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## Consistent Two to Four Degree Crystalloid Potassium Cardioplegia

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### Abstract

The use of hypothermic crystalloid potassium cardioplegia in open heart surgery has been shown to be effective in arresting the heart and protecting it from ischemic injury during aortic crossclamping. A perfusion technique for the routine delivery of 2–4° centigrade (C) crystalloid potassium cardioplegia has been employed in 116 consecutive coronary artery bypass graft procedures between October 1980 and October 1981. The cardioplegic solution is infused with a low flow roller pump through a polyvinyl chloride tubing coil immersed in an ice bath which serves as the cooling device and a Sarns pediatric bubble trap. The planned initial dose of cardioplegia is 450 ml/m<sup>2</sup> body surface area. With the initial cardioplegia infusion, the mean myocardial temperature was lowered to 14.4 ± 0.4°C (S.E.). Myocardial temperature is maintained at less than 20°C at all times. A total of 2524 ± 73 ml of cardioplegia was administered for each patient with a mean crossclamp time of 83.6 ± 2.2 minutes and a total bypass time of 156 ± 3.6 minutes.

CPK-MB and SGOT values were minimally elevated in the immediate postoperative period, but returned to normal on the second and third postoperative day respectively. Two patients in the study group died with an operative mortality of 1.7 percent. The cardioplegia infusion system we have

employed assured the delivery of crystalloid potassium cardioplegia to the myocardium at 2–4°C, provided continuous profound myocardial hypothermia, and resulted in good myocardial protection as determined by clinical variables followed postoperatively.

### Introduction

The aim of cardioplegic arrest during aortic crossclamping is the intraoperative protection against myocardial damage with the preservation of the structure and function of the myocardium. The controversy surrounding what cardioplegic solution and which ingredients provide optimal protection has yet to be resolved. However, the cardioplegic method should combine the three basic mechanisms of myocardial protection that include: a) the conservation of intracellular energy stores by the induction of rapid diastolic arrest, b) a slowing of the metabolic processes through the use of hypothermia and c) the prevention and reversal of unfavorable ischemic changes<sup>1</sup>. Hypothermic crystalloid potassium cardioplegia is currently the most widely used method of myocardial preservation during open heart surgery and has been shown to be effective in arresting the heart and protecting it from ischemic injury<sup>2–6</sup>. Though the safe period of myocardial ischemia is not known, some have safely used hypothermic potassium cardioplegia for prolonged crossclamp times of up to three hours<sup>7</sup>.

The use of multidose cardioplegic infusion with controlled infusion pressure and flow is considered the best available method of myocardial pre-

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ervation since it allows for the maintenance of profound myocardial cooling, continuous electromechanical arrest, and the washout of metabolic end products<sup>8-10</sup>. Since clinical and experimental evidence indicate that optimal protection occurs when the myocardial temperature is maintained as low as is feasible<sup>11,12</sup>, our cardioplegic delivery system was designed to provide maximally cooled solution that can be infused in a totally controlled manner. The present study evaluated the efficacy of this method by which crystalloid potassium cardioplegia at 2-4° is used to induce arrest in a consecutive series of patients undergoing coronary artery bypass graft surgery.

## Materials and Methods

One hundred and sixteen consecutive coronary artery bypass graft procedures between October 1980 and October 1981 were evaluated using a perfusion technique for the routine delivery of 2-4° crystalloid potassium cardioplegia. The cardioplegia solution contains 25 mEq/L of potassium adjusted to pH 7.8 and is hyperosmolar (See Figure 1). The planned initial dose of cardioplegia is 450 ml/m<sup>2</sup>. The cardioplegic solution was stored in a reservoir<sup>a</sup> and administered with a low flow roller pump<sup>b</sup> through a polyvinyl chloride tubing coil<sup>c</sup> (See Figure 2). The tubing coil is 3/16 inch internal diameter (I.D.) by 1/4 inch outer diameter (O.D.),

300 inches in length, and is immersed in an ice slush containing rock salt. The solution is then pumped through a pediatric bubble trap<sup>d</sup> at a controlled pressure not to exceed 80 mmHg in the aortic root. A 1/4 inch Y tubing connector distal to the bubble trap permits either cardioplegia infusion or recirculation. Temperature and pressure of the infused arrest solution are monitored at the bubble trap with a thermistor probe and an aneroid manometer. The cardioplegic solution is constantly recirculated when not being infused and is exposed to an oxygen atmosphere. Filtered oxygen is introduced at the top of the cardioplegia reservoir permitting the recirculating arrest solution to pass in close proximity to the oxygen source. This effectively raises the pO<sub>2</sub> of the cardioplegia to over 500 torr.

