Myocardial Preservation: A Comparison of Oxygenated Crystalloid and Blood Cardioplegia

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Department of Thoracic and Cardiovascular Surgery, Tohoku University School of Medicine, Sendai 980, *Division of Cardiothoracic Surgery, Department of Surgery, University of Washington School of Medicine, Seattle 98195, USA, and †the Second Department of Surgery, Yamaguchi University School of Medicine, Ube 755

TABAYASHI, K., MCKEOWN, P.P., MIYAMOTO, M., LUETDKE, A.E., THOMAS, R., BREAZEALE, D.G., MISBACH, G.A., ALLEN, M. and IVEY, T.D. Myocardial Preservation: A Comparison of Oxygenated Crystalloid and Blood Cardioplegia. Tohoku J. Exp. Med., 1990, 161 (3), 185-197 —— The purpose of this experiment was to compare myocardial protective effect after global ischemia using oxygenated crystalloid (CCcO2) and an oxygenated blood (BCcO2) cardioplegic solutions. Post-ischemic ventricular performance was studied in 2 equal (n = 7) groups of dogs subjected to 120 min of global ischemia induced at average myocardial temperatures of 8°C in the CCcO2 group and 18°C in the BCcO2 group. Left ventricular (LV) function included analysis of LV systolic function (global and regional function), LV diastolic function (chamber and myocardial stiffness) and LV relaxation was measured by sonomicrometry and Millar micrometers. Data were processed with a Dec PDP-11/23 computer. In vitro oxygen content (Vol %) measured 3.2±1.0 (CCcO2) and 9.5±0.3 (BCcO2). Percent recoveries of LV global function (LVSP, loop area, % shortening, LV dp/dt, mean Vc and E max) in the CCcO2 group were approximately the same as those in the BCcO2 group. There were no significant differences in LV regional function (loop area and % shortening) after ischemia between the two groups. The chamber and myocardial stiffness after ischemia in the CCcO2 group were almost the same as the baseline values. Values in the BCcO2 group were reduced significantly compared to the baseline level. There were significant differences in post-ischemic chamber and myocardial stiffness between the two groups. Post-ischemic maximum negative LV dp/dt in both groups decreased significantly compared to the baseline values. However, the time constant and diastolic interval after ischemia in both groups were approximately the same as the baseline values. We conclude that there were no significant differences in myocardial protective effect between the CCcO2 and BCcO2 groups, and both methods preserved the ischemic myocardium well.

oxygenated crystalloid cardioplegic; oxygenated blood cardioplegia

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Blood potassium cardioplegia (BCcO₂) has been advocated as an advantageous method of myocardial protection both experimentally and clinically (Melrose et al. 1955; Follette et al. 1978; Engelman et al. 1980; Fremes et al. 1984). The inclusion of blood in the cardioplegic solution was developed as a method to enhance its myocardial protective characteristics through increased oxygen-carrying capacity, providing metabolic substrates, hormones, and oncotic constituents (Follette et al. 1978). On the other hand, as a method of oxygen administration during ischemia, the oxygenation of crystalloid cardioplegia was developed (Engelman et al. 1980; Bodenhamer et al. 1983). It has been reported that oxygenated crystalloid cardioplegia (CCcO₂) improved myocardial preservation during ischemia (Bodenhamer et al. 1983; Guyton et al. 1985; Coetzee et al. 1986). There have been few comparisons of BCcO₂ and CCcO₂ (Engelman et al. 1980; Guyton et al. 1985) and it remains uncertain whether BCcO₂ is superior to CCcO₂. Engelman et al. (1980) reported that BCcO₂ was superior to CCcO₂, whereas Heitmiller et al. (1985) demonstrated that there were no differences between BCcO₂ and CCcO₂. However, the latter authors administrated BCcO₂ at an infusion temperature of 4°C. It is reported that this temperature is not the optimum temperature for BCcO₂ (Follette et al. 1987; Digerness et al. 1981; Magovern et al. 1982). Follette et al. (1978) reported that BCcO₂ should be administrated at an infusion temperature greater than 16°C. The purpose of this study was to compare myocardial protective effects between oxygenated crystalloid and oxygenated blood cardioplegia, in which the infusion temperatures were 18°C and 8°C, respectively.

