Effect of Potassium Cardioplegia on Myocardial Ischemia and Post Arrest Ventricular Function

Hartzell V. Schaff, M.D., Richard Dombroff, M.D., John T. Flaherty, M.D., Bernadine H. Bulkley, M.D., Grover M. Hutchins, M.D., Richard A. Goldman, M.D., and Vincent L. Gott, M.D.

SUMMARY To assess the effects of moderate potassium cardioplegia (37 mM KCl) on the severity of myocardial ischemia during arrest and on post arrest ventricular function, 32 isolated, isovolumic feline hearts were studied before, during and 1 hour after ischemic arrest. Normothermia (37°C) was maintained in 16 hearts, eight without KCl and eight with KCl. Hypothermia (27°C) was maintained in the remaining 16 hearts, eight with KCl and eight without KCl. Myocardial oxygen (PmO₂) and carbon dioxide tensions (PmCO₂) were measured by mass spectrometry. Maximum developed intraventricular pressure (max DP) and max dP/dt were used as indices of performance. Compared with normothermic or hypothermic arrest alone, the addition of potassium cardioplegia resulted in a significant reduction in the peak PmCO₂ measured during the arrest period. Hypothermia alone resulted in morphologic evidence of improved myocardial preservation and a significant reduction in peak PmCO₂ compared with normothermia. Post arrest ventricular function was best with the combination of hypothermic arrest and potassium cardioplegia (max DP = 96 ± 6% of control and max dP/dt = 99 ± 5% of control). These data suggest that the beneficial effects of potassium cardioplegia and 27°C hypothermia are additive, and that reduction in myocardial ischemia as evidenced by a reduction in peak PmCO₂, correlated with improvement in ventricular performance in the post arrest period and with preservation of myocardial structure.

ISCHEMIC CARDIAC ARREST during open heart surgery provides a tranquil operative field and thereby facilitates valve replacement, direct coronary artery revascularization procedures and the definitive correction of complex congenital anomalies. Once cardiopulmonary bypass is instituted, aortic cross-clamping totally interrupts coronary flow, resulting in fibrillation. Although observable mechanical activity soon stops, electrocardiographic evidence of energy-consuming fibrillation continues until energy substrates are depleted. By reducing metabolic activity, myocardial cooling can prolong the safe period of ischemia. In addition, various studies suggest that hyperkalemic arrest at the time of aortic cross-clamping preserves myocardial function after the ischemic period by quickly inducing electromechanical arrest and thereby reducing substrate utilization. Early experience with hypertonic potassium citrate arrest was unfavorable due to structural evidence of myocardial damage directly related to the cardioplegic solution.

More recent reports have advocated use of a moderately hyperkalemic, isosmotic solution as an adjunct to hypothermia during ischemic arrest. Utilizing such a solution, this study was designed to determine the effect of potassium cardioplegia on development of myocardial ischemia during cardiac arrest at normothermia and at 27°C hypothermia. Furthermore, the protocol allowed for examination of the relationship between severity of ischemia as assessed by myocardial gas tension changes during the arrest period and post arrest ventricular performance. Light and electron microscopic analysis was performed to determine the presence or absence of morphologic changes due to ischemia, and particularly to search for any structural changes attributable to the potassium solution itself.

Methods

Thirty-two mongrel cats weighing 2–3 kg each were anesthetized by intraperitoneal injection of sodium pentothal (30 mg/kg). After adequate anesthesia was achieved, the thoracic cavity was entered via median sternotomy and the beating heart was quickly excised. The heart was immersed in chilled (10°C) Krebs-Ringers Bicarbonate Solution (KRB), and within 1 minute was cleansed of its pericardial remnants and transferred to the perfusion apparatus (fig. 1). The ascending aorta was slipped on to a perfusion cannula at the base of a continuously overflowing fluid column 110 cm in height and was banded in place, establishing linear coronary perfusion retrograde through the aorta at a constant pressure of 81 mm Hg (fig. 1).