Cardiopulmonary bypass (CPB) is established at 34°C and the heart is kept beating and ejecting until the aorta is crossclamped. A partial occlusion clamp is placed on the ascending aorta and the proximal saphenous vein anastomoses are completed. The partial occlusion clamp is then removed and a 9 French aortic root cannula<sup>e</sup> is inserted in the ascending aorta for the infusion of the cardioplegic solution and for the subsequent venting of the heart (See Figure 3). A parallel Y-adaptor<sup>f</sup> specifically fitted for use with the aortic root cannula permits the attachment of 1/4 inch I.D. tubing. One arm of the Y adaptor is attached to the tubing originating from the bubble trap and the other arm serves as the vent return. Integral clamps on the Y-adaptor mark the direction of flow and facilitate connection of the cardioplegia and vent lines. Vented blood terminates at a 3/8 × 3/8 × 1/4 inch Y-connector approximately 8 to 10 inches below the cardiotomy reservoir<sup>g</sup> that is placed level with the operating table. A tubing clamp is placed below the Y-connector of the vent inlet. With the tip of the Y-adaptor occluded, the cardioplegia/vent circuit is then flushed with the cardioplegic solution to free the lines of air and establish a fluid filled column to the cardiotomy. Once the aorta is crossclamped and the heart is arrested, the vent may be opened if needed. The fluid filled column to the cardiotomy permits con-

### POTASSIUM CARDIOPLEGIA-CONTENTS AND CHARACTERISTICS

SODIUM	137 mEq/L
POTASSIUM	25 mEq/L
MAGNESIUM	6 mEq/L
CHLORIDE	101 mEq/L
ACETATE	26 mEq/L
GLUCONATE	23 mEq/L
CALCIUM	1.35 mEq/L
DEXTROSE	5 g/L
pH	7.8
mOsm	330
TEMPERATURE	2-4°C

FIGURE 1. Potassium Cardioplegia—Contents and Characteristics.

<sup>a</sup> Model 5M1470 cardiotomy reservoir, Travenol Laboratories, Deerfield, Ill. 60015.

<sup>b</sup> Model 5000 Heart-Lung machine console, Sarns, Ann Arbor, Mich. 48103

