ASSESSMENT OF MYOCARDIAL VIABILITY AND PROTECTION DURING CABG

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Dynamic imaging with stress echocardiography has been evaluated as a method to distinguish viable from nonviable myocardium. It is well recognized that regional left ventricular dysfunction is often reversible and exists in territories of viable myocardium.[1-4] Indeed, it is widely recognized that reversible segmental wall-motion abnormalities caused by transient myocardial ischemia are the hallmark of atherosclerotic coronary artery disease. During the past decade, stress echocardiography has emerged as a safe and sensitive method for the detection of coronary artery disease and it has been used to provide data for risk stratification during the perioperative period.[5-7]

The response of regional left ventricular function to dobutamine is useful to characterize myocardium. In the therapeutic dose range (5-20 μg/kg/min) cardiac output is augmented by an increase in ventricular contractility, heart rate, and stroke volume, and a β2-mediated decrease in systemic vascular resistance. Contractility increases at higher doses (20-40 μg/kg/min). Normal resting wall motion and the development of hyperdynamic function with increasing doses of dobutamine are hallmarks of normally perfused myocardium. The development of new wall motion abnormalities or the worsening of baseline systolic dysfunction with escalating doses of dobutamine increases myocardial ischemia. Contractile reserve, on the other hand, is consistent with viability and characterized by baseline wall motion abnormalities that improve with low-dose dobutamine.[9-11] When such a low-dose augmentation of function is followed by progressive systolic dysfunction with higher doses (biphasic response), the accuracy of predicting postoperative cardiac morbidity or changes in regional function after revascularization is enhanced even greater.[11] Regional segments that remain akinetic (or dyskinetic) despite dobutamine infusion are nonviable.

Dobutamine stress echocardiography, has a high sensitivity (85%) and specificity (88%) when compared to angiography in patients with recent myocardial infarction.[12] A review of data from several studies revealed overall sensitivity and specificity of the test for detecting ischemic heart disease to be 82% and 86% respectively.[8] Stress echocardiography has been shown to be an efficient method for identifying patients undergoing major vascular surgery who are at high or low risk of perioperative cardiac events.[13] In addition, intraoperative application of stress echocardiography enables the extent of myocardial salvage and viability during coronary revascularization surgery to be determined and therefore used to more reasonably direct therapeutic intervention.

Recently Aronson & colleagues demonstrated that functional changes following low dose dobutamine prior to CABG predicted functional changes post-CABG when complete revascularization was achieved. Four hundred and twenty segments in 30 patients were prospectively evaluated during elective CABG for regional wall motion changes at 4 stages including baseline (pose induction of general anesthesia, prior to cardiopulmonary bypass) and after low dose dobutamine (also prior to CPB) following separation from CPB (early) and one hour after administration of protamine (late). It was observed early ($p<0.0001$) and late ($p<0,0001$) functional changes for all regional myocardial wall motion scores.

Because there is increasing pressure to minimize cost and delays for preoperative patient evaluation intraoperative stress echocardiography may be particularly well suited for the use of patients who have known coronary artery disease or who are at high risk of postoperative cardiac morbidity.

An intraoperative paradigm that demonstrates postoperative outcome benefits and thereby, enables more efficient utilization and allocation of otherwise scarce resources, (e.g. ICU beds), would improve quality of care and reduce cost.

Understanding the relationship between ventricular function and coronary blood flow during coronary bypass surgery represents another limitation to provocative stress testing with echocardiography and has been limited by the inability to directly assess myocardial perfusion. Thallium Scintigraphy, for example, is predicted on characterization of cell membrane function of extract patterns of thallium with washout kinetics,[14] and is not practical during surgery. Thallium imaging uptake is normal in normal and stunned myocardial tissue, and decreased uptake is expected at rest in hibernating and infarcted tissue with redistribution of thallium at four hours in ischemic myocardial tissue following initial decreased uptake. Thallium (and other nuclear pharmaceuticals) perfusion imaging do not, however, provide a functional correlation to flow conditions, are time consuming and cannot be used to assess flow intraoperatively.

The goals of intraoperative assessment of bypass surgery include the ability to asses graft patency graft and anastomotic sites, identification that the correct stenosis are selected with adequate perfusion established and that a relationship between flow and function is understood before therapeutic intervention is initiated.

Previous techniques employed to understand coronary blood flow have included anatomic and hydraulic methods (measuring graft flow, probing anastomosis) as well as physiologic methods (intraoperative velocity measurements linked with assessment of coronary reserve). None of these techniques are routinely used today in larger part because they all have limitations. Recently, intraoperative myocardial contrast echocardiography (MCE) has been used to assess myocardial perfusion after myocardial revascularization.[15-19] MCE is a technique used to assess the integrity of the coronary microcirculation. The visualization of microbubbles by this technique assesses flow through vessels <100 μg in diameter and provides evidence for microvascular integrity which is a marker for viability.

