# The Effects of Cardioplegic Solutions on the Energy Source of the Guinea Pig Heart

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## ABSTRACT

The changes in adenosine triphosphate (ATP), creatine phosphate (CP) and lactic acid (LA) contents of guinea pig hearts were studied during the cardioplegia and recovery phase.

1) ATP and CP contents in cardiac ventricular tissue were decreased during the cardioplegia, regardless of $Ca^{2+}$ concentration in the cardioplegic solutions, and CP contents were recovered with the reperfusion of normal Tyrode solution faster than those of ATP. And there were no significant differences in the recovery of CP contents with different concentration of $Ca^{2+}$ in the cardioplegic solutions tested, while the recovery of ATP contents was faster with 15 mM $K^+$, 0.1 mM $Ca^{2+}$ cardioplegic solutions.

2) LA contents were increased during the cardioplegia and decreased with the reperfusion of normal Tyrode solution.

3) The more recovery time (up to 3 hrs), the more CP contents were recovered with the reperfusion of normal Tyrode solution faster than those of ATP. And LA contents were decreased as the duration of recovery time.

These results suggest that $Ca^{2+}$ and $K^+$ concentration in the cardioplegic solution is one of the major factors influencing the recovery of cardiac tissue from the cardioplegia.

**Key Words**: Cardioplegia, Adenosine triphosphate, Creatine phosphate, Lactic acid

## INTRODUCTION

Energy metabolism in cardiac muscle includes all processes involved in the production and utilization of adenosine triphosphate (ATP). In normal tissue, the rate of oxidative phosphorylation, ATP production system, and $O_2$ consumption are strictly coupled to the rate of ATP utilization (Vary et al, 1981; Jennings & Steenbergen, 1985).

Surgeons often induce cardiac arrest (ischemia) by aortic cross-clamping during open heart surgery. High $K^+$ cardioplegic solutions are used to stop the heart beating immediately and protection of the myocardium during cardioplegia and ischemic state is a major problem of cardiac surgery, and no ideal method has been established (Roberts et al, 1980). High $K^+$ (10~20 mM) and/or cold (15~20℃)cardioplegic solutions preserve the high energy phosphate stores by avoiding needless expenditure of these stores during cardioplegia (Roe et al, 1981;

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Kohda et al, 1985), but the characterization of the ideal composition and method of administration is incomplete (Gay & Ebert, 1973; Roberts et al, 1980). Although membrane depolarization induced by high $K^+$ solutions can be used to stop the heart immediately, $Ca^{2+}$ influx following depolarization of membrane potential is to damage the cardiac cell (Mullins, 1981; Kimura et al, 1987). The increment of intracellular $Ca^{2+}$ accumulation increases use of energy in sarcoplasmic reticulum and mitochondria and results in a decrease in the prodution amount of ATP and ischemic contracture (Opie, 1984; Reimer & Jennings, 1986). These imply that intracellular $Ca^{2+}$ concentration is one of the most important component and extracellular $Ca^{2+}$ reduction should reduce tissue injury by avoiding accumulation of intracellular $Ca^{2+}$. Therefore the attempts of reduction of $Ca^{2+}$ in the cardioplegic solutions and the use of $Ca^{2+}$ antagonists such as verapamil have been made to reduce tissue injury by avoiding intracellular $Ca^{2+}$ overload (Balderman et al, 1984; Bourdillin & Poole-Wilson, 1982; Hearse et al, 1984; Hendriks et al, 1985; Yamamoto et al, 1984). But cardioplegia with low or zero $Ca^{2+}$ cardioplegic solution can induce the abrupt $Ca^{2+}$ influx during the recovery with the solution of normal concentration of $Ca^{2+}$ and the heart was immersed in reperfusion injury (Singal et al, 1986; Sunnengren & Rovette, 1987).

In cardioplegic state $O_2$ supply was diminished and the hearts use of their ATP demand for anaerobic glycolysis. So products of the metabolism such as $H^+$, lactate, $CO_2$ and these compounds can inhibit metabolic processes and also result in myocardial acidosis (Vary et al, 1981). Lactic acid (LA), the end product of anaerobic glycolysis, accumulates in the myocytes during the cardioplegia. LA also has direct effects on cardiac myocytes that could contribute to the evolution of ischemic injury. A high LA concentration has been linked to decreased phosphorylating capabilities of mitochondria in (lactate-rich) myocardium. Recovery of ventricular function following 30 minutes of total ischemia in rat hearts is inversely related to the accumulated levels of LA (Hendriks et al, 1985; Kohda et al, 1985; Reimer and Jennings, 1986).