**MATERIALS AND METHODS**

**Experimental preparation.** Fourteen adult mongrel dogs weighing between 17.0 and 28.0 kg were divided into two groups. One group (n = 7) received the oxygenated crystalloid cardioplegia (CCcO₂) consisting of 25 mEq/liter of potassium, 2 mEq/liter of ionized calcium and 80 mmol/liter of glucose (Table 1). The osmolarity was 390 mOsm/liter and the pH was 7.4. The other group (n = 7) received the oxygenated blood cardioplegia (BCcO₂). This solution was made up of blood from a donor dog and a small amount of electrolyte solution such that the hematocrit was 15±1%. Potassium chloride was added to make a final concentration of 25 mEq/liter and the osmolarity was 396 mOsm/liter. Both crystalloid and blood cardioplegic solutions were fully oxygenated by continuous bubbling of 100% oxygen through the recirculating solution. Oxygen tension was measured with a gas analyzer (Model 113; Instrumentation Laboratories, Lexington, MA, USA), and the oxygen content was measured using a Lex-O₂-Con analyzer (Lexington Instruments, Waltham, MA, USA).

Anesthesia was induced with thiamylal sodium (Surital®; 18 mg/kg) and maintained with a mixture of alpha chloralose (50 mg/kg) and urethane (400 mg/kg). Ventilation was controlled with a constant volume respirator (Serils 600; Harvard Apparatus, Millis, MA, USA).

Rectal and esophageal temperatures were simultaneously measured with Yellow Springs telethermometers. Major vessels to the spleen were ligated to prevent splenic pooling. The heart was exposed through a median sternotomy. A 7 Fr. Mikro-tip® catheter (Millar Instruments, Inc., Houston, TX, USA) transducer was inserted into the ascending aorta via
the right carotid artery for measurement of arterial pressure. LV pressure and its first
derivative (LV dp/dt) were obtained from a 7 Fr. Mikro-tip catheter transducer inserted
through the LV apex. A polyethylene catheter was inserted into the body of the left atrium
for measurement of left atrial pressure (LAP). Pressures obtained from fluid-filled cath-
eters were measured with Statham P 23 b transducers.

Three pairs of sonomicrometric piezoelectric crystals were implanted in the left ventri-
cle. One pair was sutured to the anterior and posterior epicardial wall to obtain maximum
transverse external diameter in the plane of the LV short axis. A second pair was implant-
ed across the LV free wall to measure wall thickness. A third pair was implanted in the
subendocardial position perpendicular to the long axis of the ventricle near the left anterior
descending artery for measurement of segmental shortening. Dimensional data
were measured with a sonomicrometer (Triton Technology, Inc., San Diego, CA, USA). Orienta-
tion of the crystal pairs was confirmed by postmortem dissection of the LV.

Following systemic heparinization (3 mg/kg), arterial (Bardec 14 Fr. or 16 Fr.) and
venous perfusion cannulae (Bardec 22 Fr.) were inserted into the left carotid artery and
right atrium, respectively. A pediatric bubble oxygenator (BOS-5; American Bentley,
Irvine, CA, USA) and a roller pump (Olson Medical Sales Corp., Ashland, MA, USA) were
used for extracorporeal support. The extracorporeal system was primed with Ringer's
lactate (1,300 ml), fresh homologous blood (700 ml) and mannitol (5 ml/kg). After can-
nulation, cardiopulmonary bypass (CPB) was initiated for 3 min. Baseline measurement of
hemodynamic variables was taken 15 min after weaning from the CPB so that the hemato-
crit (HCT) could stabilize following extracorporeal hemodilution. HCT of the CCcO₂ and
BCcO₂ groups following hemodilution was 33±2% and 30±2% (NS vs. CCcO₂ group),
respectively. Hemodynamic measurements were taken under pacing at the rate of 135
beats/min.

