Cold crystalloid cardioplegia

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Cold crystalloid cardioplegia is clinically used since the mid-1960s. It is currently applied in adult and pediatric cardiac surgery patients and remains the preferred method of myocardial protection for many cardiac surgeons. This chapter gives a brief overview about the technical aspects of cold crystalloid cardioplegia application in the operating room.

Keywords: Cardioplegia; Ischemia-reperfusion injury; Myocardial protection

Introduction

Effective myocardial protection remains the key element for success in heart surgery. The clinical introduction of cold crystalloid cardioplegic solutions, beginning in the mid-1960s [1,2], may be considered an essential prerequisite for many of the more complex cardiac surgical procedures, which have been developed since that time. Since the 1990s, blood cardioplegia in its numerous variations has found broad clinical application and has added considerable complexity to the field of myocardial protection. Nevertheless, in many institutions around the world, cold crystalloid cardioplegia remains the preferred method of myocardial protection, due to its satisfactory clinical results, institutional experience, and individual surgeon’s preference.

In principle, cold crystalloid cardioplegia protects the myocardium by hypothermia and electromechanical arrest, both of which reduce the myocardium’s metabolic demands and thus, prolong its tolerance to ischemia. Based on the pharmacological mode of action, two types of cold crystalloid cardioplegic solutions may be discriminated: the intracellular and the extracellular solution type. Intracellular type crystalloid solutions contain no or low concentrations of sodium and calcium, whereas extracellular type solutions contain higher concentrations of sodium, calcium, and magnesium. Both types contain potassium between 10 and 20 mmol/l, and may have added osmotically active substances such as mannitol, local anaesthetics such as lidocaine and procaine, as well as buffers such as bicarbonate and amino acids. Examples for intracellular and extracellular crystalloid cardioplegias are Bretschneider’s solution (CUSTODIOL® – MMCTSLink 86) and Hospital of St. Thomas solution No. 2 (Plegisol®, MMCTSLink 87), respectively (Table 1).

Surgical technique

The patient is placed on cardiopulmonary bypass in the usual fashion. Although most surgeons prefer to subject the patient to mild or moderate hypothermia (34–28 °C), some surgeons apply cold crystalloid cardioplegia during normothermia, particularly if the anticipated crossclamp time is brief. After cross-clamping the aorta, the cardioplegic solution is infused into the aortic root via a catheter inserted in the ascending aorta proximal to the cross-clamp. In case of aortic valve incompetence, the ascending aorta is incised approximately 2 cm above the level of the coronaria ostia which are thereafter selectively cannulated under direct vision. For this purpose a variety of catheter designs in different diameters is commercially available. In most cases, for the left coronary ostium, a cannula 3.5–4.0 mm in diameter angled at 135°, and for the right ostium, a 90° cannula.
Table 1. Composition of cardioplegic solutions

<table>
<thead>
<tr>
<th></th>
<th>Sodium</th>
<th>Potassium</th>
<th>Magnesium</th>
<th>Calcium</th>
<th>Bicarbonate</th>
<th>Other components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Custodiol® (HTK)</td>
<td>15</td>
<td>9</td>
<td>4</td>
<td>0.015</td>
<td>–</td>
<td>Histidin, Tryptophan, potassium-hydrogen-2-ketoglutarate</td>
</tr>
<tr>
<td>Plegisol® (St. Thomas No. 2)</td>
<td>110</td>
<td>16</td>
<td>16</td>
<td>1.2</td>
<td>10</td>
<td>Lidocaine</td>
</tr>
<tr>
<td>Lactated Ringers</td>
<td>130</td>
<td>24</td>
<td>–</td>
<td>1.5</td>
<td>–</td>
<td>Lactate, chloride</td>
</tr>
</tbody>
</table>

Example for composition of intracellular (Custodiol®) and extracellular (Plegisol®) cardioplegic solutions. All numbers in mmol/l.

Video 1. The patient is cannulated in the standard fashion for CABG surgery: arterial cannulation of ascending aorta, venous return via a two-stage cannula in the right atrium, and for cardioplegia delivery an aortic root cannula with a sideline for venting. On CPB, the aorta is crossclamped, and the heart is unloaded by suction on the sideline of the aortic root cannula. When the left ventricle is sufficiently unloaded, which is usually the case after about 10–20 s, the venting sideline is closed, and infusion of cold crystalloid cardioplegia is commenced. At this point, it is important to note sufficient closure of the aortic valve, so that the cardioplegic solution flows into the coronaries rather than the left ventricular cavity. Closure of the aortic valve may be facilitated by increasing the perfusion pressure in the aortic root. The gradual cessation of mechanical and electric myocardial activity is closely observed. Cardiac arrest may be aided by external cooling with normal saline at 4°C.