Intraoperative stress-contrast echocardiography holds promise as a technique that may enable the identification of viable myocardium and differentiate ischemic dysfunction from non-ischemic dysfunction and this greatly enhances our therapeutic rationalization when treating low output syndromes. Despite this important question, no studies have yet addressed the question as to whether the identification and revascularization of dysfunctional but viable myocardium improves patient outcomes. Barill, et al.[20], reported that patients with viable myocardium treated medically had less recovery of left ventricular systolic function than those who were revascularized. Voci, et al.[21], have shown that microvascular revascularization improves functional outcome. Unfortunately, many techniques to assess revascularization only provide anatomic evidence of vessel patency rather than microvascular flow into the tissue at risk.

In patients with acute myocardial infarction and occlusion of the infarct-related artery, the presence of collateral flow by myocardial contrast echocardiography correlated with improvement in regional wall motion month after successful coronary angioplasty.[22] A subsequent study showed that in patients with documented patency of the infarct-related artery after recent myocardial infarction, there was a strong correlation between evidence of an intact microcirculation and subsequent improvement in regional wall motion. During acute myocardial infarction, patients with evidence of re-flow by myocardial contrast echocardiography in the myocardial area at risk after reperfusion therapy had greater improvement in global and regional left ventricular function on follow-up than patients with no re-flow.[23] With respect to chronic ischemia, perfusion by myocardial contrast echocardiography correlated with improvement in regional wall motion and global left ventricular function after revascularization in a population of patients with previous myocardial infarction and reduced left ventricular ejection fraction.[24]

The method and rationalization for performing intraoperative stress-contrast echocardiography has been reported and is briefly described below: The response of regional left ventricular function to the beta adrenegic receptor agonist dobutamine is useful to characterize myocardial reserve capacity. [10,11,25,26] Low dose dobutamine infusion is expected to increase regional myocardial blood flow and contractility without causing myocardial ischemia unlike high dose dobutamine, which would be expected to increase oxygen nutrient delivery mismatch in areas at risk.

Normal resting wall motion and the development of hyperdynamic function with increasing doses of dobutamine are hallmarks of normally perfused myocardium. [10,25,26] The development of new wall motion abnormalities or the worsening of baseline systolic dysfunction with escalating doses of dobutamine indicates myocardial ischemia. Contractile reserve, on the other hand, is consistent with viability and characterized by baseline regional wall motion abnormalities that improve with low-dose dobutamine. Anticipated low-dose augmentation of function would be followed by progressive systolic dysfunction if higher doses of dobutamine were used (a biphasic response).[11] The accuracy of predicting changes in regional systolic function after low dose dobutamine in chronic coronary artery disease should optimally predict function following revascularization. Left ventricular segments that remain akinetic or dyskinetic despite dobutamine infusion are nonviable and likely reflect scar. We often only infuse low dose dobutamine in order to augment baseline coronary blood flow and asses the changes in regional myocardial function reserved to be used as a gold standard to predict myocardial flow-function following revascularization.

The patients' regional function should be evaluated with intraoperative transesophageal echocardiography imaging in the transgastric short-axis, apical 4-chamber and two-chamber view, and transgastric 2-chamber view utilizing a multiple transducer. If contrast is used, then images should be recorded during and after the contrast injection. Regions of interest can be marked on the two-dimensional echocardiogram by using internal calipers to outline the segments. In the left ventricular short-axis view, the left coronary artery territory will extend from the anterior septum to the posterolateral wall. The anterior septum and anterior wall will typically be the left anterior descending territory while the lateral and posterior walls will be the circumflex artery territory. The right coronary territory will include the inferior wall and inferior septum.

The infusion of potassium rich cardioplegia solution has been instrumental in reducing the morbidity and mortality associated with open heart surgery. Optimal myocardial protection during CPB is predicated on adequate homogenous distribution of cardioplegia solution to all myocardial segments. Traditionally, the efficacy of cardioplegia perfusion has been assessed by quiescence of electrical activity on the ECG, a decrease in myocardial temperature, and direct visualization. Recently, contrast ultrasonography has been used to indicate the adequacy of cardioplegia distribution within the myocardium during cardiac surgery. [27-35]

Monitoring cardioplegia delivery with contrast ultrasound is a direct, real-time, intraoperative technique that enables the surgeon and anesthesiologist to assess the adequacy of cardioplegia distribution to all myocardial segments. Zaroff et al. [29] retrospectively investigated the relationship between immediate outcome after cardiac surgery, preoperative left ventricular ejection fraction and homogeneous delivery of cardioplegia with intraoperative contrast echocardiography in 21 patients undergoing CABG surgery. They found that low ejection fraction alone did not predict low output failure following cardiopulmonary bypass while the combination of inadequate intraoperative myocardial protection (as indicated by non-homogeneous delivery of cardioplegia to myocardial regions at risk), and low ejection fraction always predicted the need for exogenous support to separate from cardiopulmonary bypass.

