Indentifying Hibernating Hearts

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Introduction

Over the last 20 years mortality due to coronary artery disease (CAD) has markedly decreased but the incidence and prevalence of heart failure has dramatically increased, making it the leading cause of hospitalization.

In the mid 1970's it became evident that patients with severe CAD and depressed left ventricular (LV) systolic function showed significant improvement after surgical revascularization. Surgeons bypassing each graftable coronary artery without considering the contractile status of the affected myocardium lead to a "revolutionary" finding of improvement in contraction even in akinetic segments, considered as "hibernating myocardium". It was Rahimtoola in 1989 that popularized the concept of "myocardial hibernation".

Viable myocardium can be stunned or hibernating, while nonviable myocardium represents scar tissue. Stunned myocardium is usually found in the acute ischemic states representing dysfunctional myocardium that persists after reperfusion, despite the return to near normal or normal perfusion. Hibernating myocardium is defined as chronic LV dysfunction occurring secondary to prolonged chronic hypoperfusion, as a protective response of myocytes to a decrease in oxygen demand. This results in a perfusion-contraction mismatch. By

decreasing contractile work energy demand of myocytes diminishes, hence function is trade for survival.

After revascularization 25-40% of patients with ischemic cardiomyopathy (ICM) will show a significant improvement in ejection fraction. On the other hand surgical revascularization is associated with high operative morbidity and mortality in patients with systolic dysfunction, so careful selection of patients should be done. Thus, identifying and quantitating viable myocardium is important to determine outcomes. We shall review now the most commonly used cardiac imaging tests.

Thallium 201 SPECT Imaging

Tl-201 myocardial imaging is an important clinical tool for estimating myocardial perfusion, cell membrane integrity and hence, assessing myocardial viability. Peak myocardial activity occurs between 5-15 minutes after injection and it has a half- life of 73.1 hours. Tl clears more slowly from regions supplied by stenotic vessels compared to normal perfused segments; thus, an infarct appears as a cold spot on Tl 201 imaging.

The disadvantages of Tl-201 single photon emission computed tomography (SPECT) includes low spotted resolution, poor image quality in obese patients, attenuation artifacts and inability of this technique to differentiate endocardial from epicardial viability.

Dobutamine Stress Echocardiography

Dobutamine stress echo (DSE) has been used to assess myocardial viability by assessing wall motion and thickening under the influence of low dose (5 µcg/Kg/min) and intermediate dose (10-20µcg/Kg/min) dobutamine. During dobutamine infusion, there are four possible responses of an abnormal segment: (1) improvement, (2) initial improvement followed by subsequent worsening (biphasic response), (3) worsening and (4) no change. Viable myocardium is identified by improved or a biphasic response. However, a biphasic response is a better predictor of functional recovery following revascularization with a predictive value of 72%. In patients with poor acoustic windows or inability to adequately visualize all segments, transesophageal echocardiography can be applied using a similar protocol.

Yong reported recently on the value of mitral inflow pattern as predictor of viability. A refractory restrictive pattern, characterized by deceleration time (DT) <150ms and an E/A ratio >2, was associated with a high mortality and high transplantation rates. After CABG, only patients who had a DT >150 ms had an increase in LVEF. If DT was <150 ms, DSE and SPECT showed low viability indices.

DSE is a safe test with a good sensitivity and specificity, is probably the best for predicting regional and global left ventricular function recovery after revascularization.

Magnetic Resonance Imaging

Provides three dimensional data without radiation exposure, excellent spatial resolution (1-2 mm range), intrinsic soft tissue contrast, inherent sensitivity to blood and wall motion, multi-tomographic imaging capabilities, and the potential for in vivo measurement of myocardial metabolism using MR spectroscopy.

Cine MRI produces images of cardiac motion in a similar fashion to echocardiography, but is not limited by the examiner or by the patient's chest wall. Left ventricular myocardium is considered viable if the baseline wall thickness was $\geq$5.5mm or if the systolic wall thickening was $\geq$2mm.

Myocardial blood flow and cell membrane damage can be studied by gadolinium-diethilene-triaminepenta-acetic acid (Gd-DPTA). A persistent hyperenhanced pattern suggests that myocytes are destroyed, which is differentiated from an edematous zone that occurs in the vicinity of areas that have suffered ischemic episodes that did not provoke an infarction. Kim studied 50 patients with Gd-DPTA and demonstrated that myocardial contractility improved after revascularization in 256 of 329 segments (78%) with no hyperenhancement, but only in 1 of 58 segments with hyperenhancement of more than 75% of tissue. This finding occurred in hypokinetic, akinetic or dyskinetic segments.

An important advantage of contrast enhanced MRI is that it shows the transmural extent of viable myocardium, being able to differentiate between endocardial nonviable tissue and epicardial viable myocytes, due to its high spatial resolution.

