Effect of high-volume cardioplegia on small-amplitude electrical activity during cardioplegia arrest *

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Abstract. The effects of high-volume cardioplegia on the presence of small-amplitude electrical activity during cardioplegia arrest were investigated in 19 mongrel dogs. The animals were randomly assigned to receive either high-volume crystalloid cardioplegia (HV-plege) or crystalloid cardioplegia guided by continuous electrical monitoring (V-plege). Cardiac index, left ventricular stroke work index \(\frac{dp}{dt}\), and myocardial oxygen consumption were measured before bypass and following 90 min ischemia and 45 min reperfusion. Biopsies were taken for measurement of adenosine triphosphate (ATP) and examination of myocardial ultrastructure. Nine animals received HV-plege, while the remaining 10 animals received cardioplegia guided by voltage criteria. Small-amplitude electrical potentials were recorded within 10-15 min after the infusion of cardioplegia in all animals receiving cardioplegia guided by voltage criteria. Electrical activity, however, was immediately abolished by reinfusion of cardioplegia. HV-plege reduced the incidence of small-amplitude electrical activity during cardioplegia arrest but did not prevent electrical activity. Left ventricular function and myocardial ultrastructure were better preserved when cardioplegia was guided by electrical monitoring. ATP decreased similarly in both groups following cardioplegic arrest, but myocardial oxygen consumption was significantly higher following the arrest in the V-plege group. Conclusions: HV-plege does not prevent small-amplitude electrical activity and may have adverse effects on myocardial metabolic and functional recovery. [Eur J Cardio-thorac Surg (1991) 5:395-399]

Key words: Myocardial preservation – Electrophysiology – Myocardial metabolism

Cardioplegia provides myocardial protection during ischemic arrest by preventing electromechanical activity. However, more recent investigations in independent laboratories [4, 6] have reported the presence of electrical activity after cardioplegia when the heart is quiescent and the electrocardiogram is isoelectric. Small-amplitude electrical potentials have been recorded from the myocardium with specially designed plunge electrodes within 10-15 min after the initial infusion of cardioplegia and may persist for upwards of 30 min before the resumption of electromechanical activity. Although the significance of small-amplitude electrical activity during cardioplegia arrest is not fully understood, earlier investigations [7, 8] have suggested that persistent electrical activity during cardioplegia arrest is associated with impaired myocardial metabolic and functional recovery.

In an earlier experimental investigation [8] we suggested that continuous electrical monitoring during cardioplegia arrest may be necessary in order to identify residual electrical activity which may be present but unrecognized by contemporary monitoring techniques. However, it is conceivable that high-dose volume cardioplegia, administered in a multidose fashion, may prevent small-amplitude electrical activity during cardioplegia arrest. To test this hypothesis we monitored the voltage of the myocardium during cardioplegia arrest and compared myocardial metabolic and functional recovery in animals randomly assigned to receive either high-volume cardioplegia or cardioplegia guided by continuous electrical monitoring.

Material and methods

Nineteen adult dogs, weighing between 25 and 30 kg, were randomized to receive high-volume cardioplegia or cardioplegia guided by voltage monitoring during 90 min ischemia. The commercially available crystalloid cardioplegia solution contained 25 mEq potas-
sium per litre and was delivered at a temperature of 4°C. The high-volume group received 25 cm³/kg bodyweight crystalloid cardioplegia which was infused at a rate of 200 cm³/min after application of the aortic cross-clamp with reinfusion of 25 cm³/kg at 0.5-h intervals during the 90-min arrest. The voltage group received 10 cm³/kg crystalloid cardioplegia after clamping of the aorta to initiate an electrical arrest (voltage less than 15 μV). Cardioplegia was reinfused in 100-μl aliquots for any two-fold increase in the voltage until the intramyocardial voltage returned to the arrest potential of less than 15 μV. Thus, the electrical potential was always maintained below 15 μV during the entire 90 min of ischemia.