In the present study, it was intended to observe the effect of the concentration of $K^+$ and $Ca^{2+}$ in the cardioplegic solutions on the extent of recovery of ATP, CP and LA. To observe the effect of $K^+$ and $Ca^{2+}$ in the cardioplegic solution, the changes of the contents of ATP and CP, high energy phosphates, and LA, the end product of anaerobic glycolysis were measured during and after cardioplegia. And also the change of these metabolites was observed according to the recovery time.

## METHODS

### 1. Langendorff perfusion system

Guinea pigs weighing about 500~800 g were sacrificed by injecting pentobarbital (50 mg/kg) with heparin (2,000 IU/kg) intraperitoneally. The hearts were excised rapidly and cannulated via the aorta. The perfusion was made with normal Tyrode solution (composition, NaCl 133.5; KCl 4; $MgSO_4$ 1.2; $NaH_2PO_4$ 0.3; Tris 10; $CaCl_2$ 1.8; D-glucose 10 mM, pH 7.4), equilibrated with 100% $O_2$, for 30 mins with Langendorff retrograde perfusion system (flow rate, 4 to 5 ml/min). The perfusion solution was maintained at 37℃ with temperature-regulated water bath.

The cardioplegic solutions with variation of the concentration of $Ca^{2+}$ and $K^+$ were made by replacing with NaCl and maintained the osmolarity of the solution constant through all the experiments. The perfusion of the heart was made in a sequence; the normal Tyrode solution for 30 mins (control period), cardioplegic solutions with various concentration of $Ca^{2+}$ and $K^+$ for 30 mins (cardioplegia) and reperfusion with normal Tyrode solution after cardioplegia for 30 mins, 1 hr and 3 hrs respectively (recovery period).

### 2. Tissue preparation

At the end of perfusion, the heart was quickly frozen in a liquid nitrogen tank (-70℃) to stop the metabolism. The atrium and surrounding tissues were trimmed and the weight of remaining tissue was measured (ventricle weight, wet weight). The frozen tissue was homogenized (Polytron, Type PT 10/35) in ice-cold 0.8 N perchloric acid (3.25 ml $HClO_4$ to g tissue) for 30 seconds. The homogenate was centrifuged (CRU-5000 centrifuge, Damon) at 2,000 x g for 10 mins to discard large pieces of tissue. The supernatant was neutralized to pH 7.4 with 6 N KOH solution and stood for 10 mins in ice-cold bath and recentrifuged. The final supernatant (ventricular extract) was immediately used for the analysis of ATP, CP, and LA.

### 3. ATP and CP determinations

ATP and CP were determined as described by Heinz & Weisser (1985. The initial composition of the incubation solution (3 ml, pH 7.4) was triethanolamine-hydrochloride 94.5, $MgCl_2$ 23.6, $\beta$-nicotinamide adenine diphosphate 0.6, D-glucose 118.2 $\mu$mole, glucose-6-phosphate dehydrogenase 3 unit, and ventricular extract 0.1 ml. The reaction was started by adding 2 unit of hexokinase. The fluorescence intensity after 5 minutes' reaction was measured and the net amount of ATP was calculated from standard curve of ATP. After the end of the reaction, the 0.51 $\mu$mole adenosine diphosphate (ADP) solution was added and the plateau value of fluorescence intensity (F1) was taken as the reference for the CP measurement. The reaction of determination of CP was started by addition of 80 unit creatine kinase solution. The fluorescence intensity (F2) was observed and the amount of CP was calculated from the difference between F2 and F1. The amount of the ATP and CP was expressed as $\mu$mole/g wet wt.

### 4. Measurement of LA content

LA content was spectrophotometrically determined by the modified method of Marbach & Weil (1967). The ventricular extract was added to the 3 ml (final volume) of incubation solution, which contained glycine 0.459 mmole, Lactic dehydrogenase 46 unit, $\beta$-nicotinamide adenine dinucleotide 10 mg, and incubated at 37℃ for 30 mins. The optical density of the reduced form of nicotinamide adenine dinucleotide at 340 nm (Shimadzu PR-1, UV-240) was measured. The amount of LA was also expressed as $\mu$mole/g wet wt.