Modified KRB perfusate was bubble oxygenated with an O₂:CO₂ gas mixture (95%:5%), while maintaining the oxygen tension of the perfusate less than 300 mm Hg to avoid factitious elevation of myocardial oxygen tension (PmO₂). Hearts that did not spontaneously defibrillate after 2 minutes of coronary perfusion were electrically converted with pulses of 0.5–2 watt-seconds (Medrad Cardioverter Model 72103-A2). Next, the left atrial wall was excised and the
mitral valve leaflets were freed from their papillary muscle attachments, effectively venting the left ventricle and facilitating the insertion of a latex balloon in the cavity of the left ventricle (fig. 2). As depicted in the diagram, the flaccid balloon was secured with a tie around the tip of a rigid cannula which, in turn, was attached to a plastic button. The button with attached balloon was sewn into the mitral annulus with three fine cardiovascular silk sutures passed through three oversized holes in the plastic button; this also served to vent thebesian flow. A flange on one end of the button occluded the aortic outflow tract to prevent herniation of the saline-filled balloon during ventricular systole. The balloon cannula was connected via a three-way stopcock to either a low volume pressure transducer (Statham P23Db) or to a syringe in which the balloon was filled with enough saline to produce a left ventricular end-diastolic pressure (LVEDP) of approximately 10 mm Hg. With this arrangement, continuous recordings were made of left ventricular pressure and dp/dt. (Honeywell HM 1508 Visicorder; Accudata 132 Differentiator). Alterations in the LVEDP in this isovolumic preparation effected by a 1-hour ischemic period were studied.

The sinus node was crushed and all hearts were paced at 110 beats/min with a pulse amplitude of 5–7 mV (Medtronic 5880 Pacemaker). Myocardial temperature was monitored by a thermistor probe positioned in the cavity of the right ventricle via the main pulmonary artery, and all hearts were stabilized for 10–30 minutes at 35–37°C.

The myocardial gas probe was a 22 gauge stainless steel tubing covered with heat-shrinkable teflon. Over the distal 19 mm of the probe, the teflon was left in its expanded state. Myocardial oxygen and carbon dioxide molecules diffuse across the teflon membrane according to their partial pressures, passing through slots in the stainless steel tubing into a vacuum mass spectrometer (Medspect Model MS-8). Before each preparation, the mass spectrometer probe was calibrated by immersion in a water-filled tonometer (37°) which had been equilibrated with a gas mixture of known content. After a 1 mm incision was made in the epicardium, the distal 2 cm of the probe was inserted tangentially to a midmyocardial depth in the posterolateral wall of the left ventricle in the distribution of the circumflex coronary artery (fig. 2) and secured with a pursestring suture.

The KRB perfusate was filtered and not recirculated; total coronary effluent was measured volumetrically. Perfusate pH was monitored frequently and remained in the range of 7.4–7.6.

After the initial stabilization and baseline record-

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**Figure 1.** Diagram of isolated heart preparation and perfusion apparatus. Spectrom. = spectrometer, pulm. a. = pulmonary artery, L.A. = left atrium, L.V. = left ventricle.

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**Figure 2.** Diagram of isolated heart preparation. After excision and attachment to the perfusate column, hearts were instrumented with pacing wires, a mass spectrometer probe for measurement of myocardial gas tensions and a thermistor probe. The intraventricular balloon is shown before and after insertion through the left atrium. Ao = aorta, P.A. = pulmonary artery, L.V. = left ventricle, I.V. = intraventricular.
ing period, all hearts were made globally ischemic by cross-clamping the aortic inflow perfusion cannula. The 32 hearts were divided into four equal groups. Eight hearts (37°C) were made ischemic by aortic clamping and maintained at 37°C during the 60-minute ischemic period. In a second group, eight hearts (27°C) were cooled to 27°C by perfusion with cold oxygenated perfusate at 81 mm Hg pressure for 2 minutes before aortic cross-clamping. In the potassium-treated hearts, cardioplegia was induced by the intracoronary injection of 10 ml (approximately 2.5 mEq KCl per 100 g cardiac weight) of arrest solution at the time of aortic inflow clamping. This solution has an osmolality of 290 mOsm/l, a pH of 7.4, no calcium, and approximately 37 mEq/l of KCl (table 1). Potassium arrest was carried out in the third (37°C + KCl) and fourth (27°C + KCl) groups of eight hearts each under normothermic and hypothermic conditions, respectively. This was accomplished by passing a 17 gauge catheter through a port in the aortic perfusion cannula to the level of the aortic root, followed by rapid injection of the arrest solution. The aorta was simultaneously cross-clamped to assure homogeneous depolarization of the myocardium and to prevent washout of the hyperkalemic solution. Without exception, immediate and lasting arrest was achieved with this dose and mode of administration of the cardioplegic solution.