**Surgical preparation**

The animals were anaesthetized with Somnotol and ventilated with a Bird Mark 7 pressure-regulated ventilator. Pancuronium bromide (0.1 mg/kg) was administered intravenously following intubation. The chest was opened through a median sternotomy and the femoral arteries were exposed bilaterally. Heparin was then administered at a dose of 4 mg/kg. A 16F USC1 arterial catheter was inserted into the left femoral artery in preparation for cardiopulmonary bypass and an 8F USC1 catheter was positioned in the right femoral artery for continuous blood pressure monitoring. A 7F Swan-Ganz thermodilution catheter was introduced into the pulmonary artery and a 5F Millar catheter-tipped transducer was passed through the apex of the left ventricle for determination of the maximum rate of rise of left ventricular pressure (dp/dt) and for the measurement of left ventricular end diastolic pressure. A 16F USC1 catheter was then passed through the wall of the right atrium and manipulated into the coronary sinus. The flanged catheter fit snugly into the coronary sinus, which ensured that coronary sinus drainage through the catheter represented the entire coronary sinus flow. Two 34F USC1 cannulas were inserted into the superior and inferior venae cavae and cardiopulmonary bypass was established with a Medtronic impeller pump model 1810 which was infused at a rate of 200 cm³/min after application of the aortic cross-clamp with reinfusion of 25 cm³/kg bodyweight crystalloid cardioplegia reservoir.

Electrical activity was recorded from the myocardium with specially designed plunge electrodes that were positioned over the anterior surface of the left ventricle and were placed in close proximity to the thermistors which measured intramyocardial temperature. The technical details have been described in an earlier report [6]. The root mean square (RMS) of the intramyocardial voltage was monitored with an in-line Fluke R40A voltmeter and an RMS-to-DC converter. Intramyocardial voltage was recorded before clamping of the aorta during ventricular fibrillation and was continuously monitored during the arrest.

**Left ventricular function and myocardial oxygen consumption**

Cardiac index, left ventricular stroke work index and dp/dt were measured before bypass and at 90 mm Hg and 45 min reperfusion. These measurements were made at a heart rate of 150 beats per minute and at a preload of 10 mm Hg. The heart was atrially paced when the heart rate was less than 150 beats/min and left ventricular end diastolic pressure was adjusted to 10 mm Hg by infusing or withdrawing volume through the femoral arterial catheter.

Myocardial oxygen consumption was calculated from coronary sinus flow and oxygen saturations by a standard formula [10]. Coronary sinus flow was collected for a period of 60 s and the average of at least three flows was used for calculation of myocardial oxygen consumption.

**High-energy phosphates and myocardial ultrastructure**

Biopsies for investigation of adenosine triphosphate (ATP) and electron-microscopic ultrastructure were obtained with a Travenol needle before bypass and at 15 and 45 min after ischemic arrest. The method for obtaining and analyzing these specimens has been described elsewhere [7]. Photographs of electron-microscopic ultrastructure were examined by a pathologist in a blinded fashion. Each specimen was coded by a pathologist in a blinded fashion: each specimen was coded by the specimen’s relationship to the experimental protocol. Injury to the cellular ultrastructure was graded using a system described by Breyer and associates [1].

**Statistical analysis**

The results are reported as the arithmetic mean ± the standard error of the mean. Student’s t-test and analysis of variance were utilized for statistical comparisons.
Results

Nine animals received high-volume cardioplegia (HV-plege). A total of $1710 \pm 81 \text{ cm}^3$ was administered to this group during the 90-min arrest. Significantly less cardioplegia was administered to those animals receiving cardioplegia guided by voltage criteria (V-plege group): the total volume measured $566 \pm 66 \text{ cm}^3$ ($p < 0.0001$). The voltage data are illustrated in Table 1. Intramyocardial voltage, measured during hypothermic fibrillation at $30^\circ C$ and just prior to clamping of the aorta, was $662 \pm 48 \mu V$ in the HV-plege group and $556 \pm 41 \mu V$ in the V-plege group. The infusions of cardioplegia resulted in a dramatic decrease in the intramyocardial voltage in both groups, reducing the RMS voltage to less than $15 \mu V$ in all animals. Small-amplitude electrical activity occurred within 10–15 min after the infusion of cardioplegia in those animals receiving cardioplegia guided by voltage criteria. The onset of small-amplitude electrical activity was heralded by a two- to three-fold increase in the electrical potential of the myocardium (see Table 1). This group required a total of 37 infusions of cardioplegia to maintain the intramyocardial voltage below $15 \mu V$ during the arrest. Small-amplitude electrical activity was also recorded from the myocardium in those animals receiving high-volume cardioplegia. However, the higher volume of cardioplegia administered to this group reduced the incidence of small-amplitude electrical activity to a total of 26 episodes. The activity occurred within 15 min after the infusion of cardioplegia and persisted until reinfusion of cardioplegia on the half hour.