After baseline hemodynamic measurements, venous cannulae (Bardec 30 Fr.) were
inserted into the superior (SVC) and inferior (IVC) vena cavae and CPB was reinitiated.
Biatrial vents were inserted into the right and left atria. During bypass, pH was
maintained with sodium bicarbonate at the mean of 7.46±0.03; Pₐₒ₂ at 532±19 mmHg;
Pₐ_CO₂ at 19±1 mmHg; and HCT at 25±1%. Mean aortic pressure was maintained at 75±
4 mmHg by adjusting systemic perfusion to flow rates between 70 and 100 ml/kg/min.
After the preparation had stabilized, the animal was perfusion cooled to the mean rectal
temperature of 29±0.2°C, the aorta was cross-clamped and chilled cardioplegic solution (8°C
in CCcO₂ or 18°C in BCcO₂) and cardioplegic solution administrated immediately. The

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**Table 1. Composition of cardioplegic solutions**

<table>
<thead>
<tr>
<th>Determinations</th>
<th>Crystalloid</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>K⁺ (mEq/liter)</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Na⁺ (mEq/liter)</td>
<td>145</td>
<td>155</td>
</tr>
<tr>
<td>Ca²⁺ (mEq/liter)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mg²⁺ (mEq/liter)</td>
<td>3</td>
<td>1.2</td>
</tr>
<tr>
<td>Glucose (mmol/liter)</td>
<td>80</td>
<td>100</td>
</tr>
<tr>
<td>Osmolarity (mOsm/liter)</td>
<td>390</td>
<td>396</td>
</tr>
<tr>
<td>pH</td>
<td>7.4</td>
<td>7.4</td>
</tr>
<tr>
<td>Hemoglobin (g/100 ml)</td>
<td>0</td>
<td>5.8</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td>O₂ content (Vol %)</td>
<td>3.2</td>
<td>9.5</td>
</tr>
</tbody>
</table>
The initial dose of cardioplegic solution was 10 ml/kg with additional doses (10 ml/kg) infused every 30 min. The injection pressure of the cardioplegic solution was maintained between 60 and 70 mmHg by adjusting the flow rate of a separate infusion pump. Cardioplegic solution was infused over a period which averaged approximately 3 min. Cardioplegic solution returning through the right atrial vent was diverted to a discard cylinder so that it would not accumulate in the cardiopulmonary circuit. A 24 gauge hypodermic thermister (Model 524, Yellow Springs Instruments Co., Yellow Springs, OH, USA) was placed in the anterior portion of the LV septum for the continuous monitoring of myocardial temperature. Myocardial temperature was maintained at 18 ± 0.4°C in the CcO$_2$ group and 23 ± 0.2°C in the BcO$_2$ group. Cross-clamp time in all experiments was 120 min.

After removal of the aortic cross-clamp, the heart was electrically defibrillated. A beating state (no venting) was maintained for 30 min prior to removing the dog from bypass. Cardiotonic agents were not administered. Post-bypass measurements of hemodynamic variables were taken at 45 and 60 min after the removal of the cross-clamp. A biopsy specimen for determination of myocardial water content was taken from the free wall of the LV at 60 min after the removal of the cross-clamp. All experiments were performed in accordance with “The Principles of Laboratory Animal Care” formulated by the National Society for Medical Research and the “Guide for the Care and Use of Laboratory Animals” (NIH Publication #80-23, revised 1978).

Data analysis. The ECG, LV pressure (LVP), LV dp/dt and dimensional data were measured before ischemia and at 45 and 60 min after releasing the cross-clamp. Each parameter was measured at rest and during vena caval occlusion. Hemodynamic measurements at rest were taken at LV end-diastolic pressure (LVEDP) of 5 mmHg. Analog data were digitized at 5 msec-intervals with a minicomputer (PDP 11/23; Digital Electronics Corp, Marlboro, MA, USA). End-diastole was taken as the beginning of the initial upstroke of dp/dt. Onset of ejection was taken from the time of maximum positive dp/dt. End-systole was defined as the point 15 msec before maximum negative dp/dt.