During the 1-hour ischemic period, the intraventricular balloon was deflated, simulating the operative conditions of a vented, non-distended left ventricle. Temperature was controlled during the arrest period by immersion of all hearts into a separate, non-circulating, non-oxygenated perfusate bath, either warmed to 37°C by a heated water jacket or cooled to 27°C by means of ice chips in the perfusate bath. Since alteration in temperature affects principally the gas permeability constant of the teflon membrane of the mass spectrometer probe, partial pressures of oxygen and carbon dioxide recorded during the period of 27°C hypothermia were corrected by the method of Holness and Brock.

In all hearts, ischemia was terminated after 1 hour by the slow release of the aortic cross-clamp and reperfusion at 37°C. Defibrillation was performed after 3 minutes of reperfusion. All hearts in the normothermic and normothermic + KCl groups required cardioversion. Two hearts in the 27°C group and seven of eight hearts in the 27°C + KCl group defibrillated spontaneously within 3 minutes after release of the cross-clamp. Hearts were maintained, with balloons deflated, in the beating, non-working state for the first 15 minutes of reperfusion, after which the original volume was re-infused into the intraventricular balloon. After 45 minutes of reperfusion, with the final 30 minutes in the beating, working state, all hearts were quickly removed from the apparatus and the gas probe position and aortic outflow tract occlusion were confirmed. Biventricular wet weights were determined and the hearts were sectioned for histologic analysis.

Transverse sections of myocardium for light microscopy were fixed in acetate buffered 10% formalin, paraffin-embedded, sectioned and stained with hematoxylin and eosin, and phosphotungsten acid hematoxylin stains. Ischemic damage was graded on a scale of 0 to 4 + , based on the severity of injury on a complete transverse section through the mid portion of the left ventricle. The slides were reviewed blindly by two independent observers.

Samples of myocardium for electron microscopy taken after the experiment were fixed in cold 3% gluteraldehyde in 0.1 M phosphate buffer, washed with several changes of 0.1 M phosphate buffer (pH 7.4), post-fixed for 1½ hours with osmium tetroxide in sucrose-phosphate buffer, dehydrated in a graded series of alcohols and acetone and embedded in epoxy resin. Semi-thin (1 μ thick) sections of epoxy resin embedded tissues were stained with toluidine blue and examined with the light microscope. Ultra-thin sections were stained with lead citrate and uranyl acetate and examined with the electron microscope (AEI).

**Table I. Composition of Three Potassium Cardioplegic Solutions**

<table>
<thead>
<tr>
<th>Solution</th>
<th>Na (mEq/l)</th>
<th>K (mEq/l)</th>
<th>Osmolality (mOsm/l)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gay-EBert</td>
<td>90</td>
<td>37</td>
<td>290</td>
<td>7.40</td>
</tr>
<tr>
<td>Melrose</td>
<td>120</td>
<td>250</td>
<td>448</td>
<td>7.90</td>
</tr>
<tr>
<td>Lam</td>
<td>0</td>
<td>667</td>
<td>1160</td>
<td>6.60</td>
</tr>
</tbody>
</table>

**Results**

1. **Myocardial Metabolism**

The mean control myocardial carbon dioxide tension (PmCO2) in the four groups ranged from 60 ± 4 mm Hg to 69 ± 6 mm Hg before arrest, and differences were not statistically significant (fig. 3). With aortic cross-clamping and ischemic arrest at normothermia, PmCO2 rose steadily to 342 ± 18 mm Hg by the end of the 1-hour arrest period. In the group of hearts arrested with potassium and maintained at 37°C, the PmCO2 rose less rapidly to a peak value of 293 ± 12 mm Hg (P < 0.05) at the end of the arrest period. Also, after 15, 30 and 45 minutes of ischemia, PmCO2 in the normothermic potassium hearts was significantly (P < 0.005) lower than in the hearts arrested without potassium. In the group of hearts cooled to 27°C during arrest, PmCO2 rose to 232 ± 11 mm Hg after 1 hour of ischemia. With the addition of potassium cardioplegia to 27°C hypothermia, the maximum PmCO2 value during arrest was markedly lower at 119 ± 8 mm Hg (P < 0.001). Furthermore, during the arrest period the rate of rise in PmCO2 with potassium arrest at 27°C was 0.5 mm Hg/min compared to 2.9 mm Hg/min with hypothermia alone. Thus, the accumulation of myocardial CO2 during arrest was significantly reduced by the addition of potassium cardioplegia in both the 37°C and 27°C hypothermia groups.