Transmural myocardial temperature was similar in both groups and was maintained between $8^\circ$ and $10^\circ C$ with topical cooling and multidose cardioplegia. The administration of high-volume cardioplegia had no demonstrable effect on myocardial temperature, which was undoubtedly due to the fact that myocardial temperature was maintained within a range of $8^\circ – 10^\circ C$ by the application of topical cooling to the myocardium in both groups.

Left ventricular function and myocardial oxygen consumption

The indices of left ventricular function have been summarized in Table 2. We have presented the results as the decrement in each index of left ventricular function, since each animal in each group served as its own control. Left

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<th>Table 1. Intramyocardial voltage (mean ± SEM)</th>
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SAEA, Small-amplitude electrical activity

* $p < 0.003$

* $p < 0.002$
ventricular function was depressed in all animals after 90 min ischemia and 45 min reperfusion. Those animals receiving HV-plege, however, had a significantly greater reduction of cardiac index, left ventricular stroke work index and rate of rise of left ventricular pressure (dp/dt) following the arrest. Myocardial oxygen consumption was also significantly lower in those animals receiving high-volume cardioplegia. Myocardial oxygen consumption decreased by 1.4 ± 0.5 cm³/min 100 g myocardium in those animals receiving HV-plege and by 0.2 ± 0.4 cm³/min 100 g myocardium in those animals receiving V-plege (p < 0.01).

### High-energy phosphates and myocardial ultrastructure

ATP was measured in μM/g dry weight of cardiac muscle. ATP measured 34.5 ± 2 μM/g in the HV-plege group and 32.3 ± 1 μM/g in the V-plege group before bypass. Ninety minutes of ischemia and 45 min reperfusion resulted in a decrease in myocardial high-energy phosphate concentration in both groups. After 15 min reperfusion ATP had decreased by 0.3 ± 2 μM/g in the HV-plege group and by 0.7 ± 2 μM/g in the V-plege group (p < 0.5). By 45 min ATP had decreased by 4.9 ± 2 μM/g in the HV-plege group and by 4.4 ± 2 μM/g in the V-plege (p < 0.9).

Electron microscopy demonstrated significantly more damage to the myocardial ultrastructure in those animals that had received high-volume cardioplegia. Representative photomicrographs are shown in Fig. 1. Analysis of variance indicated that there was more cellular oedema (p < 0.005), increased mitochondrial disruption (p < 0.025), and disruption of myofibrils (p < 0.05) in the HV-plege group.

### Discussion

Cardioplegia protects the myocardium during elective cardiac arrest by reducing myocardial energy requirements. Myocardial oxygen consumption is lowered by preventing electromechanical activity and decreasing myocardial temperature. Although mechanical activity ceases after cardioplegia, electrical activity has been recorded from the myocardium during cardioplegia arrest by independent investigators [4, 6]. The electrical activity is of small amplitude and low frequency, becomes apparent within 10–15 min after the infusion of cardioplegia, and may persist for as long as 30 min before the resumption of gross electromechanical activity [8]. Spectral analysis of the recordings of small-amplitude electrical activity has shown that the fundamental frequency lies within a range of 3.0–3.5 Hz and that the waveform resembles that of ventricular fibrillation, although the electrical potentials are of a much smaller amplitude [6, 8]. Our laboratory has further characterized small-amplitude electrical activity by measuring the voltage of the myocardium during cardioplegia arrest [8]. The infusion of cardioplegia reduces the voltage of the hypothermic fibrillating heart at 30°C from a range of 400–800 μV to less than 20 μV. The onset of small-amplitude electrical activity is heralded by a two- to three-fold increase in the magnitude of the electrical potential, the increase in the electrical potential coinciding with the onset of small-amplitude fibrillation. Although the significance of small-amplitude electrical activity is not fully understood, we have shown that small-amplitude electrical activity during cardioplegia arrest may cause impaired myocardial metabolic and functional recovery [7, 8].