## RESULTS

The tissue contents of ATP, CP and LA were measured during the cardioplegia and the recovery of the heart (Fig. 1 and 2). The amount of ATP, CP and LA in the control period were $2.9\pm0.5$, $2.1\pm0.4$ and $7.7\pm1.2$ $\mu$mole/g wet wt, respectively. A 30-minute period of cardioplegic solution administration was chosen because it consistently resulted in severe loss of ATP to improve during the recovery period (Dewitt et al, 1983). During perfusion of the cardioplegic solution containing 15 mM $K^+$, guinea pig ventricular tissue contents of ATP were significantly decreased ($p<0.05$) to $0.9\pm0.2$ and $0.9\pm0.1$ with 0.1 mM and 1.8 mM $Ca^{2+}$ in the cardioplegic solution. CP contents were significantly decreased ($p<0.05$) to $0.7\pm0.1$ and $1.0\pm0.2$ with 0.1 mM $Ca^{2+}$ and 1.8 mM $Ca^{2+}$. And the amount of LA was increased to $12.5\pm2.4$ and $11.2\pm0.7$ with 0.1 mM $Ca^{2+}$ and 1.8 mM $Ca^{2+}$ (Fig. 1). With the cordioplegic solution containing 25 mM $K^+$, the amount of the metabolites was measured. The tissue contents of ATP were significantly decreased ($p<0.05$) to $0.9\pm0.2$ and $1.3\pm0.2$ with 0.1 mM $Ca^{2+}$ and 1.8 mM $Ca^{2+}$. CP contents were decreased, with no significance ($p>0.05$), to $0.9\pm0.3$ and $0.9\pm0.2$ with 0.1 mM $Ca^{2+}$ and 1.8 mM $Ca^{2+}$. LA amount was increased, with no significance ($p>0.05$) to $8.7\pm3.5$ and $8.4\pm0.9$ with 0.1 mM $Ca^{2+}$ and 1.8 mM $Ca^{2+}$ (Fig. 2).

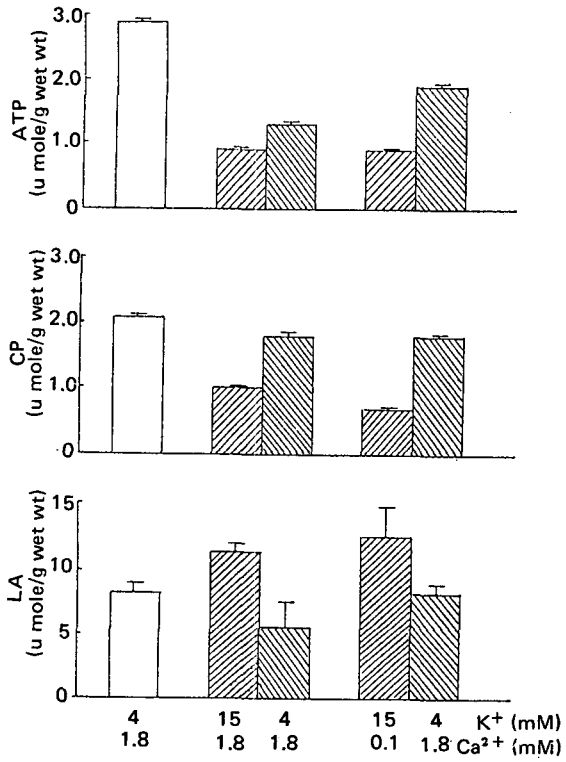


**Fig. 1.** Effect of $Ca^{2+}$ concentration of low $K^+$ (15 mM) cardioplegic solutions on the content of ATP, CP and LA of guinea pig hearts. Guinea pig hearts were perfused with 15 mM $K^+$ cardioplegic solutions of various $Ca^{2+}$ concentration for 30 minutes and reperfused with normal Tyrode solution. After a series of reperfusion, whole heart tissue was quickly frozen under liquid nitrogen. ATP and CP of ventricular tissue were measured fluorometrically and LA was spectrophotometrically (see METHODS for details). The sequence of pictures is as follows; control(□), cardioplegia (▨) and recovery (■). All values are Mean± SD of 3 to 6 experiments.

* Significantly different from the control values in each group ($p<0.05$).

\# Significantly different from the value of the cardioplegia in each group ($p<0.05$).

