

Original Article***Evaluation of a Variable Ratio Cardioplegia System***

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Keywords: myocardial protection, cardioplegia delivery, potassium

ABSTRACT

Gish Biomedical has designed a blood cardioplegia delivery system (MyoManager™) which is purported to provide rapid control of blood and crystalloid solution ratios for myocardial preservation. The present study was designed to evaluate the ability of this device to provide cardioplegia solutions of specific hematocrit and potassium ion concentrations ([K+]).

An in vitro circuit was designed whereby a blood perfusate with a [K+] of 5 mEq/L was mixed with a base crystalloid solution containing 210 mEq/L of K+. Data was collected at several blood to crystalloid ratios (1:1, 4:1, 8:1, 16:1, 25:1), and at four delivery rates (100, 150, 200, 250 ml/min). Predicted and observed values of total cardioplegia volume, hematocrit, crystalloid volume, and [K+] were statistically (ANOVA) analyzed, and statistical significance accepted at $p < 0.05$.

There were no statistically significant differences observed at any flows or ratios in hematocrit. However, at 100 ml/min flow rates, the crystalloid delivery volume difference of 2.4 ± 2.0 ml was significantly higher than that observed at 250 ml/min, 1.5 ± 1.5 ml ($p < 0.02$) and at 200 ml/min flow rates, 1.5 ± 1.6 ml ($p < 0.02$). There was no statistical significance in [K+] difference between flows across all ratios. However, within ratios, a significant difference in [K+] at 100 ml/min, 1:1 blood to crystalloid ratio, was observed ($p < 0.0001$) versus all other ratios and flows. The only statistically significant difference that was shown in total cardioplegia delivery volume was observed between 100 and 200 ml/min ($p < 0.04$) when analyzed across all ratios.

The data suggests that the MyoManager™ effectively provides precise control of [K+] and hematocrit at cardioplegia flows greater than 100 ml/min.

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INTRODUCTION

During cardiopulmonary bypass (CPB) all myocardial protective strategies are directed towards preventing irreversible ischemic and/or reperfusion injury. This is accomplished both mechanically and pharmacologically by decreasing metabolic activity through the arrest of mechanical activity, and the conservation of high energy phosphate stores (1). In doing so, there is a lowered demand for both oxygen and nutrients, with a concomitant reduction in utilization. Since the late 1800's, many different techniques have been attempted to perform this function. In the mid 1950's, administration solutions were formulated that provided immediate arrest through the disruption of ionic gradients across the myocardial sarcolemma (2,3). In 1973, Gay and Ebert re-examined hyperkalemic cardioplegia and formulated a base solution that has served as the foundation of modern day extracellular solutions (4). In the 1970's, Buckberg proposed using blood in cardioplegia solutions to enhance oxygen delivery and improve buffering capacity, reducing overall ischemic injury (5). This process has become widely accepted and is utilized in the majority of open heart procedures today (6).

Controversy continues concerning the optimum myocardial protection technique, with significant debate centered on both temperature issues and on pharmacological preservation solutions. In an attempt to lower myocardial oxygen consumption, decrease energy demand, and reduce myocardial oxygen turnover, and thus decrease the rate of enzymatic activation, cold delivery of cardioplegia (8-9°C) has been widely accepted (7). In an attempt to maintain ultrastructure stability, maintain myocardial oxygen and lactate extraction, decrease conduction disturbances, decrease cellular derangement, and shorten bypass and cross clamp time, normothermic cardioplegia delivery has been proposed (8). Both techniques are currently in use and the benefits of one technique over the other remain to be proven.

During CPB, the potassium concentration ($[K^+]$) needed in cardioplegia solutions may vary dependent upon the point of the operation. A high potassium solution is used to achieve rapid arrest, while a lower potassium solution, designed for multi-dose use during the course of the operation, has been used as a maintenance solution (9), especially during continuous infusion technique. Many different techniques are currently being used to deliver varying $[K^+]$, with most requiring the switch to a low dose solution after the initial high dose has been infused (9). Modern blood delivery cardioplegia circuits mix blood and crystalloid solutions in a fixed ratio, control thermic delivery via a heat exchanger, and deliver the solution under pressure to the coronary circulation (9,10).