<sup>c</sup> Cobe Laboratories, Lakewood, Co. 80215

<sup>d</sup> Model 6301, Sarns, Ann Arbor, Mich. 48103

<sup>e</sup> Model 10012, DLP Inc., Walker, Mich. 49504

<sup>f</sup> Model 10003, DLP Inc., Walker, Mich. 49504

<sup>g</sup> Model Q2204, Bentley Laboratories, Inc., Irvine, Ca. 92714

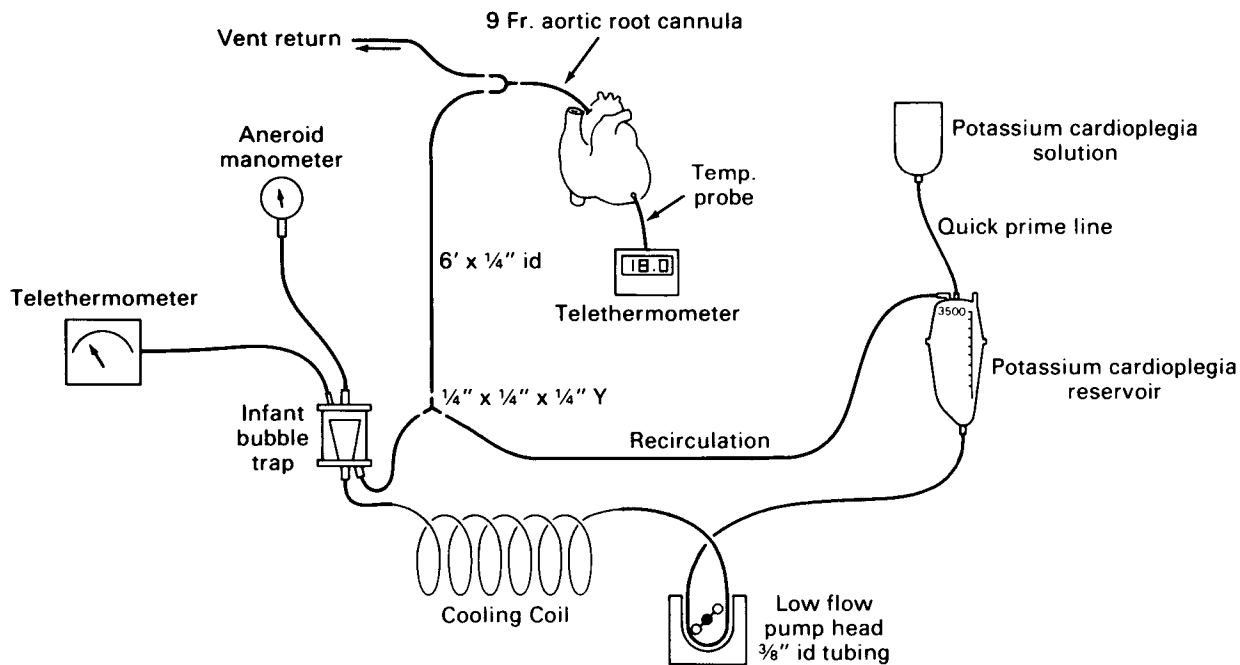


FIGURE 2. Cardioplegia Delivery System.

trolled siphon drainage and prevents the retrograde aspiration of air into the opened coronary arteries during the distal anastomoses of a non-occlusive proximal lesion or from the vent aortotomy. Topical cooling was frequently used in conjunction with aortic root infusion of the potassium arrest solution to enhance myocardial cooling. After the distal anastomoses are completed, the aortic root cannula is removed prior to removing the aortic crossclamp and the patient is systemically rewarmed. A needle thermistor<sup>h</sup> placed in the anterior septum provides a continual digital readout of the myocardial temperature during the crossclamp period. The myocardium is maintained below 20°C at all times. After the crossclamp was removed, most patients' hearts began beating spontaneously. Those in ventricular fibrillation were immediately defibrillated with a 5 to 10 watt-second shock.

All patients were oxygenated with a bubble oxygenator<sup>i</sup> primed with 4.7% albumin in a bal-

anced electrolyte solution containing 20–25 grams of dextrose. Flow rates during CPB ranged from 2.2 L/min/m<sup>2</sup> at 37°C to 1.6 L/min/m<sup>2</sup> at 24°C. A 21 or 24 French straight aortic cannula<sup>j</sup> was inserted in the ascending aorta and the right atrium was cannulated with a 46–34 French two-stage venous cannula<sup>k</sup>.

All serum enzyme determinations were made on an Abbott VP bichromatic analyzer<sup>l</sup>. The creatine phosphokinase-MB (CPK-MB) isoenzyme was measured by the method of immunoinhibition<sup>13</sup> and checked with the electrophoresis method<sup>m</sup> to insure accuracy. The normal value at our institution for CPK-MB is less than 20 (IU/L) or less than 6% of the total CPK. Normal value for the total CPK is 33–194 IU/L and for the serum glutamic-oxaloacetic transaminase (SGOT) is 13–38 IU/L. Only those patients with complete sets of values

<sup>h</sup> Model NTM100, Wilton Webster Laboratories, Altedena, Ca. 91001

<sup>i</sup> Model 422-21, Cobe Laboratories, Lakewood Co. 80215

<sup>j</sup> Model 8888-591073, 591099, Sherwood Medical Products, St. Louis, Mo. 63103

<sup>k</sup> Model 8274, USC Div. C. R. Bard, Santa Ana, Ca. 92705

<sup>l</sup> Abbott Laboratories, Pasadena, Ca. 91030

<sup>m</sup> Helena CPK-US electrophoresis procedure, Helena Laboratories, Beaumont, TX 77704