Parameters analyzed were calculated as follows:

I) $D_{\text{int.}} = (D_{\text{ext.}} - 2h)$

II) \( \% \text{ shortening} = \frac{\text{NEDD}_{\text{int.}} (\text{NESSL}) - \text{NESD}_{\text{int.}} (\text{NESSL})}{\text{NEDD}_{\text{int.}} (\text{NESSL})} \times 100 \)

III) \( C = \Pi (D_{\text{ext.}} - h) \)

IV) \( \text{mean } V_{cf} = \frac{\text{EDC} - \text{ESC}}{ET \times \text{EDC}} \)

V) \( V = 1.014 \times (D_{\text{int.}})^{1.155} \)

VI) \( \text{LVP} = E_{\text{max}} (V - V_0) \)

VII) \( \epsilon = \ln \frac{C}{C_{\text{co}}} \)

VIII) \( \sigma = 1.36 \times \frac{(D_{\text{ext.}} - h)}{h} \times \text{LVP} \)

IX) \( \text{LVP} = \alpha (e^{\alpha t} - 1) \)

X) \( \sigma = \alpha' (e^{\alpha' t} - 1) \)

XI) \( \frac{dP}{d\epsilon} = \beta P + \alpha \beta \)

XII) \( d\sigma/d\epsilon = \beta' \sigma + \alpha' \beta' \)

XIII) \( \ln \text{LVP} = -\frac{1}{T} t + A \)

$D_{\text{int.}}$ = internal minor axis diameter, $D_{\text{ext.}}$ = external minor axis diameter, $h$ = wall thickness, NEDD$_{\text{int.}}$ = normalized end-diastolic internal diameter, NESD$_{\text{int.}}$ = normalized end-systolic internal diameter, NEDSL = normalized end-diastolic segment length, NESSL = normalized end-systolic segment length, $C$ = midwall minor axis circumference, mean $V_{cf}$ = mean velocity of circumferencial fiber shortening, EDC = end-diastolic midwall minor axis circumference, ESC = end-systolic midwall minor axis circumference, ET = ejection time,
V = LV volume (Suga and Sagawa 1974), Emax = slope of LV end-systolic pressure-volume relationship, Vo = volume intercept, ε = strain, Co = minimum diastolic midwall circumference, σ = midwall circumferential stress, α = elastic constant of pressure-strain relationship, β = constant of chamber stiffness, α’ = elastic constant of stress-strain relationship, β’ = constant of myocardial stiffness, dP/dε = derivative of pressure over strain, dσ/dε = derivative of stress over strain, T = time constant, t = time, A = curve-fit parameter.

Loop area was constructed by plotting LV pressure on the ordinate and the minor external diameter or the segment length on the abscissa. The area of these loops corresponds to the total work of the LV. The minor diameter was normalized by dividing the measured length by pre-arrest EDDext (Theroux et al. 1976) and then multiplying by a constant of 30 mm. Segment length was normalized to an initial value of 10 mm and calculated similarly. Co was measured during maximum vena caval occlusion. Emax and the static diastolic curve were generated by selecting data from 10 to 20 cycles during an approximately 20 sec vena caval occlusion (Rankin et al. 1977; Sodums et al. 1984). DP/dε and dσ/dε correspond to the instantaneous chamber and myocardial stiffness of the LV at a specific LVP and stress (Alyono et al. 1984). T was calculated by fitting formula XIII (Weiss et al. 1976), beginning with LVP at the time of maximum negative dP/dt, and ending when LVP was 5 mmHg higher than LVEDP. The degree of LV relaxation is expressed by the time constant.

Water content. Myocardial water content was determined by weighing the myocardium (Mettler ME 22 analytic scale, Mettler Instrument Corp., Hightstown, NJ, USA) in the fresh state (wet weight) and then desiccating the samples for 48 hr at 80°C for determination of dry weight. Water content, expressed as a percent of wet weight, was calculated as:

\[
\left(1 - \frac{\text{dry weight}}{\text{wet weight}}\right) \times 100
\]

Statistical analysis. Results were expressed as mean±s.e. Comparison of variables obtained at baseline with measurements taken during the postischemic period was made with the paired t-test. The unpaired t-test was used to determine the significance of differences between the CcO2 and cO2 groups. Differences were considered to be statistically significant for p values less than 0.05.