Although critical, coronary artery stenosis may impair antegrade delivery of cardioplegia solutions through the aortic root and thereby contribute to perioperative ischemia and infarction, it has been shown with intraoperative contrast ultrasonography that retrograde infusion of cardioplegia provides myocardial distribution to areas subserved by the left anterior descending and left circumflex coronary arteries even in the presence of complete stenosis of these vessels. [30] Furthermore, retrograde perfusion of cardioplegia in humans has been reported to provide information regarding transmural distribution of cardioplegia with the ratio of endocardial to epicardial flow 1.46±0.27 and 1.39±0.33 in the left ventricular free wall and interventricular septum respectfully. [30]

In general, retrograde delivery of cardioplegia for myocardial protection is an approach fostered by coronary venous and arterial anatomy. Its efficacy is highly predicated on individual coronary venous drainage patterns which vary greatly. Winkelman et al.[32] has shown that retrograde delivered cardioplegia through a balloon tip coronary sinus catheter, is not distributed equally to the right ventricle and interventricular septum. They use intraoperative contrast echocardiography and online videodensitometric analysis to demonstrate that right ventricular free wall opacification was significantly less (peak pixel intensity 48+9) compared to the posterior septum (peak pixel intensity 89+12) or anterior septum (peak pixel intensity 107+10), following retrograde delivered cardioplegia.

In a related study by Allen et al.[33] it was confirmed that retrograde cardioplegia provided poor ventricular myocardial perfusion when assessed by contrast echocardiography and coronary ostial drainage. The poor perfusion was unable to meet the myocardial demands of the right ventricle as assessed by oxygen extraction during retrograde perfusion. Villanueva et al., [34]in an experimental protocol used radiolabeled isotropes and myocardial contrast echocardiography to evaluate microvascular flow and nutrient delivery during retrograde and antegrade delivery of cardioplegia. They concluded that microvascular and nutrient flow rates were lower during retrograde delivery due to microvascular differences between coronary arterial and venous systems. Myocardial cooling was however equally efficient with either delivery techniques suggesting that the clinical benefits of retrograde delivery was primarily cooling and substrate replenishment was better achieved (at similar flow rates and temperatures) with antegrade delivery. Their data however, presumed normal coronary artery anatomy and did not consider the influence of collateralization. In patients with ischemic heart disease, predicting the distribution of cardioplegia and understanding its contribution to myocardial protection in each individual patient is difficult without direct assessment during delivery.

Quintilio et al.[35]used intraoperative myocardial contrast echocardiography to determine the myocardial distribution of cardioplegia during combined antegrade and retrograde delivery. They showed that overall myocardial opacification was greater after retrograde delivery in patients with three vessel disease undergoing elective CABG surgery. However, collateral circulation was the most important determinate for adequacy of myocardial cardioplegia delivery. If adequate collaterals were present, than retrograde delivery offered no advantage for distribution of cardioplegia to regions at risk. On the other hand, they did show that aortic root delivery may not provide adequate myocardial protection in the subset of patients without evidence of significant collateral circulation. In a related study we employed intraoperative myocardial contrast echocardiography (MCE) during coronary artery bypass grafting (CABG) surgery to determine the contribution of collateral blood flow for regional myocardial cardioplegia distribution when delivered antegrade and retrograde.[36] The role of the preoperative electrocardiogram and coronary angiogram for determining the distribution of cardioplegia in fifteen patients (all with total occlusion of their right coronary artery), was also evaluated and compared to direct assessment with intraoperative MCE. Coronary angiograms were evaluated and compared to direct assessment with intraoperative MCE. In that study, coronary angiograms were evaluated for native epicardial anatomy and evidence of collateral coronary circulation supplying the right ventricle, left ventricular apex, and interventricular septum. Evaluation of the preoperative electrocardiograms (ECG) were also performed and prediction of regional distribution of cardioplegia was compared to delivery of cardioplegia determined with myocardial contrast echocardiography using Albunex®. Eighty-seven out of ninety (97%) segments were analyzed for cardioplegia distribution at the time of cardiopulmonary bypass during delivery of cardioplegia. It was demonstrated that the preoperative angiogram and EKG poorly predicted regions at risk for incomplete cardioplegia distribution. Antegrade delivery of cardioplegia was distributed to the right ventricle in 31% of patients despite 100% occlusion of the right coronary artery, whereas retrograde delivery of cardioplegia to the right ventricle only occurred 20% of the time. It was concluded that in the presence of 100% occlusion of the right coronary artery, retrograde cardioplegia delivery is not often observed and antegrade delivery of cardioplegia to the right ventricle is not expected unless coronary collateral circulation is well developed. Furthermore, compared to intraoperative contrast echocardiography, the preoperative angiogram and ECG were not predictive of coronary collateral circulation and therefore not predictive of cardioplegia distribution to the right ventricle.

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