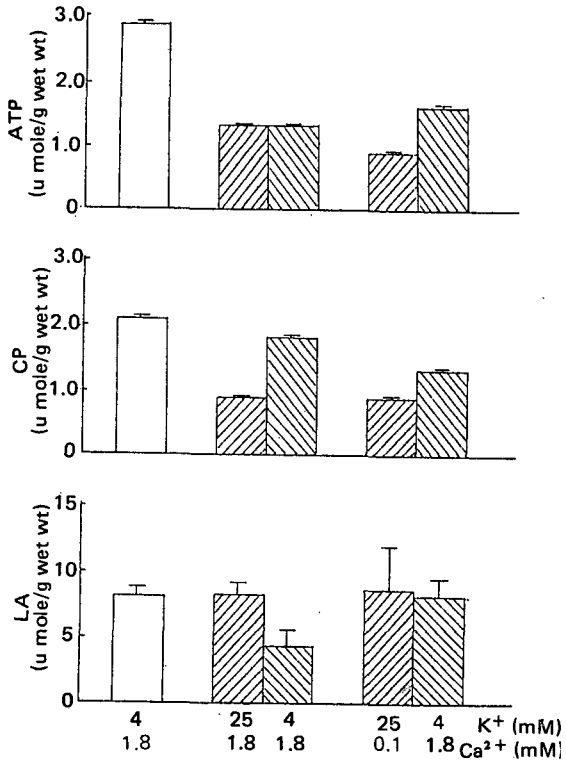


**Fig. 2.** Effect of $Ca^{2+}$ concentration of high $K^+$ (25 mM) cardioplegic solutions on the content of ATP, CP and LA of guinea pig hearts. Guinea pig hearts were perfused with cardioplegic solutions containing 25 mM $K^+$, 1.8 mM $Ca^{2+}$ for 30 minutes and reperfused with normal Tyrode solution. After a series of perfusion, whole heart tissue was quickly frozen under liquid nitrogen. ATP, CP and LA of ventricular tissue were measured as described in Fig. 1 (see METHODS for details). The sequence of pictures is as follows; control (□), cardioplegia (■) and recovery (■). All values are means±SEM of 3 to 6 experiments.

* Significantly different from the control values in each group ($p<0.05$).

Reperfusion of normal Tyrode solution following the cardioplegia increased the contents of ATP and CP of guinea pig ventricular tissues. After the cardioplegia, the heart was reperfused with normal Tyrode solution for 30 minutes and the tissue contents of ATP, CP and LA were measured. ATP contents were recovered to 1.9±0.3, 1.3±0.3, 1.6±0.6 and 1.3±0.3 $\mu$mole/g wet wt from the cardioplegia of 15 mM $K^+$, 0.1 mM $Ca^{2+}$, 15 mM $K^+$, 1.8 mM $Ca^{2+}$, 25 mM $K^+$, 0.1 mM $Ca^{2+}$ and 25 mM $K^+$, 1.8 mM $Ca^{2+}$ CP contents were also recovered to 1.8±0.4, 1.