RESULTS

Cardioplegic oxygenation. Samples for the oxygen content were taken from the cardioplegic delivery system at an infusion temperature of 8°C in the CCcO2 and 18°C in BCcO2 groups. Oxygen content in the CCcO2 and BCcO2 groups was 3.2±0.1 vol % and 9.5±0.3 vol % (p <0.01 vs. CCcO2 group), respectively.

Left ventricular systolic function. LV systolic function was assessed from global and regional function.

Fig. 1 illustrates the percent recovery of global functional parameters. Percent recovery of left ventricular systolic pressure (LVSP) in the CCcO2 and BCcO2 groups was 78±5% and 70±5% (n.s. vs. CCcO2 group) at 45 min after ischemia, and 83±7% and 76±5% (n.s. vs. CCcO2 group) at 60 min after ischemia, respectively. Loop area of the minor external diameter in the CCcO2 and BCcO2 groups was 114±26% and 90±12% (n.s.) at 45 min, and 129±18% and 102±15% (n.s.) at 60 min, respectively. Percent shortening of the minor internal diameter of the CCcO2 and BCcO2 groups was 94±9% and 107±17 (n.s.) at 45 min, and 103±3% and 114±18% (n.s.) at 60 min, respectively. LV dp/dt in the
Fig. 1. Percent recoveries of left ventricular global function at 45 and 60 min after ischemia in the CCcO² (■■■) and BCcO² (□□□) groups. n = 7. LVSP, left ventricular systolic pressure; Loop area, left ventricular pressure-minor external diameter loop area; % Shortening, % shortening of normalized minor internal diameter; LV dp/dt, maximum positive first derivative left ventricular pressure; Mean Vcf, mean velocity of circumferential fiber shortening; Emax, slope of left ventricular end-systolic pressure-volume relationship; CCcO², oxygenated crystalloid cardioplegia; BCcO², oxygenated blood cardioplegia.

Fig. 2. Percent recoveries of left ventricular regional function at 45 and 60 min after ischemia in the CCcO² (■■■) and BCcO² (□□□) groups. n = 7. Loop area, left ventricular pressure-segment length loop area; % Shortening, % shortening of normalized segment length; CCcO², oxygenated crystalloid cardioplegia; BCcO², oxygenated blood cardioplegia.
CCcO₂ and BCcO₂ groups was 82±5% and 95±9% (n.s.) at 45 min, and 99±7% and 117±12% (n.s.) at 60 min, respectively. Mean $V_{CF}$ in the CCcO₂ and BCcO₂ groups was 85±9% and 102±12% (n.s.) at 45 min, and 93±6% and 110±13% (n.s.) at 60 min, respectively. Emax in the CCcO₂ and BCcO₂ groups was 81±11% and 100±14% (n.s.) at 45 min, and 77±9% and 89±8% (n.s.) at 60 min, respectively.

Fig. 2 illustrates percent recovery of regional functional parameters. The loop area of the segment length in the CCcO₂ and BCcO₂ groups was 107±13% and 83±13% (n.s.) at 45 min, and 123±23% and 93±18% (n.s.) at 60 min, respectively. Percent shortening of segment length in the CCcO₂ and BCcO₂ groups was 92±4% and 107±6% (n.s.) at 45 min, and 96±4% and 99±8% (n.s.) at 60 min, respectively. Thus, there were no significant differences in the global and regional functional recoveries between the CCcO₂ and BCcO₂ groups.

Left ventricular diastolic function. LV diastolic data are presented in Table 2. The minimum diastolic midwall circumference (Co) in the CCcO₂ and BCcO₂ groups did not change significantly after ischemia, compared to Co at baseline. Constants of chamber ($\beta$) and myocardial ($\beta'$) stiffness in the BCcO₂ group were decreased significantly ($p<0.01$ or $p<0.05$) at 45 and 60 min after ischemia compared to $\beta$ and $\beta'$ in the BCcO₂ group at baseline.