The increase in concern with myocardial manage-

ment during extracorporeal circulation has brought about a need for technology to augment the accuracy of delivery of cardioplegia to assure that cardiac protection is adequately achieved. One manufacturer has recently introduced a microprocessor controlled instrument (MyoManager™)^a to accomplish this task by integrating the control of crystalloid/blood ratios in a single set. The present study was designed to quantitatively assess, in an *in vitro* setting, the efficacy of the MyoManager™ (MM) to deliver varying ratios of blood and crystalloid volumes.

MATERIALS AND METHODS

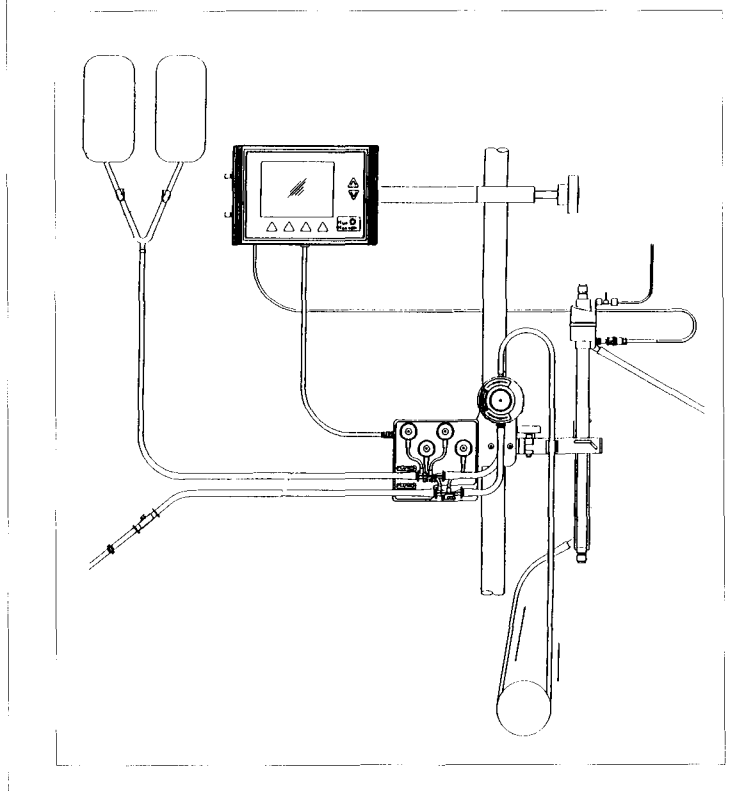
DEVICE DESCRIPTION

The device is a variable rate cardioplegia delivery system that enables the user to alter the ratio of blood to crystalloid solutions from 1:1 to 50:1, and also provide delivery of either all blood or all crystalloid. The device operates on a single-line system with mixing of blood and crystalloid solutions occurring proximal to a roller pump, via a variable ratio rheostat. The cardioplegic mixture is then pumped to an aluminum heat exchanger with bubble chamber, and is passed through an integrated 160 micron filter before being delivered to the patient.

SOLUTION AND BLOOD PREPARATION

A high potassium solution was prepared by adding 210 mEq of KCl to a 1000 ml of 0.9% sodium chloride. This quantity

Figure 1: MyoManager™ Schematic



a Myomanager, Gish Biomedical, Irvine, CA

was chosen to coincide with a clinical blood cardioplegia ratio of 8:1 (blood to crystalloid) with an end-delivery $[K^+]$ of 28 mEq/L. Expired human blood, received from the American Red Cross, was processed with a cell washing device^b to produce a packed red cell mass with a mean $[K^+]$ of approximately 5 mEq/L. The starting hematocrit was set at 25 ± 2% by the addition of a balanced electrolyte solution.