With release of the cross-clamp, PmCO2 rapidly fell toward normal values, and no significant differences were noted after 45 minutes of reperfusion. However, 5 minutes after reperfusion PmCO2 in the hypothermic potassium arrested hearts was only 67 ± 4 mm
Hg, a value which was significantly lower ($P < 0.005$) than the PmCO$_2$ in the group with hypothermia alone.

There were no significant differences in PmO$_2$ among the four groups (fig. 4). Generally, PmO$_2$ fell rapidly to very low levels (2–12 mm Hg) in all groups during the first 15 minutes of ischemia and then stabilized at these low levels until release of the aortic cross-clamp. With cross-clamp release, a transient rise and overshoot in PmO$_2$ was noted, representing a reactive hyperemic response.

II. Ventricular Performance

After 60 minutes of normothermic ischemia and 45 minutes of reperfusion the hearts recovered only 42.6 ± 6.9% of their control maximum dP/dt and 25.9 ± 5.9% of control maximum developed pressure (figs. 5 and 6). With the combination of normothermic ischemia and potassium arrest, max dP/dt returned to 69 ± 11.7% of pre-arrest control levels and maximum developed pressure recovered 49.5 ± 7.4% of its control value. Hypothermic ischemia alone resulted in a preservation of 80.1 ± 12.1% and 67.4 ± 10% of control max dP/dt and developed pressure, respectively. However, the addition of potassium cardioplegia to hypothermic ischemia resulted in preservation of 99 ± 5.3% max dP/dt and a 96 ± 5.6% recovery of control maximum developed pressure ($P < 0.05$ vs 27°C arrest group).

III. Alterations in Left Ventricular End-Diastolic Pressure

After 60 minutes of normothermic ischemia and 45 minutes of reperfusion, the LVEDP, following reinfusion of the same volume which had resulted in a LVEDP of 10.3 ± 0.4 mm Hg in the pre-arrest period, exhibited a mean increase of 37.6 ± 7.2 mm Hg (fig. 7). Addition of potassium cardioplegia to normothermic ischemia resulted in an increase of 25.3 ± 6.7 mm Hg over a pre-arrest control LVEDP of 8.4 ± 0.6 mm Hg. After hypothermic ischemia the observed rise in LVEDP was 25.9 ± 4.7 mm Hg over a pre-arrest level of 10.4 ± 0.8 mm Hg. However, the combination of hypothermia and potassium cardioplegia resulted in a mean increase of only 14.8 ± 2.5 mm Hg over a pre-arrest LVEDP of 11.3 ± 0.7 mm Hg ($P < 0.05$ vs 27°C arrest group).
Percent Recovery of Developed LV Pressure

![Graph showing percent recovery of developed LV pressure with different conditions and time points.]

FIGURE 5. Return of ventricular function in the reperfusion period appears inversely related to the myocardial carbon dioxide tension recorded during ischemic arrest. Thus, hearts arrested with potassium cardioplegia and maintained at 27°C during arrest (27°C KCl) returned to essentially 100% of pre-arrest developed pressure. Poorest results occurred in the groups subjected to unmodified normothermic arrest. These hearts had the greatest myocardial carbon dioxide values at the end of ischemia and during the reperfusion period could maintain only approximately 30% of pre-arrest developed pressure. Hypothermia alone (27°C) and normothermic potassium cardioplegia (37°C KCl) gave intermediate results, attaining 67% and 50% of pre-arrest developed pressure respectively. LV = left ventricle.

IV. Alterations in Cellular Morphology

Light microscopic changes

Study of the transverse sections of myocardium from all specimens showed some cells of the myocardium.

