of induced hypothermia during CPB is a fundamental requirement for both myocardial and systemic protection, and further influences the rheological behavior of blood. A survey by Robertson et al. of more than 1400 United States surgeons indicates that blood cardioplegia is the solution of choice during cardiac operations (23). Experimental data indicate that blood-based cardioplegia provides superior preservation as compared

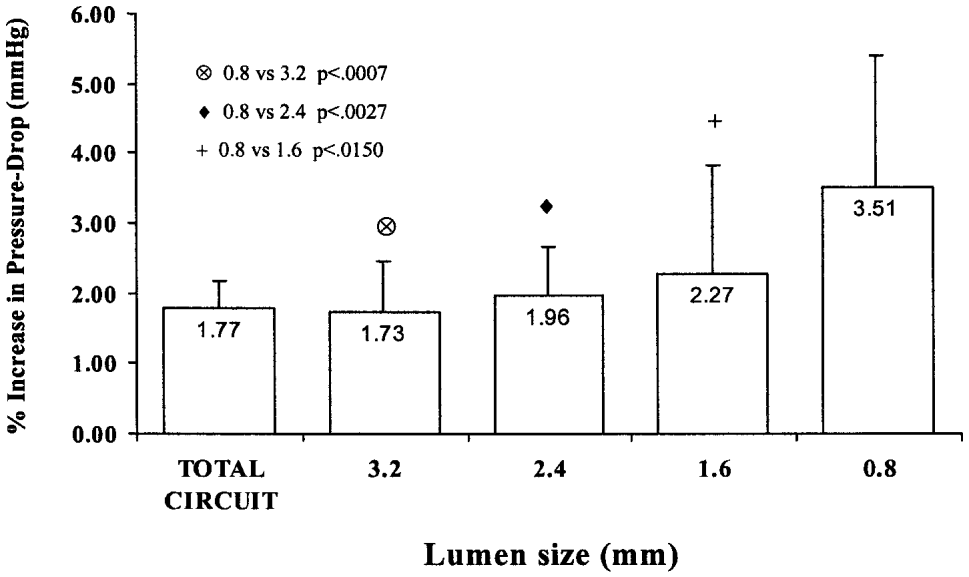

Figure 5. Mean percentage increase in pressure drop across all circuit conduits when temperature is decreased from 37°C to 6°C.

to crystalloid solutions, because of its enhanced oxygen-carrying capacity, limitation of hemodilution, and oncotic, buffering, and antioxidant benefits (10–14). However, concerns over the use of cold blood cardioplegia arise from: the possibility of producing unfavorable shifts in the oxygenation dissociation curve, which inhibit oxygen unloading at the cellular level; the potential of cold agglutinin activation and blood sludging if temperatures under 15°C are used, and the prospect of less effective distribution of blood solution beyond coronary stenoses, as compared to less viscous asanguineous solutions (1,11). In their survey, Robertson et al. determined that 92.6% of all surgeons polled infused their cardioplegia solution at less than 12°C, and 58.6% preferred infusion at less than 6°C (23). Hypothermia decreases flow by inducing direct vasoconstriction and increasing blood viscosity (40). The viscosity of whole blood has been reported to increase approximately 20 to 25% for every 10°C drop in temperature (41). A comparison of the relative changes in viscosity between crystalloid and blood cardioplegia solutions at varying temperatures has been demonstrated by other authors (42,43). In their in vitro investigation of cardioplegia delivery system pressures, Kato et al. determined a negligible difference between delivery line pressures of blood (Hct 20%) and crystalloid solutions across all flow rates tested at 37°C (44). However, at 8°C, delivery line pressure was significantly higher at all flow rates with blood cardioplegia than with crystalloid solution.