Although there have been considerable improvements in the composition of chemical cardioplegia and the techniques of delivery, there is still no reliable monitoring technique that may be used to guide the administration of cardioplegia. Myocardial temperature is monitored by most surgeons during cardioplegia arrest. However, profound myocardial hypothermia does not guarantee optimal metabolic and functional recovery. Furthermore, numerous earlier investigations have demonstrated that electrical activity may reoccur despite the fact that the myocardial temperature is maintained within the range of 10°–15°C [4, 6–9]. Wilson and associates [12] monitored intramyocardial pH during cardioplegic arrest and found that progressive acidosis occurred during profound hypothermia and that the acidosis was not ameliorated by the use of cardioplegia. Khuri and colleagues [5] monitored intramyocardial pH in 40 patients undergoing cardiac operations. Myocardial protection was provided with a combination of systemic cooling, multidose crystalloid cardioplegia and topical cooling. Accumulation of hydrogen ions occurred in some of these patients during ischemic arrest. Although acidosis was associated with a poor outcome, continuous intramyocardial pH monitoring did not predict the requirements for cardioplegia. More recently, our laboratory has suggested that electrical monitoring may provide useful data for guiding the administration of cardioplegia, since myocardial electrical activity reflects the presence of myocardial metabolic activity during cardioplegia arrest [8, 9]. Electrical monitoring of the myocardium during cardioplegia arrest requires a complex monitoring system that may not be easily introduced into the clinical setting. Thus, we have investigated the effects of high-volume cardioplegia on the electrical status of the myocardium in order to determine whether an increase in the volume of cardioplegia would prevent residual electrical activity.

High-volume cardioplegia reduced the incidence of small-amplitude electrical activity but did not prevent electrical activity during cardioplegia arrest. Furthermore, high-volume cardioplegia may have adversely affected myocardial metabolic and functional recovery.
Cardiac index, left ventricular stroke work index and the maximum rate of rise of left ventricular pressure were significantly lower in those animals receiving high-volume cardioplegia. Although the decrease in left ventricular function may have resulted from the presence of persistent electrical activity during cardioplegia arrest, the marked disruption of myocardial ultrastructure observed in this group would more likely have resulted from the cardioplegia technique. Examination of myocardial ultrastructure demonstrated an inordinate degree of cellular oedema and damaged intracellular organelles. This degree of injury has only been observed in animals that have had prolonged small-amplitude electrical activity that has persisted for 30–45 min during ischemic arrest [7]. Considering that large volumes of cardioplegia were administered every 30 min, that myocardial temperature was maintained within a range of 8°–15°C, and that small-amplitude electrical activity was never present for more than 10–15 min before the reinfusion of cardioplegia, one must assume that the large volume of cardioplegia administered to the HV-pleg group must have influenced the degree of cellular injury by promoting myocardial oedema. However, since myocardial metabolic and functional recovery were impaired in both groups, one must surmise that the non-oxygenated cardioplegia solution may not have fully protected the myocardium during the 90 min ischemia. This conclusion is supported by the observation that left ventricular function decreased in both groups after the arrest and also by the observation that high-energy phosphates tended to be lower in both groups during the period of reperfusion.

Early investigations that have examined the effects of high-volume cardioplegia on myocardial functional recovery have met with conflicting results. DeWitt and colleagues [2] reported increased washout of adenine nucleotides and impaired functional recovery following the use of high-volume cardioplegia while Saydjari and associates [11] suggest that high-volume cardioplegia improved myocardial protection. Engelman and associates [3] examined the effects of high-volume cardioplegia in 41 patients undergoing myocardial revascularization. Early metabolic recovery, as indicated by increased myocardial oxygen consumption and decreased lactate production, was somewhat better in those patients receiving high-volume cardioplegia. The benefits, however, were shortlived, and within 20 min following the arrest both groups had attained similar levels of myocardial metabolic recovery. Although the effects of high-volume cardioplegia on myocardial metabolism are uncertain, our data suggest that high-volume cardioplegia may increase cellular water and impair myocardial functional recovery, as indicated by increased myofibrillar and mitochondrial destruction and increased cellular oedema.

Our data indicate that the onset of small-amplitude electrical activity usually occurs within 10–15 min after the infusion of cardioplegia and that the electrical potentials persist in the absence of electromechanical activity until cardioplegia is reinfused. High-volume cardioplegia does not prevent small-amplitude electrical activity, and may actually potentiate myocardial injury. We therefore suggest that small volumes of cardioplegia should be reinfused every 15 min during cardioplegia arrest in order to minimize the incidence of small-amplitude electrical activity.

References


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