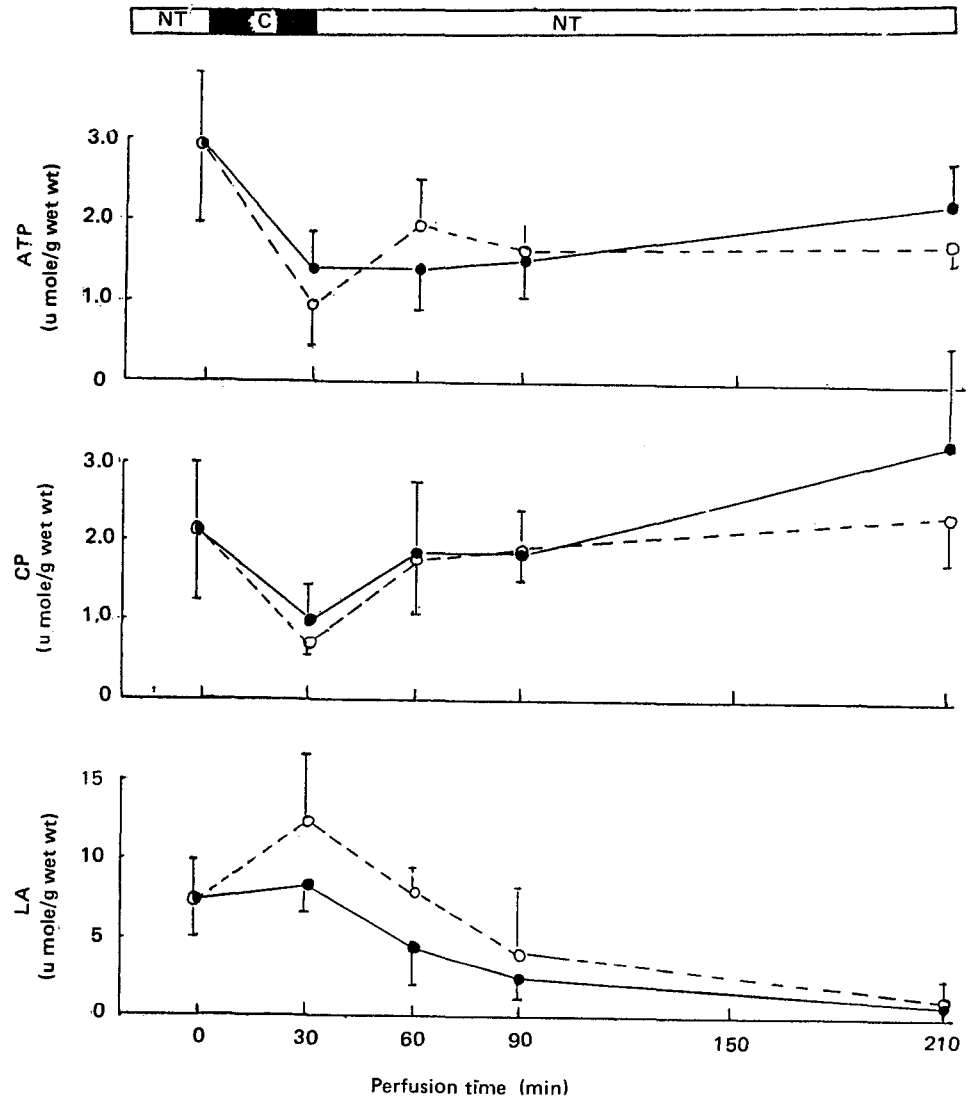


**Fig. 3.** Recovery of ATP, CP and LA contents after the cardioplegia with 25 mM $K^+$, 1.8 mM $Ca^{2+}$ and 15 mM $K^+$, 0.1 mM $Ca^{2+}$ cardioplegic solutions. Guinea pig hearts were perfused with cardioplegic solutions (○) of 25 mM $K^+$, 1.8 mM $Ca^{2+}$ (●) and 15 mM $K^+$, 0.1 mM $Ca^{2+}$ (○) for 30 minutes and reperfused with normal Tyrode solution (NT). After a series of perfusion, whole heart tissue was quickly frozen under liquid nitrogen. ATP, CP and LA of ventricular tissue were measured as described in Fig. 1 (see METHODS for details).

$8\pm0.6$, $1.3\pm0.5$ and $1.8\pm0.4$ $\mu$mole/g wet wt respectively. The amounts of LA after the cardioplegia were decreased to $8.0\pm0.8$, $5.5\pm1.8$, $7.7\pm2.0$ and $4.6\pm1.2$ respectively.

The increase in LA content was not significant with 25 mM $K^+$-cardioplegia, and 1.8 mM $Ca^{2+}$-cardioplegia reduced LA content after 30 minutes' reperfusion significantly. These data imply that low $Ca^{2+}$ concentration in the cardioplegic solution decreases ATP and CP contents and high $K^+$ increases ATP and CP contents. However, ATP content after 30 minutes' reperfusion of normal

Tyrode solution was larger with 0.1 mM $Ca^{2+}$ cardioplegia.

In order to investigate whether this increase in ATP content after 0.1 mM $Ca^{2+}$ cardioplegia is due to a decreased contractility during reperfusion (not shown in this paper), the recovery phases of ATP, CP and LA were measured over 3 hours. After the cardioplegia induced with 25 mM $K^+$ and 1.8 mM $Ca^{2+}$, ventricular tissue content of ATP was recovered to 1.3±0.3 (at 30 mins), 1.51±0.3 (1 hr) and 2.1±0.3 (3 hrs) but did not return to the control level (2.9±0.5). CP content was recovered to 1.8±0.4 (30 mins), 1.8±0.1 (1 hr) and 3.3±0.7 (3 hrs) from 2.1±0.4. LA content was recovered to 4.6±1.2 (30 mins), 2.7±0.5 (1 hr) and 1.1±0.2 (3 hrs)(Fig. 3) below the control level. After the cardioplegia induced with 15 mM $K^+$,0.1 mM $Ca^{2+}$ solution, ATP content was recovered to 0.9±0.3 after 30 mins but was not increased further even after 3 hours' reperfusion, 1.6±0.1 (1 hr) and 1.7±0.1 (3 hr). CP was 1.8±0.4 (30 mins), 1.4±0.3 (1 hr) and 2.3±0.3 (3 hrs). LA content was decreased by 8.0±0.8 (30 mins), 4.2±2.2 (1 hr) and 1.2±0.4 $\mu$mole/g wet wt (3 hrs) (Fig. 3).

The recovery of ATP after the cardioplegia of 15 mM $K^+$, 0.1 mM $Ca^{2+}$ was halted, compared to that after the cardioplegia of 25 mM $K^+$, 1.8 mM $Ca^{2+}$.