In their comparison of regional distribution of blood and crystalloid cardioplegia at similar infusion rates, Robertson et al. showed that blood cardioplegia demonstrated better rheologic properties resulting in improved microvascular flow characteristics, and thus provided better post-stenotic delivery, produced faster arrest and more effective cooling than less viscous crystalloid solutions (45). Robertson demonstrated that the more viscous blood cardioplegia solution resulted in a slower runoff through the unobstructed coronary arteries and produced higher aortic root pressure and better perfusion of the vascular bed beyond the obstructed vessel. Our research is in agreement with theirs because we were unable to show differences in flow distribution with lowering temperatures. This was true despite the increase in viscosity present when temperatures were decreased from 37 to 6°C. However, when infusion pressure was standardized, Landymore and Kinley found no difference in the post-stenotic distribution between blood and crystalloid solutions as correlated to regional myocardial temperature changes (42). We chose to let perfusion pressure vary as a consequence of temperature because control at the vascular level remains a function of lumen size and vasomotor activity. By doing this, we measured significant increases in pressure drop, which were most profound with the smallest lumen size.

Proposed strategies of continuous warm blood cardioplegia and titration delivery of cardioplegic agents during continuous infusion reduce the volume of crystalloid, and thus increases solution viscosity, of the CP solution. Minimally diluting cardioplegic solutions is proposed as an alternative to the standard 4:1 dilution of blood:crystalloid ratios. Despite the large difference in viscosity between blood and asanguineous cardioplegic solutions, we failed to demonstrate a difference in flow distribution. Our study was designed to determine whether viscosity would affect volumetric distribution during administration of cardioplegic solutions. The difference in viscosity between all-blood and crystalloid solutions was striking at 6°C (the temperature of cardioplegia solution during infusion). The

viscosity of the blood solution was 2.5 times greater than the asanguineous solution, but the magnitude of viscosity change had relatively little influence on post-stenotic distribution. However, concerns are raised when one considers using blood-based solutions with more extreme reduction of cardioplegia solution temperature. Although these points may represent reasonable, hypothetical limitations to the homogeneous distribution of blood cardioplegia at very low temperatures, we found that the reduction of the temperature of the blood cardioplegia solution from 37 to 6°C did not demonstrate any significant impairments.

Limitations

Given the complexity of the various biological processes that occur in vivo, it is not possible to design an in vitro model that precisely duplicates how hematocrit and temperature affect viscosity in the microvasculature. Because the conduits used in this extracorporeal circuit lack the permeability and elasticity of the coronary vasculature, direct correlation of the significance of this analysis of CP delivery to in vivo regulation of myocardial coronary perfusion cannot be made. However, these data are valuable and indicate that rheological changes in solution occur and is related to the change in viscosity. Our experiment was designed to test the relative distributions of blood and crystalloid cardioplegia solutions under the most rigid conditions that might exist clinically. First, we made the hematocrit value of the blood cardioplegia solution 38% and reduced the temperature to 6°C to maximize the viscous changes that might occur within the circuit.

The results of this study indicate that reducing blood viscosity may not enhance volume delivery in a simulated setting of moderate coronary arterial stenosis. Further studies are needed to examine these problems to determine a more effective combination of agents and interventions to be used for optimal delivery of cardioplegia to all myocardial regions. A more precise understanding of hemorheology in the presence of stenotic lesions may result in improved strategies to enhance cardioplegia distribution.