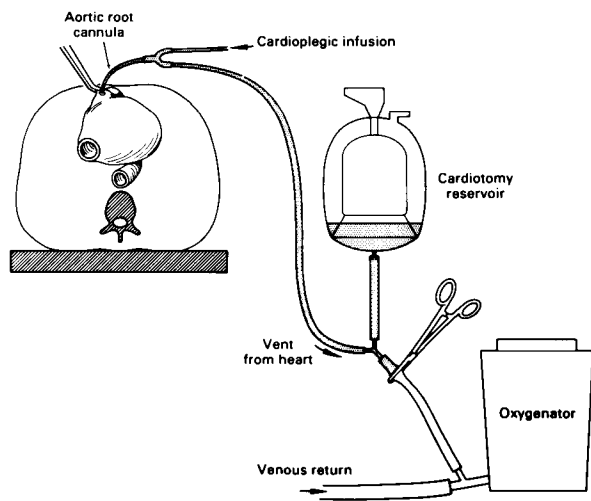


FIGURE 3. Aortic Root Vent Technique.

for each specific serum enzyme were analyzed for this study.

### Patient Profile

A mean of just over 4 vessels were grafted per patient with a range of 1–7 anastomoses per patient (See Table 1). There were 71 males (61%) and 45 females (39%) in the group. The mean age was 56 years and the mean body surface area was 1.86 m<sup>2</sup>. The mean total dose of cardioplegia administered per patient was 2524 cc with a mean aortic crossclamp time of 83.6 minutes and a total bypass time of 156.6 minutes.

TABLE 1  
Patient Profile

Parameter	Mean ± SE ± SD			Range
Age	55	0.9	9.2	34–71
Height (cm.)	169	0.9	9.4	150–196
Weight (kg.)	76	1.4	15.4	46–135
BSA (m <sup>2</sup> )	1.86	0.02	.20	1.42–2.48
Vessels Grafted	4.2	0.1	1.3	1–7
Total CPB Time (min)	156.6	3.6	38.6	61–292
Total Aortic Cross Clamp Time (min)	83.6	2.2	23.9	24–139
Total Cardioplegia Infused (cc)	2524	73	786	800–6000

### Results

Potassium cardioplegia dose, time of infusion on CPB, and myocardial temperature were recorded for the initial and three subsequent (cooling) infusions (See Table 2). The mean initial infusion dose of 848 cc (456 cc/m<sup>2</sup>) of cardioplegia dropped the mean myocardial temperature from 34°C to 14.4°C. The mean time between the first and second infusion of cardioplegia was 23 minutes. All subsequent infusions of cardioplegia were approximately one half of the initial arresting dose. By the Pierson correlation coefficient, there was a positive correlation between the initial myocardial temperature and the initial volume of potassium cardioplegia infused ( $r = 0.49$ ,  $P < 0.05$ ).

Blood for the determination of CPK-MB and CPK were drawn upon admission to the intensive care unit (ICU), at 6–8 hours postoperatively, 12 hours postoperatively, and on the second postoperative day (See Figures 4 and 5). Of 116 patients, 64 had completed CPK-MB isoenzyme and 68 total CPK values. The mean CPK-MB upon admission to the ICU was 23 IU/L and peak values occurred at 6–8 hours after surgery increasing to 25 IU/L. Thereafter, the CPK-MB decreased and was 14 IU/L by the second postoperative day. Of these 64 patients, 7 patients had moderate CPK-MB isoenzyme elevations (CPK-MB 20–50 IU/L) and 1 patient exhibited a severe elevation (CPK-MB > 50 IU/L) on the second postoperative day. There was no correlation between the peak CPK-MB at 6–8 hours postoperatively and the aortic crossclamp time. The total CPK showed a similar pattern of elevation and decrease. However, the peak total CPK occurred 12 hours after surgery increasing to 652 IU/L and decreasing on the second postoperative day to 588 IU/L. The SGOT was measured upon admission to the ICU, 12 hours postoperatively and 24 hours thereafter on postoperative day 2 and 3 respectively (See Figure 6). In this group, 63 of 116 patients had completed SGOT determinations. The mean SGOT upon admission to the ICU was 37 IU/L. This value peaked at 12 hours after surgery increasing to 50 IU/L. Decreases were observed thereafter and returned to normal by the third postoperative day.