| Table 2. Left ventricular diastolic function during baseline and at 45 and 60 min after ischemia |
|-----------------------------------------------|-----------------------------------------------|
| Variables                      | CCcO₂                          | BCcO₂                          |
|                               | Baseline | 45 min | 60 min | Baseline | 45 min | 60 min |
| Co (mm)                        | 119±4    | 120±5  | 119±5  | 113±5    | 110±5   | 112±6  |
| $\alpha$ (mmHg)                | 10.9±3.4 | 21.7±7.5 | 16.3±9.1 | 3.2±1.3 | 18.0±10.9 | 6.8±2.5 |
| $\beta$                        | 3.9±0.7  | 3.9±1.4 | 6.2±2.0 | 8.3±1.6 | 3.8±0.9* | 5.1±0.9* |
| $dp/d\varepsilon_5$ (mmHg)     | 51±3     | 52±4   | 56±6   | 58±5    | 45±1*   | 47±1   |
| $dp/d\varepsilon_10$ (mmHg)    | 70±4     | 72±9   | 87±14  | 99±13   | 64±5*   | 73±5*  |
| $dp/d\varepsilon_15$ (mmHg)    | 90±7     | 92±16  | 119±24 | 141±21  | 84±9**  | 98±9*  |
| $\alpha'$ (g/cm²)              | 18.6±3.7 | 22.8±6.2 | 18.1±7.8 | 7.5±2.1 | 19.4±6.6* | 11.5±2.8 |
| $\beta'$                       | 7.6±0.7  | 6.8±1.1 | 8.6±1.5 | 10.8±1.4 | 6.7±0.9** | 8.1±0.7* |
| $d\sigma/d\varepsilon_10$ (g/cm²) | 118±14  | 187±16 | 182±20 | 175±11 | 169±12 | 163±10 |
| $d\sigma/d\varepsilon_30$ (g/cm²) | 328±14  | 323±20 | 352±27 | 389±34 | 302±15* | 324±14* |
| $d\sigma/d\varepsilon_50$ (g/cm²) | 467±22  | 459±39 | 523±53 | 605±62 | 436±30* | 486±26* |

Values are expressed as mean±s.e. *$p<0.05$ vs. baseline; **$p<0.01$ vs. baseline. Co, minimum diastolic left ventricular midwall circumference; $\alpha$, elastic constant of the pressure-strain relationship; $\beta$, constant of chamber stiffness; $dp/d\varepsilon_5$, 5, 10, 15, instantaneous left ventricular chamber stiffness determined at 5, 10, 15 mmHg of left ventricular pressure, respectively; $\alpha'$, elastic constant of the stress-strain relationship; $\beta'$, constant of myocardial stiffness; $d\sigma/d\varepsilon_10$, 30, 50, instantaneous left ventricular myocardial stiffness determined at 10, 30, 50 g/cm² of stress, respectively; CCcO₂, oxygenated crystalloid cardioplegia; BCcO₂, oxygenated blood cardioplegia.
The relationship between instantaneous chamber stiffness \((dp/dE)\) and LVEDP and that of instantaneous myocardial stiffness \((d\sigma/dE)\) to myocardial stiffness are shown in Fig. 3. DP/dE in the CCo2 group at 45 min after ischemia was almost the same as the baseline values over a wide range of LVEDP (5 to 15 mmHg) (Fig. 3A). DP/dE in the CCo2 group at 60 min after ischemia was increased above the baseline values, but there was no significant difference compared to the baseline (Fig. 3A). Post-ischemic dP/dE in the BCo2 group was decreased significantly \((p < 0.05 \text{ or } p < 0.01)\) below the baseline level (Fig. 3B). D\sigma/dE in the CCo2 group at 45 and 60 min after ischemia was approximately equal to baseline values over a wide range of LV circumferential stress (10 to 50 g/cm²) (Fig. 3C). Post-ischemic d\sigma/dE in the BCo2 group was not significantly different at 10 g/cm² of stress, but at 30 and 50 g/cm² it was decreased significantly \((p < 0.05)\), compared to the baseline level (Fig. 3D).