REFERENCES

1. Buckberg GD. Strategies and logic of cardioplegia delivery to prevent, avoid, and reverse ischemic and reperfusion damage. J Thorac Cardiovasc Surg. 1987;93:127–39.
2. Lazar HL, Khoury T, Rivers S. Improved distribution of cardioplegia with pressure controlled intermittent coronary sinus occlusion. Ann Thorac Surg. 1988;46:202–7.
3. Becker H, Vinten-Johansen J, Buckberg GD, Follette DM. Critical importance of ensuring cardioplegic delivery with coronary stenoses. J Thorac Cardiovasc Surg. 1981;81:507–15.
4. Grondin CM, Hélias J, Vouhé PR, Robert P. Influence of critical coronary artery stenosis on myocardial protection through cold potassium cardioplegia. J Thorac Cardiovasc Surg. 1981;82:608–15.
5. Hilton CJ, Teubl W, Acker M, et al. Inadequate cardioplegic protection with obstructed coronary arteries. Ann Thorac Surg. 1979; 28:323–32.
6. Murphy CO, Chih P, Gott JP, Guyton RA. Microvascular reactivity after crystalloid, cold blood and warm cardioplegic arrest. Ann Thorac Surg. 1995;60:1021–7.
7. Allen BS, Winkelman JW, Hanafy H, et al. Retrograde cardioplegia does not adequately perfuse the right venticle. J Thorac Cardiovasc Surg. 1995;109:1116–26.
8. Ardehali A, Gates RN, Laks H, et al. The regional capillary distribution of retrograde blood cardioplegia in explanted human hearts. J Thorac Cardiovasc Surg. 1995;109:935–40.
9. Gates RN, Laks H, Drinkwater DC, et al. Gross and microvascular distribution of retrograde cardioplegia in explanted human hearts. Ann Thorac Surg. 1993;56:410–7.
10. Buckberg GD. Update on current techniques of myocardial protection. Ann Thorac Surg. 1995;60:805–14.
11. Axford-Gatley RA, Wilson GJ, Feindel CM. Comparison of blood-based and asanguineous cardioplegic solutions administered at 4°C. J Thorac Cardiovasc Surg. 1990;100:400–9.
12. Vinten-Johansen J, Hammon JW. Myocardial protection during cardiac surgery. In: Gravelee GP, Davis RF, Utley JR, eds. Cardiopulmonary Bypass: Principles and Practice. Baltimore: Williams & Wilkins; 1993;155–206.
13. Singh AK, Farrugia R, Teplitz C, Karlson KE. Electrolyte vs. blood cardioplegia: Randomized clinical and myocardial ultrastructural study. Ann Thorac Surg. 1982;33:218–27.
14. Chen YF, Lin YT. Comparison of blood cardioplegia to electrolyte cardioplegia on the effectiveness of preservation of right atrial myocardium: Mitrochondrial morphometric study. Ann Thorac Surg. 1985;39:134–8.
15. Young DF, Cholvin NR, Roth AC. Pressure drop across artificially induced stenoses in the femoral arteries of dogs. Circ Res. 1975;36: 735.
16. Gould KL. Dynamic coronary stenosis. Am J Cardiol. 1980;45:286.
17. Schlant RC, Walker BF. Anatomy of the heart. In: Alexander RW, Schlant RC, Fuster V, eds. Hurst's The Heart, Arteries, and Veins. New York: McGraw-Hill; 1998;50–51.
18. Certificate of calibration for ASTM kinematic viscometer. Technical Glass Products, Inc., Dover, NJ. 1996.
19. Zaroff J, Aronson S, Lee BK, et al. The relationship between immediate outcome after cardiac surgery, homogeneous cardioplegia delivery, and ejection fraction. Chest. 1994;106:38–45.
20. Landymore R, Colvin S, Isom W, Cullford A. The effect of cardioplegia on myocardial cooling during coronary artery bypass. J Thorac Cardiovasc Surg. 1982;82:832–6.
21. Lazar HL, Roberts AJ. Recent advances in cardiopulmonary bypass and the clinical application of myocardial protection. Surg Clin North Amer. 1985;65:455–69.
22. Parington MT, Acar C, Buckburg GD, et al. Studies of retrograde cardioplegia. I. Capillary blood flow distribution to myocardium supplied by open and occluded arteries. J Thorac Cardiovasc Surg. 1989; 97:605–12.
23. Robinson LA, Schwartz GD, Goddard DB, et al. Myocardial protection for acquired heart disease surgery: Results of a national survey. Ann Thorac Surg. 1995;59:361–72.
24. Duarte IG, Shearer ST, Mac Donald MJ, et al. Myocardial distribution of antegrade cold crystalloid and tepid blood cardioplegia. Ann Thorac Surg. 1998;65:1610–6.
25. Aldea GS, Austin RE, Flynn AE, Coggins DL, Husseini W, Hoffman JIE. Heterogeneous delivery of cardioplegic solution in the absence of coronary artery disease. J Thorac Cardiovasc Surg. 1990;99:345–53.
26. Rao V, Cohen G, Weisel RD, et al. Optimal flow rates for integrated cardioplegia. J Thorac Cardiovasc Surg. 1998;115:226–34.
27. Mitchell BA. Optimal perfusion flow rates for cardiopulmonary bypass. J ExtraCorpor Technol. 1991;22:165–83.
28. Stammers AH. Advances in myocardial protection: The role of mechanical devices in providing cardioprotective strategies. In: Stammers AH, ed. Cardiopulmonary Bypass: Emerging Trends and Continued Practices. Boston: Little, Brown and Company; 1996;61–84.
29. Cokelet GR. A commentary on the 'In vitro viscosity law. Biorheology. 1997;34:363–7.
30. Chien S. Hemorheology in clinical medicine. Clin Hemorheol. 1982; 2:137.