CIRCUIT PREPARATION

A test circuit was constructed according to the manufacturer's recommendations (Figure 1). The circuit was modified to allow precise measurements of both blood and crystalloid cardioplegia solution. The circuit was primed with a balanced electrolyte solution and thoroughly debubbled (total priming volume of 180 ml). A 2500 ml reservoir was positioned 30 cm above the variable rate rheostat of the cardioplegia circuit, and a heater-cooler maintained a temperature of 38°C. Blood flow was created by a twin roller pump^c set to 100% occlusion. It is important to note that the MM was designed to work with a positive pressure created from the arterial pump. Back pressure was created by applying a Hoffman clamp to the distal portion of the infusion line to mimic pressure resistance caused by cardioplegia catheters and coronary artery resistance.

INITIATION OF TRIALS

The procedure was devised to evaluate the ratios of blood to crystalloid at 1:1, 4:1, 8:1, 16:1, and 25:1, and flow rates of 100, 150, 200, and 250 ml/min. Before the initiation of each change of ratio the circuit was rinsed with 200 ml at the desired ratio. This was done to ensure the system was voided of the residual effects of previous trials or priming. At the desired flow rate and ratio, approximately 100 ml of total volume of cardioplegia was measured with a graduated cylinder. At the completion of each trial the volume displacement of cardioplegia was measured. The crystalloid measurement was then compared to the readings indicated on the visual display to assess accuracy. The difference in the volumes of the cylinders was determined and used to ascertain that the selected ratios at the given flow rates were met.

DATA COLLECTION

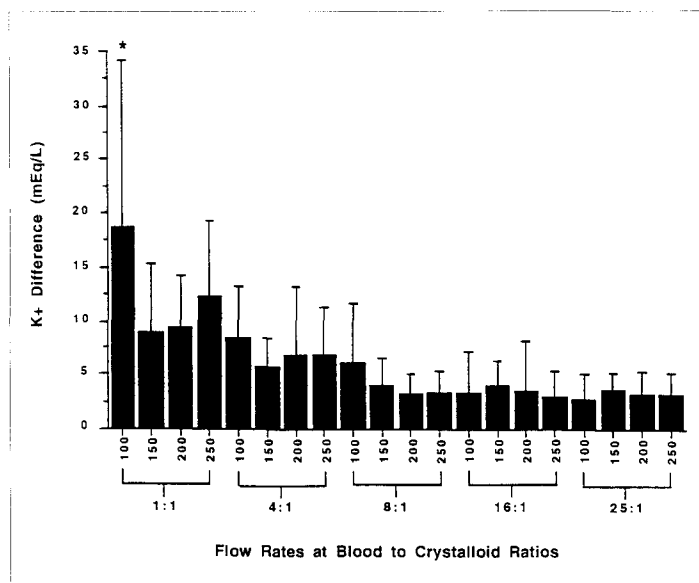
As a secondary assessment that the set ratios were obtained, the hematocrit and $[K^+]$ of each sample were measured and compared to values calculated. Hematocrits were taken at each

Table 1: Crystalloid difference from expected delivery volume

	100 ml	150 ml	200 ml	250 ml
1:1	3.25 ± 2.1	3.1 ± 2.2	2.5 ± 2.6	2.8 ± 2.3
4:1	2.5 ± 1.4	2.0 ± 1.5	2.1 ± 1.5	1.8 ± 1.3 ^f
8:1	3.4 ± 2.8	1.5 ± 1.4 ^{a,b,f}	1.4 ± 1.4 ^{a,b,f}	1.6 ± 1.1 ^{a,f}
16:1	2.0 ± 1.7	1.5 ± 0.9 ^{a,b,f}	0.9 ± 0.6 ^{a,b,c,d,e,f}	0.9 ± 0.6 ^{a,b,c,d,e,f}
25:1	1.0 ± 0 ^{a,b,d,f}	0.8 ± 0.9 ^{a,b,c,d,e,f}	0.6 ± 0.5 ^{a,b,c,d,e,f}	0.8 ± 0.7 ^{a,b,c,d,e,f}

a = p < 0.04 vs. 100 ml/min 1:1; b = p < 0.04 vs. 150 ml/min 1:1; c = p < 0.04 vs. 200 ml/min 1:1; d = p < 0.03 vs. 250 ml/min 1:1; e = p < 0.04 vs. 100 ml/min 4:1; f = p < 0.04 vs. 100 ml/min 8:1