The serum potassium and blood glucose were measured routinely throughout the intraoperative

TABLE 2  
Hypothermic Potassium Cardioplegia Data

	Volume (cc)			Temperature (°C)			Time between Infusion (min)		
	Mean	SE	SD	Mean	SE	SD	Mean	SE	SD
Initial Infusion	848	21	224	14.4	0.4	4.6	23.4	1.2	12.4
Second Infusion	375	14	155	14.6	0.3	3.6	20.5	1.2	12.2
Third Infusion	381	15	159	13.8	0.3	3.4	21.0	1.4	13.3
Fourth Infusion	382	19	177	13.4	0.4	3.0			

period (See Figures 7 and 8). There was a significant difference between the pre CPB and post CPB values ( $P < 0.05$ ) for both the serum potassium and blood glucose. Prior to CPB the mean serum potassium was 4.0 mEq/L and this increased to 4.3 mEq/L after CPB. Serum potassium levels during CPB were observed to increase with the length of the procedure. Blood glucose levels (See Figure 8) remained mildly elevated throughout the intraoperative period and were highest on bypass prior to aortic crossclamping and cardioplegia infusion. This was expected because of the 20–25 grams of dextrose used in the prime and the additional 5 grams per liter in the cardioplegic solution.

The mean urine output recorded on CPB was 883 cc. The creatinine and blood urea nitrogen (BUN) on the second postoperative day were decreased from the preoperative values (See Table 3). The creatinine was 1.2 mg/dl preoperatively and decreased to 1.0 mg/dl on the second postoperative day. The BUN also showed a corre-

sponding decrease from the preoperative value of 17 mg/dl to 12 mg/dl on the second postoperative day. The hematocrit and hemoglobin measured prior to CPB were 34% and 11.6 g/dl respectively, and these were decreased as expected because of hemodilution to 21% and 7.2 g/dl upon the completion of CPB (See Table 4). Postoperatively, 10 patients (9%) required pharmacologic support with catecholamines and 6 of these patients (5%) also required the intra-aortic balloon pump for temporary cardiac support after bypass. Of the total group, 93 patients (81%) received sodium nitroprusside for the treatment of systemic hypertension. There were 2 deaths in the group for a mortality of 1.7%. One woman died after failing to be weaned from bypass and one man died a day prior to discharge due to arrhythmias.

## Discussion

The use of hypothermic crystalloid potassium cardioplegia has been shown to be effective in re-

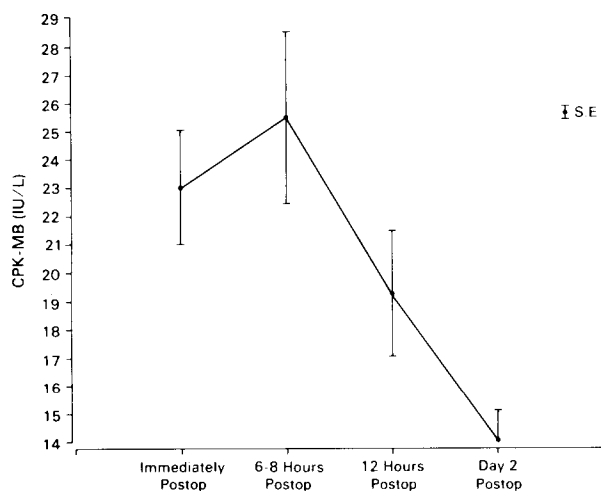


FIGURE 4. The Postoperative CPK-MB.