## DISCUSSION

The development of lethal injury in the ischemic myocardium is closely related to the level of tissue ATP. $O_2$ deprivation in cardiac tissue during the cardioplegia results in the accumulation of intracellular $Ca^{2+}$ due to the change of $Ca^{2+}$ pump and/or $Na^+$-$Ca^{2+}$ exchange mechanism (Katz & Reuter, 1979; Mullins, 1981). Increment of intracellular $Ca^{2+}$ activity activates the activity of actomyosin ATP ase, increases the hydrolysis of ATP, causes the myocardial contracture and resulted in myocardial cell damage (Hearse et al, 1977; Opie, 1984; Reimer & Jennings, 1986).

Ischemia reduce the oxygen supply to the myocardial cells and reduce the rate of ATP production by oxidative phosphorylation in mitochondria (Opie, 1984). Synthesis of high energy phosphate continues in the ischemic tissue (low blood flow) but at a much reduced rate compared with aerobic conditions, because anaerobic glycolysis is the only source of new high energy phosphate, producing 3 moles of ATP per mole of glucose derived from breakdown glycogen to lactate. In severely ischemic myocardium, little plasma glucose is available and the amount of ATP which can be produced via glycolysis is limited by a) the cellular supply of glycogen, b) the inhibition of glycolysis as the intracellular environment becomes more acid, and c) the destruction of nucleotides during metabolism, which cannot be resynthesized in anaerobic hearts during cardioplegia.

The production of lactate was rapidly increased during cardioplegia and decreased in reperfusion with normal Tyrode solution. In cardioplegic state about 80 to 90% of high energy phosphate was produced due to anaerobic glycolysis and accumulated lactate (Jennings et al, 1978). Myocardial acidosis, resulted from accumulation of lactate and proton has a variety of potentially deleterious consequences, including inhibition of various metabolic pathways, such as enzymes of the glycolytic pathway.

It is widely accepted that high $K^+$ cardioplegia immediately stops the heart beating and preserves the high energy phosphate stores. But during the sustained membrane depolarization induced by high $K^+$ cardioplegia, ATP is consumed to pump out $Na^+$ and maintain $Na^+$ gradient for $Na^+$-$Ca^{2+}$ exchange transport, with much reduced resynthesis due to the ischemia. As the ischemic condition continues, cellular high energy phosphate would be depleted and consequently lactate would be accumulated as shown in Fig. 2. And intracellular $Na^+$ and $Ca^{2+}$ also would be accumulated as previously reported Katz & Reuter, 1979; Roe et al, 1981; Kohda et al, 1985;

Kimura et al, 1986. Since $Na^+$ pumping activity is dependent upon membrane potential, the degree of intracellular $Na^+$ accumulation can be reduced by high $K^+$ cardioplegia, in a way that the 25 mM $K^+$ cardioplegia induces more depolarization which consequently spare cellular energy sources than 15 mM $K^+$ cardioplegia does as shown in Fig. 1 and 2. Even though intracellular $Ca^{2+}$ accumulation is reported as one of main factors in inducing cell damage during the ischemia (Katz & Reuter, 1979), 1.8 mM $Ca^{2+}$ cardioplegia seems to spare more ATP and CP than 0.1 mM $Ca^{2+}$ cardioplegia does. It may be explained that low $Ca^{2+}$ is coupled to $Na^+$ accumulation during the cardioplegia resulting in increased utilization of ATP. It is also supported by enhanced LA accumulation during the 0.1 mM $Ca^{2+}$ cardioplegia as shown in Fig. 3.

Reperfusion provides $O_2$ supply to tissue and returns pH to normal value and increases the mitochondrial $Ca^{2+}$ uptake (Vaughan-Jones et al, 1983). Thus ATP production in reperfusion is mainly dependent on aerobic glycolysis. The results of our present study shows that approximately 50% compared to control value of ATP and about 70% of CP was recovered and ATP was recovered more slowly. And also ATP is direct energy source of contraction and used immediately after production. Although the rate of ATP production is normal the rate of use of ATP was small due to decreased contractile activity and thus the net amount of ATP was high. And other studies indicate that under some experimental conditions purine nucleotide pools may remain depleted for many days following ischemic event (Renlund et al, 1984; Swain and Holmes, 1986).

Fig. 1 also shows that ATP content after 30 minutes reperfusion following the cardioplegia containing 15 mM $K^+$ and 0.1 mM $Ca^{2+}$ was larger than others. In the previous study reperfusion after cardioplegia containing 15 mM $K^+$ and 0.1 mM $Ca^{2+}$ resulted in an enhanced influx of $Ca^{2+}$ via $Na^+$-$Ca^{2+}$ exchange transport during reperfusion (Suh et al, 1988). An abrupt $Ca^{2+}$ influx during the reperfusion would cause myocardial cells severely damaged so that contractile strength is impaired. Thus net content of ATP can be larger if the ATP consumption is also decreased due to decreased contractility (Swain & Holmes, 1986). The cell damage due to low $Ca^{2+}$ cardioplegia is also responsible for slower recovery of ATP content as shown is Fig. 3.

