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Limited Sanguineous Reperfusion Reduces Ventricular Fibrillation Following Intermittent Cold Crystalloid Cardioplegic Arrest

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Abstract

Background: Cold crystalloid cardioplegic arrest remains a well recognised method of myocardial protection. This strategy does not allow for a controlled hyperkalaemic sanguineous reperfusate, known as a "hot shot" which is administered under constant flow and pressure conditions in order to limit reperfusion injury. We investigated the use of intermittent, antegrade cold crystalloid cardioplegia (St Thomas' I solution) combined with a limited flow normokalaemic sanguineous reperfusion and measured the outcome in terms of the incidence of reperfusion ventricular fibrillation.
Methods: Patients requiring coronary revascularization of at least two coronary arteries, including an internal thoracic artery (ITA) anastomosis, were studied in this prospective randomized trial. Myocardial protection was by intermittent, antegrade cold crystalloid cardioplegia. In the control group (n=100), after completion of the distal anastomoses, the heart was reperfused by releasing the aortic and ITA clamps concomitantly. In the study group (n=100) the ITA was allowed to perfuse the heart for 3 minutes before the aortic cross-clamp was removed. The presence of reperfusion ventricular fibrillation from the moment of reperfusion until weaning from cardiopulmonary bypass was recorded.
Results: Mean ischaemic times varied marginally between the study and control groups (study 35.60±8.65, control 35.79±10.64, p=0.89). The incidence of ventricular fibrillation decreased with an increase in the number of grafts and was significantly lower in the study group (double grafts 2/9, 22.2% vs 19/25, 76.0% p=0.004; triple grafts 2/39, 4.9% vs 16/33, 48.5% p<0.001; and quadruple grafts 2/45, 4.4% vs 13/35, 28.7% p<0.001).
Conclusions: This strategy of myocardial protection combines the advantages of conventional crystalloid cardioplegia with the added benefit of limited sanguineous reperfusion. It is cost-effective and simple to apply. The results suggest a beneficial effect with regard to reperfusion-induced injury, as evidenced by a significantly reduced incidence of reperfusion ventricular fibrillation.

Keywords: crystalloid cardioplegia; sanguineous reperfusion; ventricular fibrillation

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Introduction

A still and bloodless operative field provides the surgeon with optimal conditions to perform delicate coronary anastomosis, while effective myocardial protection avoids myocardial injury during this process.1 Cold crystalloid cardioplegia has been the cornerstone of this strategy by inducing electromechanical arrest and further reducing oxygen demand with hypothermia.2 In spite of demonstrable improvements attributed to blood-based hyperkalaemic solutions,3,4 including superior preservation of myocardial and coronary endothelial function, 5,6 especially in the setting of a dysfunctional or ischaemic myocardium,7-9 crystalloid solutions remain in widespread use. The technique of warm substrate-enhanced sanguineous reperfusion, delivered under controlled flow and pressure, is recognized as a valuable adjunct to blood-based cardioplegia, but is not part of the crystalloid protocol. Popularly known as the 'hot shot', it provides endogenous oxygen free radical scavengers and prevents myocardial substrate derangement.10,11 However, simple normokalaemic blood reperfusion, under certain conditions, and without substrate enhancement, may still attenuate reperfusion injury by providing acid-base homeostasis via the bicarbonate buffering system.12 The method of its administration may partly reproduce the controlled pressure and flow conditions in the hot shot, by limiting the initial blood flow during early reperfusion.

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The occurrence of early ventricular fibrillation (VF) after cross-clamp removal is a manifestation of reperfusion injury,13 the consequences of which also include myocardial stunning,14 microvascular obstruction15 and myocardial necrosis.16 Reperfusion-induced arrhythmias are reduced by cardioplegic protection during ischaemia and their occurrence bears an inverse relationship to ischaemic time.17 The prevention of VF by pharmacologic means has been attempted with a view to reducing subsequent myocardial damage.18

In this study we retained the protocol of antegrade intermittent cold crystalloid cardioplegic arrest and combined this with limited sanguineous normokalaemic reperfusion, initially allowing flow only via the ITA, before establishing full reperfusion by cross-clamp removal. We measured the occurrence of early VF as a marker of reperfusion injury and investigated this method of reperfusion as a possible means of attenuating this injury.

Methods

Patients requiring coronary revascularization of two or more coronary arteries, including at least one internal thoracic artery (ITA) anastomosis, were randomized to a control or study group in this prospective trial. Patients requiring routine or urgent (performed during the same week as referral) surgery were recruited whereas patients requiring emergency surgery were excluded. Informed consent was obtained from each patient and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priory approval by our institution's human research committee.

Normothermic cardiopulmonary bypass was employed. After application of the aortic cross-clamp, cold crystalloid cardioplegia (St Thomas' I solution) was administered into the aortic root as an initial dose of 500ml, and continued when necessary if complete cardiac standstill and uniform cooling was not attained (figure 1).

