SUPPLEMENTAL MATERIAL

Variants and Evidence Supporting Common Myocardial Preservation Practices

Cardioplegia Type (Common Varieties: Blood, Crystalloid, Microplegia)

Cardioplegia has been the focus of immense investigation, with blood and crystalloid being the most commonly used. Crystalloid was introduced as an arresting agent and may have theoretical advantages over its blood counterpart in terms of increased visualization afforded during construction of the anastomoses, reduced cost, and equivalency of some clinical endpoints.\(^1\) Nonetheless, in a randomized trial of 140 patients undergoing urgent CABG surgery for unstable angina, patients protected with blood (n=70) relative to crystalloid cardioplegia had lower rates of mortality (0 vs. 5%, p<0.05), MI (4 vs. 14%, p<0.05) and LOF (10% vs. 19%, p<0.05).\(^2\) Moreover, in a meta-analysis by Guru, blood cardioplegia was associated with significant reductions in rates of LOF relative to crystalloid cardioplegia [LOF, (OR 0.54, p=0.006), although non-significant reductions in MI (OR 0.78, p=0.19) and mortality OR 0.80, p=0.44)].\(^1\) Another variant of cardioplegia is microplegia, which delivers precise constitution and amounts of cardioplegia. Its theoretical advantages lie in its ability to mix pure blood with potassium.\(^3\) While a limited body of knowledge supports microplegia’s use, prior work has found it to be a safe alternative for delivering cardioplegia\(^4\), and reducing myocardial edema.\(^5\)

Cardioplegia Temperature (Common Varieties: Cold, Tepid, Warm)

A number of temperature practices exist, including delivery of cold (<28°C), tepid (28-34°C), and normothermic (35+°C) cardioplegia. While hypothermic delivery seeks to reduce the heart’s metabolic demand and provide myocardial preservation for extended periods of ischemic arrest\(^6\), \(^7\), generation of adenosine tri-phosphate (ATP) is
Normothermia theoretically improves myocardial preservation by maximizing oxygen extraction, decreasing lactate production, preserving aerobic metabolism and myocardial enzymatic functions. The Warm Heart Investigators reported its advantage, relative to hypothermia.\(^9\) Due to the detrimental effects of overly warming the brain during normothermia, clinicians may use tepid cardioplegia, which theoretically provides the beneficial effects of warm heart surgery while offsetting risk of neurological injury.\(^9\) Another variant of a cardioplegia temperature strategy is the utilization of terminal warm blood cardioplegia ("hot shot") down the aortic root prior to removing the aortic cross clamp to reperfuse the heart and increase cardiac output. Hot shots are utilized to remove toxic by-products\(^{11}\), such as lactate, by neutralizing oxidative free radicals, thereby facilitating transition to aerobic metabolism and ATP production.\(^{12,13}\)

**Cardioplegia Dosing (Common Varieties: Continuous, Intermittent)**

Surgeons may deliver cardioplegia continuously or intermittently. Continuous cardioplegia theoretically is advantageous due to its mimicking native coronary blood flow and mitigating the potential for increased acidosis in between dosages in the setting of intermittent cardioplegia. Continuous cardioplegia, however, may cause a "wet" field and thereby obstruct the surgeon’s vision. As a consequence, some surgeons may prefer intermittent cardioplegia. Louagie conducted a small randomized trial of 70 patients undergoing intermittent (n=35) or continuous cold retrograde cardioplegia during isolated CABG,\(^{14}\) and showed that while balancing existed between the two groups in terms of pre- and intra-operative variables, patients with continuous cardioplegia had improved left ventricular stroke work index and hemodynamic performance, and reduced need for post-operative inotropic support. Nonetheless, patients receiving continuous
crystalloid cardioplegia may become hemodiluted or develop edema, and thus may be pharmacologically managed to remove water content and normalize serum potassium.15

**Cardioplegia Route of Delivery** (Common Varieties: Antegrade, Retrograde, Combination)

A number of options exist for delivering cardioplegia, including: antegrade (through aortic root, coronary ostia or via the bypassed grafts), retrograde (through the coronary sinus), or some combination of routes. A number of theoretical advantages exist to support the use of antegrade cardioplegia (whether delivered intermittently or continuously), including its mimicking of native coronary flow and ease of delivery. Its use may be restricted or of limited benefit in situations of aortic insufficiency or altered distributions of the coronary circulation secondary to coronary artery disease. Surgeons may deliver antegrade cardioplegia down the newly formed grafts, which may theoretically target myocardial preservation to the most underserved territories. The use of retrograde delivery has several theoretical benefits, including: (1) its ability to deliver cardioplegia independent of the presence or extent of coronary artery disease or aortic insufficiency, and (2) its use does not interrupt the conduct of the operation. Nonetheless, the theoretical benefit of retrograde delivery may be limited by: (1) a difficult patient anatomy that precludes its placement in the coronary sinus, and (2) its imperfect ability to perfuse the septum and right ventricle. Retrograde delivery may be associated with adverse sequelae (MI, myocardial edema and hemorrhage) during periods of excessive retrograde perfusion pressure. Jasinski and colleagues undertook a randomized study of 158 patients undergoing CABG surgery, with 89 receiving retrograde cold blood cardioplegia, and 69 receiving antegrade cold blood cardioplegia.16 While early outcomes (inotrope usage and ischemic events) favored retrograde delivery, no differences were present by 24 hours post-operatively. These findings were similar to
those reported among 224 first-time CABG patients randomized to either antegrade or retrograde cardioplegia. Given these findings, and the theoretical benefits of each approach, many surgeons may choose a hybrid approach, whereby they deliver both antegrade and retrograde cardioplegia. Onorati investigated this approach among 148 consecutive patients undergoing CABG for left main disease. In this small observational study, 87 patients underwent antegrade delivery alone, while 61 received antegrade ischemic arrest followed by retrograde cardioplegia. They found no difference in EF or wall motion abnormality, although Troponin I was higher as were rates of atrial fibrillation among patients receiving antegrade cardioplegia delivery alone.
REFERENCES