Creatine phosphate content was increased rapidly in reperfusion and almost 70% compared to normal value was recovered. The rapid increase in CP content has been interpreted to indicate that energy production by the mitochondria is not limiting in postischemic myocardium. Repletion of nucleotide pools is limited by the availability of purine and pyrimidine substrates. Commonly the pH of cardioplegic solution containing 1.8 mM $Ca^{2+}$ could be lowest among the various cardioplegic solution. The production of lactate was rapidly increased during cardioplegia and decreased in reperfusion with normal Tyrode solution. The net amount of lactate in 15 mM $K^+$ cardioplegic solution was greater than in 25 mM $K^+$. Thus the smallest amount of $Ca^{2+}$ and the poor $O_2$ supply resulted in decrement of ATP by oxidative phosphorylation and increased the amount of ATP by anaerobic glycolysis. In reperfusion lactate production was remarkedly decreased. In reperfusion after cardioplegia containing 1.8 mM $Ca^{2+}$ the net amount of lactate was small.

The results of this study suggest that the concentrations of $Ca^{2+}$ and $K^+$ in the cardioplegic solution have significant roles in influencing the recovery of cardiac tissue from the cardioplegia. And it is also implied that intracellular $Na^+$ activity, which is modulated by ATP-dependent $Na^+$pump and $Na^+$-$Ca^{2+}$ exchange transport, has a major role in metabolisms of high energy phosphates. Further studies on direct measurements of intracellular $Na^+$ activity and the ionic compositions of cardioplegic solution based on the theoretical calculation of $Na^+$-$Ca^{2+}$ exchange transport are needed to enrich

our understanding of cardiac muscle under cardioplegic condition and recovery.

## REFERENCES


Baldelmann SC, Chan AK & Gage AA (1984). Verapamil cardioplegia: Improved myocardial prevention during global ischemia. *J Thorac Cardiovasc Surg* 88, 57-66

Bourdillin PD & Poole-Wilson PA (1982). The effects of verapamil, quiescence, and cardioplegia on calcium exchange and mechanical function in ischemic rabbit myocardium. *Circulation Res* 50, 360-368

Dewitt DF, Jochim KE & Behrendt DM (1983). Nucleotide degradation and functional impairment during cardioplegia: Amelioration by inosine. *Circulation* 67, 171-178

Gay WA & Ebert PA (1973). Functional, metabolic, and morphologic effects of potassium-induced cardioplegia. *Surgery* 74, 284-290

Hearse DJ, Garlick PB & Humphrey SM (1977). Ischemic contracture of the myocardium: Mechanism and prevention. *Am J Cardiol* 39, 986-993

Hearse DJ, Yamamoto F & Shattock MJ (1984). Calcium antagonists and hypothermia: the temperature dependency of the negative inotropic and antiischemic properties of verapamil in the isolated rat heart. *Circulation* 70 (suppl I), 1-54

Heinz F & Weisser H (1985). *Methods of enzymatic analysis*, 3rd edit, Verlag Chemie, Weinheim, and Academic Press, New YorK. Vol. VIII, 507-514

Hendriks FFA, Jonas J, van der Laarse A, Huysmans HA, Van Rijk-Zwikker GL & Schipperheyn JJ: Cold ischemic arrest: comparison of calcium-free and calcium-containing solutions. *Ann Thorac Surg* 39, 321-317

Jennings RB, Hawkins K, Lowe JE, Hill ML, Klotman S & Reimer KA (1978). Relation between high energy phosphate and lethal injury in myocardial ischemia in the dog. *Am J Pathol* 92, 187-207

Jennings RB & Steenbergen Jr C (1985). Nucleotide metabolism and cellular damage in myocardial ischemia. *Ann Rev Physiol* 47, 727-749

Katz AM & Reuter H (1979). Cellular calcium and cardiac cell death. *Am J Cardiol* 44, 188-190

Kim DH, Cragoe Jr EJ & Smith TW (1987). Relations among sodium pump inhibition, Na-Ca and Na-H exchange activities, and Ca-H interaction in cultured chick heart cells. *Circ Res* 60, 185-193

Kimura J, Miyamae S & Noma A (1987). Identification of sodium-calcium exchange current in single ventricular cells of guinea-pig. *J Physiol* 384, 199-222

Kimura J, Noma A & Irisawa H (1986), Na-Ca exchange current in mammalian heart cells. *Nature* 319, 596-597

Kohda Y, Tominaga R, Ueno Y, Andoh H, Nakano E & Tokunaga K (1985). Effects of cardioplegia on myocardial metabolism during hypothermic ischemia. *Jap Circulation J* 49, 75-80

Marbach EP & Weil MH (1967). Rapid enzymatic measurement of blood lactate and pyruvate. *Clin Chem* 13, 314-318

Mullins LJ (1981). *Ion transport in heart.* Raven Press, New York, p 20-43

Opie LH (1984). The Heart: *Physiology, metabolism, pharmacology and therapy*. Grune & Stratton, Inc.