Figure 2: Potassium deviation from expected values. * = p < 0.0001 vs. all other ratios across all flows



sample and determined in duplicate on a calibrated centrifuge. After four minutes of spinning at 10,200 RPM, the tubes were removed from the centrifuge and hematocrit levels were measured. Prior to centrifugation, 3 ml of blood were placed into a vacuum tube and analyzed for $[K^+]$ ^d. All data was loaded onto a personal computer in spreadsheet format. Differences were then analyzed with one way and two way ANOVA with a commercially prepared statistics program^e. Statistical significance was accepted at the p 0.05 level. All data were expressed as mean ± standard deviation of the mean.

RESULTS

The hematocrit difference between calculated and observed values was found not to be statistically significant. The difference in the measured crystalloid delivery and the observed readings was found to be statistically significant at the 100 ml/min level compared to both 200 ml/min and 250 ml/min (p < 0.01).

b Cell Saver 3, Haemonetics Corporation, Braintree, MA
 c Stockert, Sorin Biomedical, Irvine, CA
 d Ectokam, Kodak, Rochester, NY
 e Super Anova, Abacus, Berkley, CA

Figure 3: Potassium difference at 100 ml/min flow. * = p< 0.01 vs 1:1

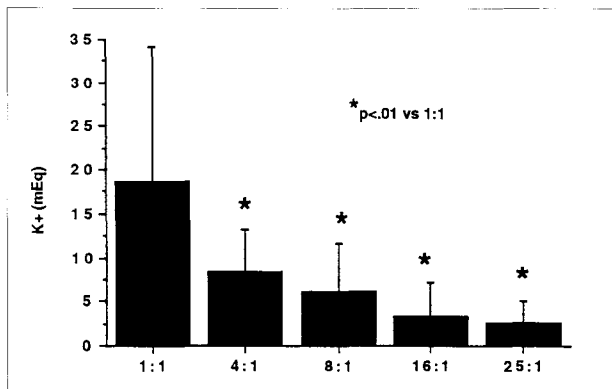


Figure 4: Potassium difference at 150 ml/min flow. * = p< 0.005 vs 1:1