This initial dose was followed by additional 100ml doses after each distal anastomosis. This additional dose was omitted before the last (ITA) anastomosis to the left anterior descending artery (LAD). No topical cooling of the heart was employed. Patients were prospectively randomized into a control or study group. In the control group (n=100) the aortic cross-clamp was removed concomitantly with ITA reperfusion. In the study group (n=100) the ITA was allowed to perfuse the heart for 3 minutes before the aortic cross-clamp was removed (figure 2). Cardiopulmonary blood flow was transiently reduced during cross-clamp removal. Manipulation of the heart was avoided during the 3 minute ITA reperfusion period in the study group and during the 3 minutes after cross-clamp removal in the control group. The occurrence of VF was recorded from the moment of reperfusion, by whichever method, until the weaning of the patient from cardiopulmonary bypass.

Table 1. Patient characteristics

	study	control	p value
age	58.8±8.8	57.2±9.2	0.21
female	15	8	0.12
ischaemic time*	35.60±8.65	35.77±10.64	0.89
ejection fraction**	63.57±13.65	60.76±14.36	0.16
urgent surgery	31	24	0.36
EuroSCORE	4.96±1.56	4.99±1.99	0.91

* mean ischaemic time for entire groups
** ejection fraction measured by ventriculography

Statistical Methods

Means and standard deviations were used to measure central tendency and dispersion for continuous variables and frequency tables and crosstabs were used to describe categorical variables. The Independent samples t-test was used to compare mean ages and mean ischaemic times between the study and control groups given that both variables satisfied the normality assumption. The Mann Whitney test was used to compare the initial dose of cardioplegia in the two groups, which did not satisfy a normal distribution. The chi square test was used to compare the incidence of ventricular fibrillation in the study and control groups for different number of grafts. In both tests a 0.05 level of significance was adopted.

Results

Age (study 58.8±8.8, control 57.2±9.2, p=0.21), gender distribution (study 15% female, control 8% female, p=0.12) initial cardioplegia dose (study 584.5±143.5ml, control 590.2±133.6ml, p=0.856), and overall ischaemic times were similar in both groups (study 35.60±8.65, control 35.79±10.64, p=0.89). Study and control characteristics are presented in table 1. The distribution of grafts per case and their respective ischaemic times are shown in figure 3.

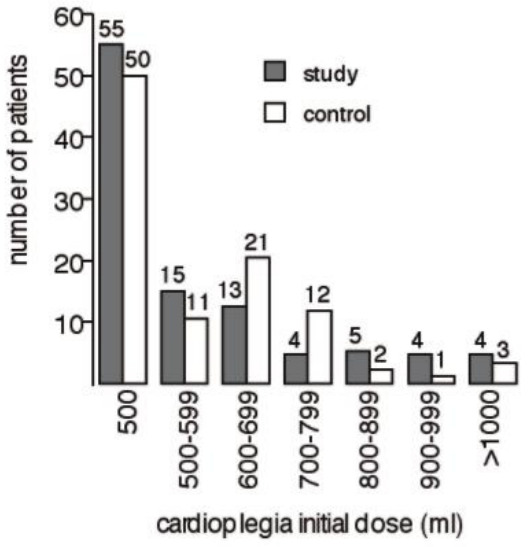

Figure 1. Initial dose of cardioplegia

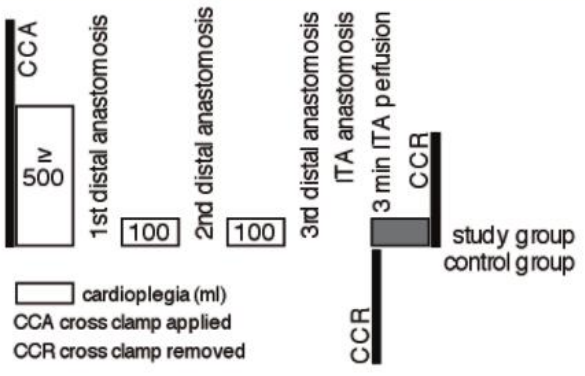

Figure 2. Protocol for myocardial protection

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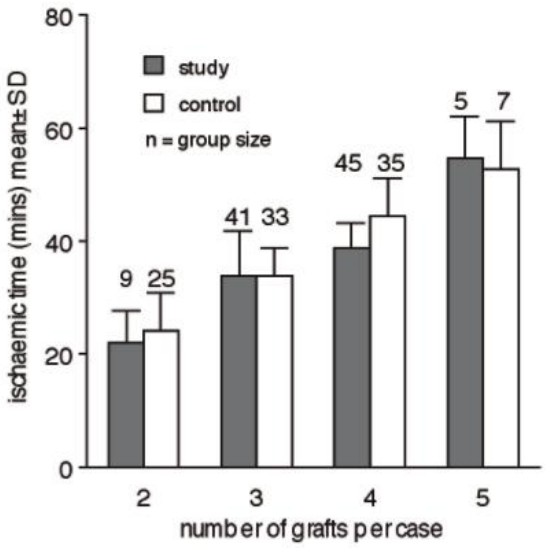