Positron Emission Tomography

Positron emission tomography (PET) has become a very useful tool in the assessment of myocardial viability. It can quantify regional blood flow and assess regional metabolic activity independent of flow, providing better image resolution and correction for body attenuation, overcoming the major limitations of Tl-201 SPECT.

During fasting, fatty acids are the primary fuel for producing high-energy phosphates in normal myocardium; breakdown of fatty acids via β-oxidation in the mitochondria is very sensitive to oxygen deprivation. Whenever ischemia occurs, myocyte metabolism shift towards greater glucose utilization to generate high-energy phosphates. However, the amount of energy produced via glycolisis is not enough to sustain contractility.

PET evaluates viable myocardium by finding enhanced or preserved metabolic activity in the presence of decreased blood flow to dysfunctional myocardial regions. F-fluorodeoxyglucose (FDG) has emerged as the best marker of regional glucose utilization. Myocardial blood flow is assessed in most protocols with nitrogen-13 ammonia (13N) or Rubidium-35 or Oxygen-15. Three patterns of blood flow and metabolism in dysfunctional myocardial areas could be seen: (1) Normal blood flow associated with normal or enhanced glucose uptake, consistent with normal pattern or stunning. (2) Flow-metabolism match concordant reduction of 13N and 18 FDG, consistent with scar. (3) Flow metabolism-mismatch greater reduction of 13N compared with FDG consistent with hibernation.

PET has become the reference test to detect viable myocardium. However, it has been limited due to high cost, regional availability and the complexity in generating the radioisotopes.

Conclusions

Patients with low ejection fraction (EF), multivessel CAD, and preserved myocardial viability that undergo revascularization have lower perioperative mortality and morbidity, and greater long-term survival than similar patients with poor myocardial viability.

Hibernating myocardium must be reperfused, but a decision making process has to be initiated before revascularization is recommended, since these patients who would probably benefit the most, are at the same time the ones at the highest surgical risk. The perioperative mortality rate of patients with severe ICM is between 15-20%, with a 72-75% survival at 3 years. There is a clear improvement in symptoms and up to 40% of these patients will show a significant improvement in LVEF.

For patient selection we suggest following these steps:

1) Assessment of patient's symptoms. It should not be limited to angina or inducible ischemia, but also to the presence of symptoms of heart failure.
2) Severity of angina may not correlate with the degree of myocardium at risk, so evaluating the amount of viable myocardium allows a better understanding of the risks and benefits of surgery.

3) Document the extent of CAD by coronary angiogram and have a coronary anatomy suitable for revascularization.

4) Assess the extent and severity of ventricular dysfunction. ICM patients with an EF between 20-35% and a left ventricular end diastolic diameter less than 70mm/m2, do best.

5) Assess the degree of significant viable myocardium by two different noninvasive imaging modalities. Patients with normal EF and those with coronary anatomy not suitable for revascularization do not need to be evaluated for viability.

Once the adequate patient has been identified, the next question is how much viable clinical myocardium is enough to guarantee improvement from revascularization. Based on the review of many studies we can conclude that the greater the amount of viable myocardium found, the better the outcome and prognosis of patients after revascularization. Therefore it is our recommendation that at least 25% of the LV needs to be viable to overcome the risk of surgical revascularization.

Several requirements need to be fulfilled in order to show improvement in myocardial function after revascularization:

1) The segments must be viable.

2) There must not be extensive preoperative subendocardial infarctions.

3) Adequate perfusion needs to be restored surgically.

4) Distal arterial sites must be able to accept a bypass graft.

5) Avoid perioperative infarction and late graft closure.

6) Optimal techniques for cardiac preservation during surgical revascularization.

7) Prolonged duration of cross clamping needs to be avoided.

Our experience suggests that a reasonable approach is to perform a combination of Tl-201 SPECT or PET with DSE, or to use contrast enhanced MRI. We propose using the 17-segment model agreed by the AHA Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging.

About the Author: Dr. Holger Salazar is Board Certified in Internal Medicine, Cardiovascular Disease, Echocardiography and Nuclear Cardiology. He completed training in Internal Medicine at New York Medical College in New York, where he also served as Assistant Chief Medical Resident. He continued his training in Cardiovascular Disease at Tulane University in New Orleans. Went on to complete an Advanced Cardiac Imaging Fellowship at the Cleveland Clinic Foundation in Cleveland. He was an Assistant Professor of Medicine at Tulane University before joining The Stern Cardiovascular Center in 2006. His area of expertise includes cardiac imaging, clinical cardiology, valvular disease, heart failure and preventive cardiology. He can be contacted at The Stern Cardiovascular Center 901-271-1000.