Reimer KA & Jennings RB (1986). Myocardial ischemia, hypoxia, and infarction. Chapter 53 in "*The heart and cardiovascular system*", edited by Fozzard HA et al, Raven Press, p 1133-1201

Renlund DG, Gerstenblith G, Lakatta EG, Jacobus WE, Kallamn CH & Weisfeldt ML (1984). Perfusate sodium during ischemic functional and metabolic recovery in the rabbit heart. *J Mol Cell Cardiol* 16, 795-801

Roberts AJ, Abel RM & Alons DR (1980). Advantages of hypothermic potassium cardioplegia and superiority of continuous versus intermittent aortic cross-clamping. *J Thorac Cardiovasc Surg* 79, 44-58

Roe BB, Hutchinson JC, Fishman NH, Ullyot DJ & Smith DL (1981). Myocardial protection with cold, ischemic, potassium-induced cardioplegia. *J Thorac Cardiovasc Surg* 73, 366

Singal PK, Lee SL, Ganguly V & Dhalla NS (1986). Reversibility of ultrastructural, contractile function and $Ca^{2+}$ transport changes in guinea pig hearts after global ischemia. *Can J Physiol Pharmacol* 64, 1368-1375

Suh CK, Park SR, Park HS, Lee YH & Kang BS (1988).

A study on the cardioplegic solutions and the cardioplegia of guinea pig heart. *Korean J Physiol* 22, 1-12

Sunnergren KP & Rovetto MJ (1987). Myocyte and endothelial injury with ischemia reperfusion in isolated rat hearts. *Am J Physiol* 252, H12411-H1217

Swain JL & Holmes EW (1986). Nucleotide metabolism in cardiac muscle. Chapter 44 in "*The heart and the cardiovascular system*", edited by Fozzard HA et al, Raven Press

Vary TC, Reibel DK & Neely JR (1981). Control of energy metabolism of heart muscle. *Ann Rev Physiol* 43, 419-430

Vaughan-Jones RD, Lederer WJ & Eisner DA (1983). $Ca^{2+}$ ions can affect intracellular pH in mammalian cardiac muscle. *Nature* 301, 522-524

Yamamoto F, Braimbridge MW & Hearse DJ (1984). Calcium and cardioplegia. The optimal calium content for the ST. Thomas' Hospital cardioplegic solution. *J Thorac Cardiovasc Surg* 87, 908-912

## ═국문초록═

## 심근 정지 용액이 심근의 에너지원에 미치는 영향

연세대학교 의과대학 생리학교실

**박 혜 수·박 소 라·이 영 호**
**김 인 숙·서 창 국·강 복 순**

심근정지용액의 조성이 심근정지 및 심근정지 후 회복기의 에너지원에 미치는 영향을 조사하기 위해 guinea pig 심실 균질액에서 adenosine triphosphate (ATP), creatine phosphate (CP) 및 lactic acid (LA)의 변화를 관찰하여 다음과 같은 결과를 얻었다.

1) ATP 및 CP 양은 심근정지동안은 감소하고 회복기에는 다시 증가하였으며, 심근정지 후 정상용액으로 30분간 회복시켰을 때에는 ATP 양의 회복이 CP에 비해 느린것을 알 수 있었다.

2) LA 양은 심근정지동안은 증가하고 회복기에는 다시 감소하였다.

3) 심근정지 후 회복시간을 길게할수록 ATP 및 CP 양의 회복은 증가하였으며 CP 양이 더 많이 회복되었다.

4) LA 양도 회복시간을 길게할수록 감소하였다.

이상의 결과를 종합하여 볼 때, 심근정지용액의 $Ca^{2+}$ 및 $K^+$ 농도는 심근정지후 회복시 심근세포의 에너지원인 ATP, CP 및 lactic acid 양에 영향을 미친다고 생각된다. 이 연구 결과를 토대로 심근세포내 $Na^+$과 $H^+$ 활성도의 변화 및 심근세포의 산증(acidosis)에 관한 연구를 첨가하면 심근정지시의 심근보호기전을 규명하는데 도움이 될 것으로 생각된다.