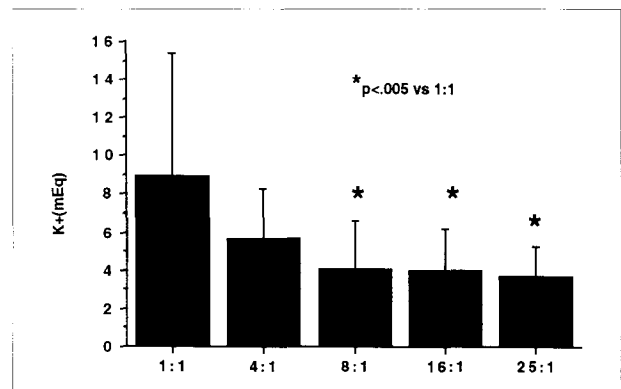


Figure 5: Potassium difference at 200 ml/min flow. * = p< 0.01 vs 1:1

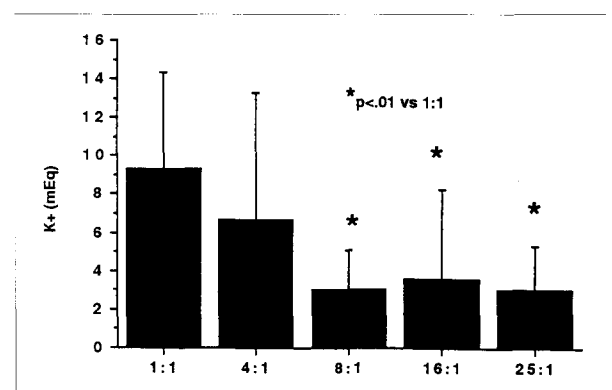
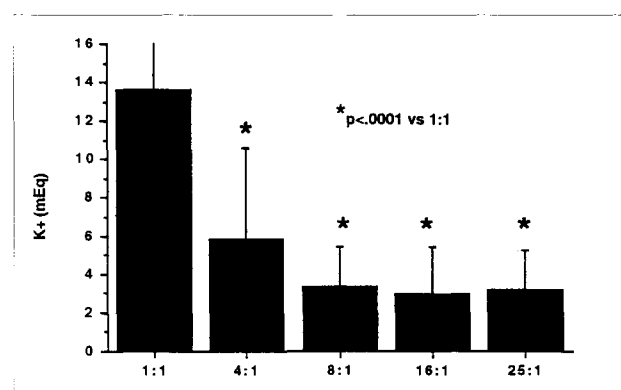


Figure 6: Potassium difference at 250 ml/min flow. * = p< 0.0001 vs 1:1



At low blood to crystalloid ratios, specifically at reduced flow rates, we observed a decrease in accuracy of the MM reported delivery of crystalloid (Table 1).

Differences between measured and calculated [K⁺] were shown not to be significant between flows, across all ratios, when analyzing the data within flow rates. However, a greater difference was seen at lower flows and lower blood to crystalloid ratios; specifically at 100 ml/min and a ratio of 1:1 (p=0.0001) vs. all other ratios across all flows (Figure 2).

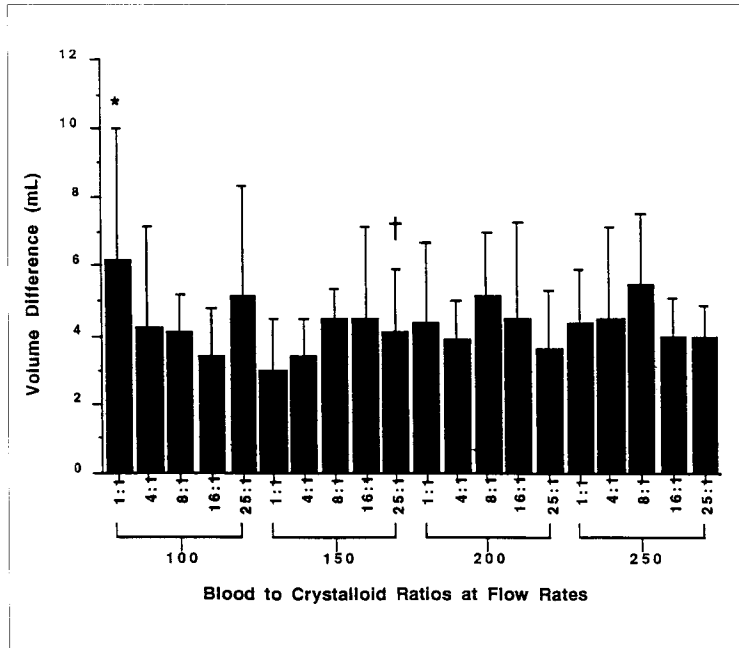
Further evaluation of the [K⁺] showed that as flow rate increased, the accuracy of potassium delivery also increased with significance (p 0.01) seen when comparing 1:1 ratios to all others (Figures 3-6).

Total cardioplegia delivery volume reported by the MM were compared to those observed experimentally; a significant difference (p<0.03) was observed between 100 ml/min and 200 ml/min across all ratios. A range in difference of 3-6 ml was seen at all flows across all ratios (Figure 7).