Video 2. Due to aortic regurgitation, antegrade cardioplegia delivery required selective cannulation of the coronary ostia in this patient. Venous drainage has been accomplished by bicaval cannulation. Bicaval cannulation and total CPB allow suction removal of the cardioplegic solution from the right atrium to minimize hemodilution. After aortic crossclamp, the ascending aorta is incised approximately 2 cm above the level of the coronary ostia which are thereafter selectively cannulated under direct vision. The right atrium is incised and clear cardioplegic solution is removed by suction upon its exit from the coronary sinus. with a diameter of 3.0–3.5 mm, will suffice. Possible pitfalls during selective cardioplegia administration directly into the coronary ostia, which must be avoid-
ed, are the displacement and subsequent embolisation of coronary calcifications and inadequate cardioplegia delivery due to unrecognised coronary abnormalities, such as separate ostia for the LAD and LCX. Once the route for antegrade cardioplegia delivery is established (either aortic root catheter or selective delivery in coronary ostia), the infusion of iced (4°C) cold crystalloid cardioplegia is commenced. The total volume of infused cardioplegic solution and the rate of infusion varies greatly depending on the applied solution and institutional experience. As a rule of thumb, perfusion pressure for antegrade delivery may be kept between 50 and 80 mmHg and a volume around 1000 ml will suffice for adequate cardioplegic arrest in most adult patients. Some surgeons prefer to continue cardioplegia infusion for 1 or 2 min after complete cessation of all mechanical and electric activity of the heart. If the heart resumes electrical activity during the procedure or if a prolonged cross-clamp time is anticipated, additional doses of 200 to 500 ml of the cardioplegic solution may be administered at intervals. It has to be considered, that the administered volume of crystalloid cardioplegic solution contributes substantially to hemodilution during CPB. In the case of bicaval venous cannulation with total CPB, this hemodilution effect can be minimized by incision of the right atrium and suction removal of the circulated cardioplegic solution upon its exit from the coronary sinus. Optionally, cold crystalloid cardioplegia can also be administered in a retrograde fashion via the coronary sinus by use of a coronary sinus cannula, with or without a self-inflating cuff. Perfusion pressure during retrograde cardioplegia infusion may not exceed 40 mmHg to avoid myocardial edema formation (Videos 1 and 2, and Photo 1).

Results

Since its clinical introduction in the late 1960s, the efficacy of myocardial protection by cold crystalloid cardioplegia has been demonstrated in numerous studies [3,4]. More recently, the clinical outcome after cold crystalloid cardioplegia has been compared to
Photo 1. Cannulae for cardioplegia delivery. From top to bottom: coronary sinus cannula for retrograde cardioplegia delivery (MMCTSLink 88), two cannulae for direct antegrade cardioplegia delivery into the coronary ostia: 135° cannula for left and 90° cannula for right coronary artery and cannula for cardioplegia delivery into the aortic root (MMCTSLink 89).

current techniques of blood cardioplegia in controlled randomised clinical trials [5–9]. The CABG Patch Trial enrolled high risk patients with coronary artery disease and found no difference in early or late survival, despite significantly higher post-operative morbidity in the cold crystalloid cardioplegia group [5]. In CABG patients not specifically stratified for high risk, mortality and post-operative morbidity showed no significant difference between blood and cold crystalloid cardioplegia [6]. Myocardial damage during CABG surgery, evaluated by measuring creatinine kinase-MB (CK-MB) and cardiac troponin I (cTnI) release, was significantly lower in patients who received warm blood cardioplegia as in comparison to patients with either cold crystalloid or blood cardioplegia [7]. Interestingly, no difference was seen between cold crystalloid and cold blood cardioplegia [7]. In paediatric patients, results of randomised studies seem to indicate better myocardial preservation by blood cardioplegia in comparison to crystalloid solutions. One study found in cyanotic paediatric patients with the application of blood cardioplegia better conservation of cellular metabolism measured by ATP levels, however, no difference was seen in mortality and post-operative morbidity [8]. Another randomised trial in paediatric patients showed better preservation of myocardial metabolism and improved left ventricular function early after weaning from CPB in the blood cardioplegia group [9]. As in the latter study, this investigation showed no difference in clinical outcome between the different cardioplegia groups [9].

Lately, new pharmacological agents, such as free radical scavengers and Na⁺/H⁺ exchange inhibitors have been investigated as additives to crystalloid cardioplegic solutions [10–12]. However, a clear clinical benefit in terms of improved patient outcome remains to be demonstrated for these cardioplegia additives.

How common is the use of crystalloid cardioplegia currently? According to a recent survey, conducted in the UK and Ireland, 84.3% of surgeons used cardioplegia and 15.7% used intermittent cross-clamp and fibrillation techniques for on-pump CABG. Of those, who used cardioplegia, 83.5% chose blood cardioplegia and 16.5% crystalloid cardioplegia [13].

Discussion

Cold crystalloid cardioplegia has been clinically used for almost 40 years. However, there is still considerable controversy regarding the ‘ideal’ cardioplegic technique and solution, not only with respect to different crystalloid cardioplegia solutions, but in particular with respect to crystalloid versus blood cardioplegia. Although recent randomised trials have shown improved metabolic and functional myocardial preservation with blood cardioplegia, a clear clinical benefit in terms of decreased mortality and morbidity was not consistently demonstrated in the comparison between blood and crystalloid cardioplegia. Therefore, institutional and the individual surgeon’s experience remain the most important determinants of myocardial protection strategy at this moment.

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