FIGURE 6. Percent recovery of max dP/dt paralleled recovery of developed pressure. At both 37°C and 27°C the addition of potassium cardioplegia resulted in improved ventricular function as assessed by return of max dP/dt in isovolumic hearts.

![Graph showing percent recovery of dP/dt with different conditions and time points.]

INCREASE IN LVEDP AFTER 45 MINS. REPERFUSION

![Bar graph showing increase in LVEDP with different conditions.]

\[ \Delta \text{LVEDP} \text{(mm Hg)} \]

- p<.05 vs 27°C

37°C | 37°C-KCl | 27°C | 27°C-KCl
---|---|---|---
5 | 15 | 20 | 25
10 | 20 | 25 | 30
15 | 25 | 30 | 35
20 | 30 | 35 | 40
25 | 40 | 45 | 50

During the reperfusion period, the intraventricular balloon was refilled with the same volume of saline which produced a left ventricular end-diastolic pressure (LVEDP) of 10 mm Hg in the heart before arrest. After 45 minutes of reperfusion, LVEDP was elevated in all hearts but was highest in the normothermic arrest group (37°C) and least elevated in hearts arrested with potassium cardioplegia and maintained at 27°C (27°C + KCl). Intermediate elevations of LVEDP occurred in the normothermic potassium (37°C + KCl) group and 27°C hypothermic group (27°C).
Figure 8. Light micrographs of a portion of near normal left ventricular myocardium (A) from a heart subjected to hypothermic anoxic arrest. Intercellular spaces (arrow) suggesting interstitial edema are present. Shown in B is a portion of myocardium from the same heart which shows more intercellular edema, cell swelling and contraction band (CB) formation within the swollen cells. (A & B, Hematoxylin and eosin, × 6000)

Dium containing prominent contraction bands (fig. 8). Widened spaces between myocardial cells suggesting intercellular edema was present throughout, but were most marked in the portions of myocardium containing contraction band injury. Although contraction band injury was present to some degree in all specimens, there were differences in the severity of these lesions between the groups. Grading contraction band injury on a scale of 0 to 4 +, the normothermic group without potassium averaged 1.8, the normothermic group with potassium 1.8, the hypothermic group without potassium 1.1, and the hypothermic group with potassium 0.9. Major differences were seen between those hearts treated with hypothermia and those treated without hypothermia. In contrast, only minor differences were seen between the hypothermic
group treated with potassium plus hypothermia and the group treated by hypothermia alone, but the potassium-treated group tended to show less contraction band injury.

**Ultrastructural changes**

Cells which appeared to be swollen and contain contraction bands by light microscopy showed similar changes by electron microscopy. Swollen cells contained large intracellular vacuoles and spaces (fig. 9) and the sarcolemma was frequently lifted up from the cytoplasm (fig. 10). Mitochondria were swollen, showing cleared spaces and disruption of the usual orderly cristal pattern. Granular densities were prominent in many of the swollen mitochondria (fig. 4). Within the swollen cells, groups of myofibrils often contained contraction bands in which several sarcomeres were compressed together, disrupting the usual in-register appearance of the sarcomeres. Although these ultrastructural changes occurred in all specimens, they were clearly least prominent in the groups of hearts subjected to hypothermic arrest, and most prominent in those subjected to normothermic arrest. Hearts in

**Figure 9.** Electron micrographs from the left ventricles of hearts subjected to ischemic arrest with hypothermia and potassium (A) and with hypothermia alone (B). Intercellular spaces (arrow) are prominent and some mitochondria (M) are swollen. Mitochondrial swelling and disruption and contraction bands (CB) are present in B. (A & B, × 16,000)

**Figure 10.** Left ventricular myocardium after ischemic arrest with hypothermia and potassium (A) and hypothermia alone (B). The plasma membrane or sarcolemma (SL) is lifted away from the myofibrils, and there is clearing of space between the myofibrils suggesting intercellular edema. A contraction band (CB) is present in A. The intercalated disc (ID) at the junction of two cells is not disrupted by the cell swelling. (A & B, × 16,000)
the hypothermic potassium arrest group appeared to show slightly less injury than the hearts subjected to hypothermic arrest alone, but the differences between these two groups even at the electron microscopic level were not marked.