31. Slack SM, Turitto VT. Fluid dynamic and hemorheologioc considerations. Cardiovasc Pathol. 1993;2:11S–21S.
32. King CL. Circulatory mechanics and blood propulsion. In: Stammers AH, ed. Cardiopulmonary Bypass: Emerging Trends and Continued Practices. Boston: Little, Brown and Company; 1996;4–10.
33. Srivastava VP. Particle-fluid suspension model of blood flow through stenotic vessels with applications. Int J Biomed Comput. 1995;38: 141–54.
34. Guyton AC, Hall JE. Overview of circulation: Medical physics of pressure, flow, and resistance. In: Guyton AC, Hall JE, eds. Textbook of Medical Physiology. Philadelphia: WB Saunders; 1996; 167–9.
35. Jandl JH. Physiology of red cells. In: Jandl JH, ed. Blood: Textbook of Hematology. Phildelphia: Library of Congress; 1996;151–2.
36. Barbee JH, Cokelet GR. The Fahraeus effect. Microvasc Res. 1971; 3:6–16.
37. Turitto VT. Blood viscosity, mass transport, and thrombogenesis. Prog Hemost Thromb. 1982;6:139–77.
38. Dormandy JA. Measurement of whole blood viscosity. In: Lowe GDO, Barbenel JC, Forbes CD, eds. Clinical Aspects of Blood Viscosity and Cell Deformability. Berlin: Springer; 1981;67–78.
39. Burch GE, DePasquale NP. Hematocrit, viscosity and coronary blood flow. Dis Chest. 1965;48:225–32.
40. Rand PW, Lacombe E, Hunt HE, Austin WH. Viscosity of normal human blood under normothermic and hypothermic conditions. J Appl Physiol. 1964;19:117–22.
41. Cooper JR, Slogoff S. Hemodilution and priming solutions for cardiopulmonary bypass. In: Gravelee GP, Davis RF, Utley JR, eds. Cardiopulmonary Bypass: Principles and Practice. Baltimore: Williams & Wilkins; 1993;126–8.
42. Landymore RW, Kinley CE. Effects of crystalloid and blood cardioplegic solutions on myocardial cooling during myocardial revascularization. Can J Surg. 1984;27:257–9.
43. Taft KJ, Stammers AH, Jones CC, Dickes MS, Pierce ML, Beck BS. Cardioplegia flow dynamics in an in vitro model. Perfusion. 1998.
44. Kato NS, Buckberg GD, Cushen CK, Whitwam CR. Inaccuracies and variability of indirect pressure measurements during cardioplegia administration. Ann Thorac Surg. 1994;58:1188–91.
45. Robertson J, Buckberg G, Vinten-Johansen J, Leaf JD. Comparison of distribution beyond coronary stenoses of blood and asanguineous cardioplegic solutions. J Thorac Cardiovasc Surg. 1983;86:80–6.
46. Lipowsky HH, Firrell JC. Microvascular hemodynamics during systemic hemodilution and hemoconcentration. Am J Phyiol. 1986;250: H908–22.