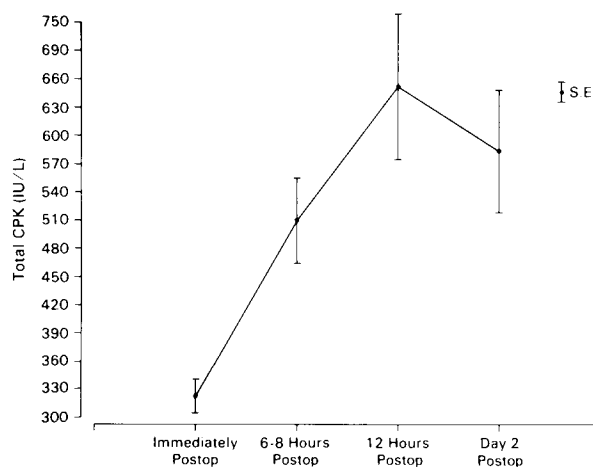


FIGURE 5. The Postoperative Total CPK.

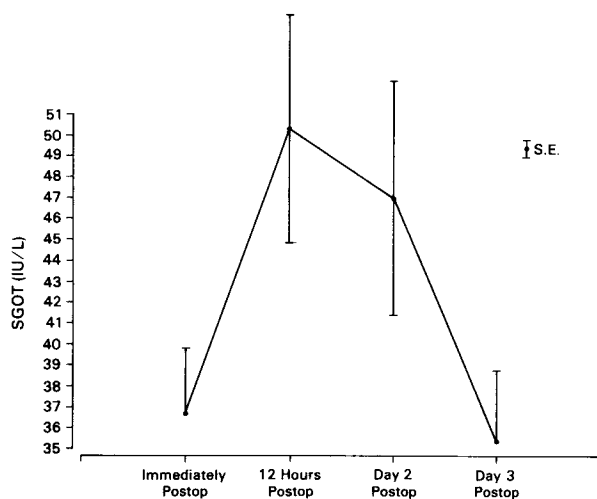


FIGURE 6. The Postoperative SGOT.

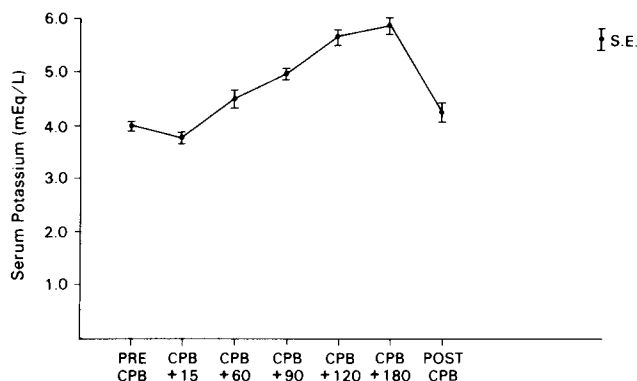


FIGURE 7. The Intraoperative Serum Potassium.

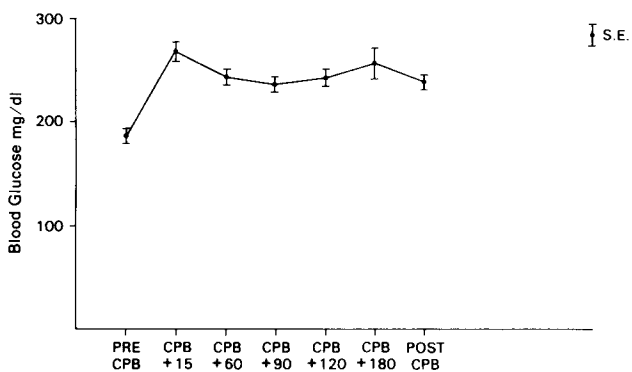


FIGURE 8. The Intraoperative Blood Glucose.

TABLE 3  
Creatinine and BUN Preoperatively  
and on Postoperative Day 2

	Preoperative			Postoperative		
	Mean	SE	SD	Mean	SE	SD
Creatinine (mg/dl)	1.2	0.06	0.6	1.0	0.06	0.7
BUN (mg/dl)	17	0.8	8.2	12	0.8	8.2

ducing ischemic injury and allows the technical advantage of performing delicate coronary artery bypass grafting on a flaccid non-beating heart.