Discussion

This study demonstrates the additive beneficial effects of potassium cardioplegia and hypothermia on ischemia during a period of aortic cross-clamping and on preservation of ventricular function following reperfusion. Potassium cardioplegia reduced myocardial CO2 production both in hearts maintained at normothermia (37°C) and in hearts cooled to 27°C (hypothermia). Return of cardiac performance and preservation of cellular morphology following reperfusion was best in those hearts which were arrested with potassium and maintained at 27°C during the ischemic period. Contrary to the findings of Engleman et al.,18 there was no evidence of additional morphologic myocardial injury associated with the use of potassium cardioplegia by light or electron microscopy. These data thus confirm the safety and benefits of an isosmotic, moderately hyperkalemic, cardioplegic solution.

Lam et al.14 first employed potassium chloride cardioplegia during ischemic cardiac arrest in dogs. Following this work and Melrose's preliminary study with potassium citrate,4 Effler et al. utilized potassium cardioplegia clinically.6 The initial enthusiasm for chemical cardioplegia using the Melrose solution was, however, short-lived, as many workers reported refractory ventricular fibrillation, ineffective cardiac action15–18 and frank myocardial necrosis which could be distinguished histologically from ischemia induced changes.8,9,19,20 Tyers et al.21 implicated the high potassium concentrations employed by both Melrose6 (240 mEq/l) and Lam19 (600 mEq/l), shown in table 1. In addition, the Melrose solution is hypertonic. Although recent studies have demonstrated beneficial effects of hypertonic mannitol (360 mOsm/l) on the performance of post-ischemic myocardium,22,23 it is possible that the deleterious effects of the Melrose solution may in part be the result of excessively high tonicity (448 mOsm/l).

Gay and Ebert10 reported the use of isosmotic, moderately hyperkalemic cardioplegia in an isolated, perfused heart preparation. The results of this and subsequent studies demonstrated further preservation of myocardial energy substrates and ventricular contractility compared to unmodified ischemia.21,24–26 Mundth et al.27 recently demonstrated additional functional preservation with the combination of potassium arrest and hypothermia (10–14°C) compared to unmodified hypothermia alone in both normal and hypertrophied hearts. Post-ischemia, less creatine phosphokinase was found in coronary sinus blood when potassium cardioplegia was used in combination with hypothermia than when hypothermia was employed alone.

In this study a correlation was demonstrated between peak PmCO2 during the arrest period and morphologic evidence of ischemic injury following reperfusion. After 60 minutes of ischemic arrest and subsequent reperfusion, all specimens showed some degree of cellular swelling and focal contraction band necrosis. Contraction band necrosis is a distinctive form of myocardial cell damage which is characterized by the formation of dense eosinophilic transverse bands within the cytoplasm (fig. 8). Foci of contraction band injury are found frequently in patients who have undergone cardiac surgery with cardiopulmonary bypass28,29 and have been produced experimentally by prolonged coronary occlusion followed by 20 minutes or more of reperfusion.30 Following reflow, myocardial cells swell, contraction bands form and electron dense granular deposits form within mitochondria (figs. 9–11). It is not clear whether cell swelling at the time of reflow is itself important in the development of the injury.31 We have found that hearts in which the highest PmCO2 levels were reached during the ischemic period demonstrated the poorest ventricular function after reperfusion and the most morphologic evidence of ischemia and/or reperfusion injury. Conversely, the combination of potassium cardioplegia and 27°C hypothermia during the arrest period resulted in the lowest peak PmCO2 during arrest, the best ventricular function during the reperfusion period, and the best preservation of cellular morphology at both light and electron microscopic levels.

After aortic cross-clamping (and thus total cessation of coronary flow), available tissue oxygen is rapidly depleted and PmO2 falls. In order to generate high energy phosphates under these anaerobic conditions, myocardial glycogen stores must be utilized to provide substrate for glycolytic pathways. As glycogen stores are depleted, ATP utilization will exceed production. Since ATP hydrolysis is associated with the generation of hydrogen ions, buffering of these hydrogen ions by the bicarbonate buffer system would result in the generation of a CO2 molecule for each hydrogen ion buffered. Under conditions of zero coronary flow there would be no washout and the concentration of carbon dioxide and other metabolic end products such as lactate would be expected to rise.52 Rovetto et al.53 recently demonstrated the inhibition of the glycolytic enzymes glyceraldehyde-3-phosphate dehydrogenase and phosphofructokinase under ischemic conditions.39 Therefore, with inhibition of glycolytic enzymes by intracellular acidosis coupled with depletion of substrate and high energy stores, the generation of CO2 molecules should cease, and a plateau in the PmCO2 curve would be expected.