Figure 3. Mean ischaemic time ±SD clustered by group and number of grafts. Figures above bars indicate group size

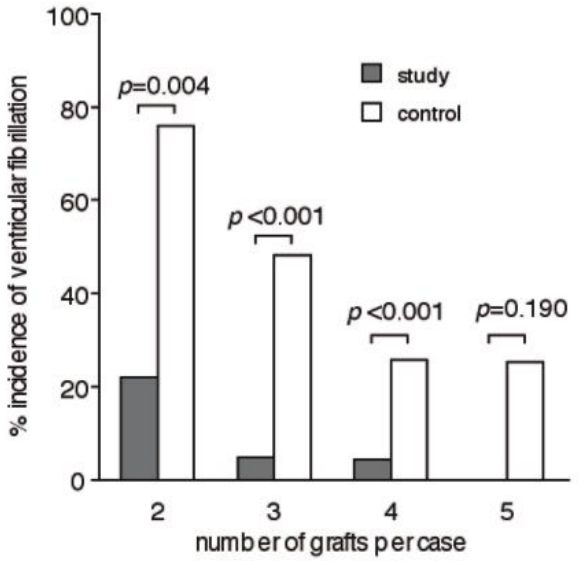

Figure 4. Incidence of ventricular fibrillation clustered by group and number of grafts

In the absence of VF, both control and study patients exhibited complete electrical quiescence or infrequent contractions during the 3 minutes of reperfusion. The incidence of ventricular fibrillation decreased with an increase in the number of grafts, down to a baseline of around 28% in the control group, and was significantly reduced in the study group for double (2/9, 22.2% vs 19/25, 76.0% p=0.004), triple (2/39, 4.9% vs 16/33, 48.5% p<0.001) and quadruple grafts (2/45, 4.4% vs 13/35, 28.7% p<0.001). VF did not occur with quintuple grafts in the study group, while it occurred in 2/7 patients (28.6%) in the control group (figure 4).

Discussion

Although the separate manifestations of ischaemia-reperfusion injury are expressed to varying degrees depending on the length of ischaemia, it is generally accepted that their expression is quantitatively related to the magnitude of the ischaemic insult. Thus, infarct size19 and global ventricular dysfunction20 although attenuated by cardioplegic protection, bear a direct relationship to ischaemic duration. The incidence of reperfusion VF has been shown, in a blood-perfused animal model, to exhibit an inverse relationship with ischaemic time, even after crystalloid cardioplegia administration.17 This relationship is also manifest in the clinical setting of this study of global ischaemia and reperfusion during coronary surgery. The attenuation of reperfusion arrhythmias can therefore be interpreted as a surrogate of other deleterious effects of ischaemia-reperfusion.

Diverse strategies have been investigated with the aim of reducing reperfusion injury, especially in the percutaneous coronary intervention setting.21-24 The hot shot was popularized to provide such a protection in the surgical setting of global ischaemia. Our method of reperfusion differs from the hot shot not only in its composition, but also in its limited distribution, with reperfusion initially confined to the LAD territory. In spite of these fundamental differences this method of reperfusion significantly reduced the incidence of VF.

For the many surgeons who still employ crystalloid cardioplegia, we describe a simple modification of reperfusion, which significantly reduces reperfusion VF, a marker of other, more serious manifestations of the ischaemia-reperfusion injury. This method is simple to apply, does not significantly lengthen the surgery, incurs no additional equipment or cost, and significantly reduces the incidence of reperfusion VF thereby reducing the necessity for topical defibrillation.25

Limitations

The study is relatively small and confined to a single surgeon practice. Patients who required emergency surgery were excluded and it is possible that in such cases this method of reperfusion may have been more beneficial. Other parameters of reperfusion injury, such as markers of myocardial damage, were not investigated in this study.

Conclusion

In conclusion we describe a method of limited sanguineous normokalaemic reperfusion via the internal thoracic artery, in the setting of coronary revascularisation using intermittent cold crystalloid cardioplegia. This simple, no-cost protocol significantly diminished the incidence the incidence of ventricular fibrillation, a marker of reperfusion-induced injury, and should improve myocardial protection and efficacy of the cold crystalloid cardioplegia technique.

Declarations of interest

The authors declare no conflicts of interest.

Acknowledgements

The authors agree to abide by the requirements of the “Statement of publishing ethics of the International Cardiovascular Forum Journal” [26].

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