DISCUSSION

The earliest methods of cardioplegia delivery consisted of infusions of pharmacological solutions directly into the aortic root, coronary sinus, or left ventricle, via hand held syringes (11). Unfortunately, such methods caused a nonhomogeneous distribution of solution, and led to the need for more precise and controlled delivery techniques that assured uniform distribution. Many clinicians switched to a pressurized bag method in which a bag of crystalloid solution was placed in a pressure infusion wrap, and cardioplegia was infused at a semi-controlled rate, dependent upon the degree of pressure and the bore of the cardioplegic needle (12,13). Although the results were better than previous methods, it was evident that such systems suffered from a lack of safety features that included inaccurate or unknown flow delivery rates, absent pressure monitoring and control systems, perfunctory air handling capacity, dependence primarily upon sanguineous solutions, and a lack of temperature control.

Figure 7: Difference in total cardioplegia delivery. * = p 0.05 vs. 250 ml/min 1:1; 150 ml/min 4:1, 200 ml/min 4:1; 200 ml/min 16:1. † = p 0.05 vs. 150 ml/min 4:1



Vertrees et al described a simple circuit that utilized a coronary perfusion reservoir, a coil submerged in iced water and a roller pump (14). The system was a significant improvement over the pressurized bag technique, as it included a means to trap air and to measure pressure within the circuit. The roller pump produced faster cooling and resulted in significantly higher aortic perfusion pressures which provided better distribution of cardioplegia in the presence of critical coronary stenosis (15).

Despite the significant improvements in cardioplegic delivery systems, inadequate myocardial protection is still a primary factor influencing post-cardiotomy mechanical failure resulting from perioperative myocardial ischemic, hypoxic, or reperfusion injury (16). It is clear that the need exists for a more precise control of cardioplegia to assure that adequate myocardial protection is achieved. Although the optimum reperfusion strategy has yet to be elucidated, cardioplegia delivery devices that can rapidly modify the reperfusate composition and hemodynamic delivery conditions are needed. New generations of cardioplegia delivery devices that improve myocardial protection need to incorporate the following: a more regulated hemodynamic control of delivery flow and pressure, accurate and precise delivery of chemicals and nutrients with immediate ability to regulate delivery concentration, varying delivery of blood to crystalloid ratio, and enhanced safety. The availability of such devices is imperative since patient conditions during cardiac surgery are dynamic and mandate rapid intervention.

Effective myocardial protection is assured only through the precise interface of both disposable and non-disposable compo-

nents of the cardioplegia delivery system, which function *in toto* to assure safe, precise and accurate administration of cardioplegic solutions. The MM was designed to accurately deliver set ratios of blood to crystalloid solutions. The device is an in line point-in-time analyzer with approximately a three second lag from actual values to displayed. In order to evaluate the device's ability to accurately deliver set ratios of blood to crystalloid, end point samples were analyzed and hematocrits obtained. These values were compared to those calculated and their differences obtained. Statistical analysis showed no significance between experimental and calculated values.

In the analysis of the device's ability to accurately deliver end-crystalloid volumes at various flows and ratios, MM reported crystalloid volume delivery was compared to that obtained experimentally. The differences between the two were analyzed and were found to be significant at lower flow rates and low ratios. This also agrees with the data obtained from analysis of end-delivery differences in [K⁺]. Potassium concentrations were obtained on blood samples taken from end-cardioplegia delivery volumes at all ratios and across all flows. The concentrations were compared to calculated values and their differences analyzed. The results showed significant differences at lower flow rates and low ratios. This may be explained by the data obtained from the end-crystalloid delivery analysis. The data illustrated that the observed crystalloid delivery was lower than that reported on the display of the MM, and may have resulted in the lower potassium values observed at lower flow rates and ratios.

Finally, upon evaluation of the device's ability to report end-cardioplegia delivery volumes, statistical analysis of the system's reading and those obtained experimentally were compared. Although we found a significant difference between 100 ml/min and 200 ml/min across all ratios, the range of differences was only 3 to 6 ml, with a deviation of only 3 ml.

In conclusion, we found the MyoManager™ to be accurate and effective in delivering desired ratios at flow rates of 150 ml/min or higher. It should be noted that the *in vitro* circuit we designed was passive in that it delivered blood and crystalloid to the pump by gravity. The system was designed to have blood delivered to flow cells at much higher pressures than used in this study.

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