MacGregor et al. correlated the finding of such a plateau during ischemic arrest with irreversible myocardial damage and the inability to resuscitate hearts after reperfusion.54 Thus, a steady rise in PmCO2 indicates continuing metabolic activity. Our data obtained in a different animal model confirm this finding and, more importantly, suggest that the rate of rise of PmCO2 during global ischemia is a quantitative index of the rate of anaerobic glycolysis. Hypothermia and chemical cardioplegia reduce rates of myocardial metabolism during global ischemia.
Furthermore, hearts demonstrating slower rates of rise of PmCO₂ during ischemic arrest were demonstrated to have better cardiac performance after reperfusion. Thus, the PmCO₂ during the period of aortic cross-clamp allows prediction of post arrest ventricular function. Measurement of PmCO₂ by mass spectrometry is particularly suited for studies of myocardial protection during ischemic arrest. Gas tensions can be monitored continuously without the requirement for serial biopsies. This technique has already been utilized successfully for intra-operative studies of patients[35] and should be useful for clinical evaluation of various methods of myocardial protection during valve replacement or coronary revascularization procedures.

Myocardial cooling has been demonstrated as an effective means of slowing the depletion of ATP and retarding the onset of irreversible, functional and morphologic deterioration associated with prolonged ischemia.[56-58] The exact degree of hypothermia required for optimal myocardial protection is not known. Several investigators have suggested that optimal post arrest function is obtained with cooling to 10-15°C. While further cooling to 4°C resulted in greater preservation of myocardial glycogen and high energy phosphate stores, while ventricular performance after reperfusion was not improved. These authors[39-41] concluded that this more extreme degree of hypothermia resulted in permanent myocardial damage, possibly due to solidification of crystallization of membrane lipids or damage to membrane-bound ATPases. A recent study from our laboratory using the isolated feline heart preparation demonstrated that cooling to 10° or 20° C, while resulting in lower peak CO₂ tensions during 60 minutes of ischemic arrest, did not result in improved recovery of ventricular function compared to cooling to 27° C.[42] The cardioplegic solution used in the present study was a modified Krebs Henseleit solution to which more potassium was added and from which all the calcium was removed. Hyperkalemic depolarization of the myocardial cell membrane, much like a physiologic depolarizing stimulus, induces a tonic contraction of the myofibril. In the presence of a normally functioning relaxing mechanism, the tension developed should gradually fade, although the membrane remains depolarized. Under conditions of global ischemia, however, normal relaxation, an energy-requiring process, would be impaired and thus, contracture would occur. This maintenance of contracture can be prevented, however, by providing a calcium-free milieu.

The term “ischemic cardiac arrest,” as it is currently used, is technically imprecise. Cardiac arrest, or the absence of all mechanical and electrical activity, does not occur immediately after aortic cross-clamping. Mechanical arrest is preceded by a variable period of agonal contraction and then by ventricular fibrillation, during which high energy substrates are being critically depleted. Even after visible mechanical fibrillation ceases, electrical activity continues, as evidenced by fine fibrillation in epicardial electrocardiograms and thus further depletion of energy stores occurs. By inducing total electrical and mechanical standstill at the time of aortic cross-clamping, hyperkalemic cardioplegia minimizes ATP consumption and thereby contributes to the maintenance of high energy phosphate and substrate stores.

The results of this study demonstrate that the combination of hyperkalemic cardioplegia and 27°C hypothermia results in additive reduction of metabolic, functional and histologic evidence of ischemia and/or reperfusion injury. Thus, cardioplegia may provide additional myocardial protection during periods of prolonged aortic cross-clamp,
particularly for hypertrophied or poorly functioning left ventricles.

References

Effect of potassium cardioplegia on myocardial ischemia and post arrest ventricular function.
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