Manley and co-workers<sup>14</sup> were the first to report the use of a low flow roller pump to administer potassium cardioplegia. The use of a low flow roller pump in conjunction with a heat exchange device or disposable coil to cool and recirculate the cardioplegic solution is currently used by many centers<sup>11,14-17</sup>. The ability to consistently cool the arresting solution and deliver it with the precise control of flow and pressure are major advantages with this technique of cardioplegia administration.

Clinical evidence indicates that the temperature and the infusion pressure at which the cardioplegia is delivered are important considerations in myocardial preservation<sup>17,18</sup>. The infusion of cardioplegia at a temperature of 4°C or less has been shown to be most effective in bringing on diastolic arrest and preserving the myocardium<sup>19,20</sup>. This allows the reduction in myocardial metabolism as well as the preservation of high energy phosphate levels. Some researchers have held that the optimal myocardial temperature is in the range of 10-15°C<sup>21</sup>, but recent evidence indicates that the colder one can keep the myocardium, the better myocardial preservation will be<sup>22</sup>. In order to achieve maximal myocardial cooling, the crystalloid cardioplegia must be delivered to the myocar-

TABLE 4  
Hematocrit and Hemoglobin before and  
after Cardiopulmonary Bypass (CPB)

	Before CPB			After CPB		
	Mean	SE	SD	Mean	SE	SD
Hematocrit (%)	34	0.5	5.5	21	0.3	2.6
Hemoglobin (g/dl)	11.6	0.2	1.9	7.2	0.1	1.0

TABLE 5  
Postoperative Treatment

	No.	Percent
Vasopressor	10	9
IABP	6	5
Sodium Nitroprusside	93	81

dium at as close to 0°C as possible. This is effectively achieved by our cardioplegia delivery system.

One of the occasional bothersome problems with the infusion of large volumes of potassium cardioplegia is hyperkalemia and the resultant delay in restoring the normal cardiac rhythm on reperfusion. This sometimes prompted the use of glucose and insulin or diuretics to lower the serum potassium level. However, we have not found it to be a significant problem as the serum potassium levels returned to normal by the end of CPB.

The CPK-MB isoenzyme is considered to be a sensitive indicator of myocardial damage<sup>23-25</sup>. Elevations in CPK-MB after cardiac surgery are well documented with the peak activity occurring approximately 6-12 hours after the release of the aortic crossclamp<sup>11,26</sup>. The transient small elevations in CPK-MB after cardiac surgery may be due to cardiac manipulation and/or electrical defibrillation<sup>26</sup>. The absolute value of the CPK-MB as well as the length of time it remains elevated are important in determining the extent of myocardial injury. After cardiac surgery, the CPK-MB reaches its peak value rapidly, but should decrease within 24-48 hours after surgery unless there has been an acute myocardial infarction<sup>24</sup>. The CPK-MB in conjunction with electrocardiographic (ECG) changes has proved useful in diagnosing acute myocardial infarction. However, in the absence of ECG changes, if the CPK-MB activity is greater than 6% of the total CPK, myocardial infarction or injury is highly probable<sup>27</sup>.

In the present study, the CPK-MB was measured by the immunoinhibition method. This technique employs the use of an antibody to the CPK-M monomer and completely inhibits CPK-MM which is the predominant isoenzyme of CPK. This does not, however, affect the B subunit activity and allows for the complete and accurate determination of the MB fraction of CPK. Because of the increased detection accuracy of the

CPK-MB isoenzyme by the immunoinhibition assay, the normal values for the CPK-MB activity are higher when compared to other methods of measurement such as electrophoresis. Hence, it is difficult to compare values from the present study with those employing other techniques for the measurement of CPK-MB. In the present study, the CPK-MB activity was minimally elevated 6-8 hours postoperatively, but returned to normal by the second postoperative day. Likewise, the SGOT showed a corresponding rise and fall similar to that of the CPK-MB isoenzyme.

Clinical evidence in the postoperative period supports the effectiveness of this technique of myocardial protection. Only a small group of patients required catecholamines or the intra-aortic balloon pump for hemodynamic support postoperatively, and results from the present study compare favorably with those using similar techniques of myocardial preservation<sup>7,15,17,28</sup>. In conclusion, the use of 2-4°C crystalloid potassium cardioplegia with this system of delivery provides excellent myocardial protection.

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