Thus, both chamber and myocardial stiffness in the CCo2 group after ischemia were approximately the same as baseline levels, while those in the BCo2 group were decreased below baseline.
Fig. 4 illustrates percent baseline $dP/d\varepsilon$ and $d\sigma/d\varepsilon$ in the CCc02 and BCc02 groups at 45 and 60 min after ischemia. Percent baseline $dP/d\varepsilon$ in BCc02 group at 45 and 60 min after ischemia was decreased significantly ($p < 0.01$ or $p < 0.05$), compared to that in the CCc02 group, over a wide range of LVEDP (5 to 15 mmHg) (Figs. 4A and B). Percent baseline $d\sigma/d\varepsilon$ in the BCc02 group at 45 and 60 min after ischemia were approximately equal to that in the CCc02 group at 10 g/cm² of stress, but at 30 and 50 g/cm² of stress it was decreased significantly ($p < 0.01$ or $p < 0.05$), compared to % baseline $d\sigma/d\varepsilon$ in the CCc02 group (Fig. 4C and D).

Thus, chamber stiffness in the BCc02 group after ischemia was lower than that in the CCc02 group, or myocardial stiffness in the BCc02 group was lower than that in the CCc02 group at high stress levels.

Data describing LV relaxation are presented in Table 3. Minimum negative LV $dP/dt$ in the CCc02 and BCc02 groups was decreased significantly ($p < 0.01$ or $p < 0.05$), compared to the baseline values. However, the time constant (TC) after ischemia in the CCc02 and BCc02 groups did not increase significantly.
The diastolic interval (DI) also exceeded the time constant by a factor of 3.5 in both groups. Thus, post-ischemic LV muscle in the CCcO$_2$ and BCcO$_2$ groups has relaxed sufficiently.

**Water content.** Water content in the CCcO$_2$ and BCcO$_2$ groups at 60 min after ischemia was 79.6 ± 0.4% and 79.0 ± 0.2% (n.s. vs. CCcO$_2$ group), respectively.

**DISCUSSION**

Surgical mortality has decreased significantly since the use of hypothermic potassium cardioplegia was introduced. Hypothermic potassium cardioplegia reduces metabolism and preserves adenosine triphosphate (ATP) and creatinine phosphate (CP) during ischemia (Roe et al. 1977). However, ATP and CP gradually deplete during ischemia, and ventricular performance rarely recovers its preischemic level if the ischemic time was prolonged (Nelson et al. 1976). A number of procedures have been attempted in order to preserve ATP and CP, and to prevent reperfusion injury (Follette et al. 1978; Engelman et al. 1980; Bodenhamer et al. 1983; Heitmiller et al. 1985; Coetzee et al. 1986; Kao and Magovern 1986).

The administration of oxygen and substrate into the cardioplegia was designed to satisfy oxygen demand, to prevent depletion of high energy phosphates, and to synthesize high energy phosphates (Follette et al. 1978; Engelman et al. 1980; Bodenhamer et al. 1983; Heitmiller et al. 1985; Coetzee et al. 1986; Kao and Magovern 1986). Blood potassium cardioplegia (BCcO$_2$) was first introduced by Melrose et al. (1955). In 1977 Follette et al. (1978) began to reexplore the use of BCcO$_2$, and described the usefulness of BCcO$_2$ experimentally and clinically. The theoretical advantages of BCcO$_2$ are the carrying capacity, buffering capacity, provision of metabolic substrate, and its oncotic property (Follette et al. 1978). Several investigators (Engelman et al. 1980; Feinded et al. 1984; Fremes et al. 1984; Iverson et al. 1984) have compared non-oxygenated
potassium cardioplegia (CCcO₂) with BCcO₂ (Engelman et al. 1980; Feindel et al. 1984; Fremes et al. 1984; Iverson et al. 1984), and concluded that BCcO₂ was superior to CCcO₂ both clinically and experimentally.

However, comparisons between the oxygenated crystalloid cardioplegia (CCcO₂) and BCcO₂ are rare (Engelman et al. 1980; Coetzee et al. 1986) and whether or not BCcO₂ is better than CCcO₂ has been uncertain. Bodenhamer et al. (1983) have suggested that CCcO₂ is an effective vehicle for oxygen delivery, providing excellent preservation of function and of myocardial ATP. These results come from a linear dissociation curve for oxygen and the increase in oxygen solubility with lower temperature (Digerness et al. 1981).

Engelman et al. (1980) compared CCcO₂ with BCcO₂, and they demonstrated that CP and ATP were better preserved with BCcO₂. Heitmiller et al. (1985) compared myocardial protection by CCcO₂ with and without calcium and that by BCcO₂ at a hematocrit of 10 or 30. They (Heitmiller et al. 1985) concluded that functional recovery with BCcO₂ of hematocrit 30 was better than that with CCcO₂ without calcium or BCcO₂ of hematocrit 10, and was the same as the functional recovery with CCcO₂ containing a similar concentration of ionized calcium. However, the BCcO₂ was administered at a temperature of 4°C.

Follette et al. (1978) showed that BCcO₂ should be administered above 16°C to prevent subendocardial sludging. Magovern et al. (1982) compared the myocardial protective effect of BCcO₂ at infusion temperatures of 20°C, 10°C and 4°C. They (Magovern et al. 1982) demonstrated that BCcO₂ was the most effective when infused at 20°C, and the use of 10°C or 4°C BCcO₂ were of no additional benefit, despite the enhancement of myocardial cooling, presumably because there was little oxygen delivery.

Digerness et al. (1981) reported that at 10°C, the CCcO₂ solution was capable of releasing all of its oxygen (4.03±0.07 Vol%), and the amount of available oxygen (4.06±0.1 Vol%) was greater than that available from a BCcO₂ solution (3.61±0.1 Vol%), but was lower than the amount of oxygen available from a BCcO₂ solution (5.08±0.16 Vol%) at 20°C. We thus infused BCcO₂ at a temperature of 18°C and CCcO₂ at 8°C. This BCcO₂ solution temperature was considered optimum in terms of high oxygen availability and myocardial cooling effect.

However, there were no significant differences in global and regional function after ischemia between the BCcO₂ and CCcO₂ groups. Results from our study are consistent with Heitmiller’s observation (Heitmiller et al. 1985) in which BCcO₂ was administered at 4°C. These findings suggest that the difference in infusion temperature (4°C and 18°C) does not influence the myocardial protective effect. Furthermore, these findings suggest that although BCcO₂ at high infusion temperature can release more oxygen than at lower infusion temperature, the effect may be offset by higher myocardial oxygen demand at high infusion temperature. However, these findings suggest that although BCcO₂ at high infusion temperature can release more oxygen than at lower infusion temperature, the effect may be offset by higher myocardial oxygen demand at high infusion temperature.
The chamber and myocardial stiffness in the BCCcO$_2$ and CCCCcO$_2$ groups was not elevated at 45 and 60 min after ischemia, and those of the BCCcO$_2$ group were lower than the baseline values, showing a good recovery of diastolic compliance. Chamber and myocardial stiffness in the BCCcO$_2$ group after ischemia were lower than those of the CCCCcO$_2$ group. Water content of the BCCcO$_2$ group was lower than it of the CCCCcO$_2$ group, although not significantly different. These findings may relate to the rheologic action of the red cell as a particle. Suaudean et al. (1982) demonstrated that the addition of washed red cells to the perfusate improved coronary perfusion flow, and reduced edema formation in the preserved canine heart. Zweifach (1940) showed that in the frog mesentery perfused with particle-free Ringer's solution, the circulation of perfusate is limited to arteriovenous capillaries, while the addition of avian red cells to the perfusate resulted in perfusion of the entire capillary bed. They demonstrated that the red cell perfusate reduced edema, compared with the bloodless perfusate.

In conclusion, the recovery of systolic function in the BCCcO$_2$ group was almost the same as that in the CCCCcO$_2$ group. Post-ischemic diastolic compliance in both groups returned completely to the baseline level. Thus, both methods of myocardial preservation provided adequate protection for 2 hrs of ischemic arrest.

References

9) Guyton, R.A., Dorsey, L.M., Craver, J.M., Bone, D.K., Jones, E.L., Murphy, D.A. &


