Myocardial Viability and Remodeling: Does Size Matter?

William A. Zoghbi, MD,* Jagat Narula, MD, PHD

Ischemic heart disease with resultant left ventricular (LV) dysfunction is the major underlying cause of heart failure and carries significant morbidity and mortality. Therapeutic endeavors to improve the prognosis of these patients have evolved over the years and include a multifaceted approach aimed at alleviating symptoms and improving ventricular function, and reducing reinfarction and sudden death, using multidrug therapy, revascularization procedures, implantable cardioverter-defibrillators and resynchronization devices. Over the past 40 years, with the introduction of the concept of myocardial viability and reversibility of LV function with revascularization and medical therapy, numerous investigations have attempted to identify how best to detect viability, particularly with various imaging modalities, and identify the most suitable candidates for revascularization with the aim to reverse remodeling, enhance ventricular function, and improve overall prognosis.

Prior to the STICH (Surgical Treatment for Ischemic Heart Failure) trial (1,2), numerous tacitly proved notions were widely believed:

1. Myocardial viability is better assessed by imaging techniques, with higher sensitivity with nuclear modalities, higher specificity with wall motion techniques, and cardiac magnetic resonance providing unique visualization of myocardial scar.
2. The mechanism of viability, ventricular remodeling, and reverse remodeling in ischemic LV dysfunction is complex at all vascular, myocardial, and molecular levels.
3. The presence of ischemia, resting and inducible, is the most predictive of recovery of function.
4. The larger the amount of viability, the larger the improvement in ventricular function after revascularization.
5. Patients with viability who undergo revascularization have a better prognosis than those treated medically or who have no viability.
6. There may be an extent of ventricular remodeling beyond which the benefits of revascularization are no longer seen despite the presence of viability.

Most of the underlying clinical investigations behind these themes, although well conducted, had some methodological issues; either they were retrospective, without control subjects, or they were not randomized, particularly when addressing the outcomes of a treatment approach (e.g., medical therapy vs. revascularization). Despite these limitations, there was general consensus that viability was important and provided an additional parameter for improving ventricular function and prognosis after revascularization, beyond medical therapy.

The STICH trial was a prospective, randomized trial evaluating whether coronary artery bypass graft (CABG) surgery is superior to optimal medical therapy (OMT) in patients with severely depressed LV function, amenable to revascularization (1). However, it was not designed to address the issue of myocardial viability in ischemic LV dysfunction, as viability testing was not mandated, and patients were not randomized on the basis of testing results. Yet its substudy on viability (2) called into question some of the generally accepted themes in myocardial viability, particularly relating to revascularization and prognosis. Has the current therapeutic era changed this paradigm, given that medical therapy, implantable cardioverter-defibrillators, and nonsurgical revascularization procedures have substantially...

From the *Cardiovascular Imaging Institute, Houston Methodist DeBakey Heart and Vascular Center, Houston, Texas; and the yIcahn School of Medicine at Mount Sinai, New York, New York. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.
evolved in the interim? Is viability testing still important in the setting of ischemic LV dysfunction? Are outcomes with OMT similar to those with CABG in such patients and does the amount of viability modulate prognosis? And last, is viability in the patient with extreme remodeling irrelevant?

In this issue of JACC, Bonow et al. (3) address the latter of these questions from the extension of the substudy on viability of STICH (2), and their study is accompanied by a thoughtful editorial by Dr. Konstam (4). In this large cohort, patients with more advanced ventricular remodeling and no viability had the worst prognosis, a finding that is in agreement with previous observations. However, no interaction was noted between treatment modality (CABG vs. OMT) and LV size or degree of viability.

Previous studies on the role of the degree of LV remodeling and viability are scarce (5-7). Numbers of patients were small, the outcome assessed was usually change in LV function rather than a clinical outcome, and patients were highly selected. The present study, in contrast, involves the large number of well-characterized patients and addresses the issues of remodeling, viability, and intervention. One facet of the findings is the comparable outcomes of revascularization and OMT in this patient population. It is the same issue that surfaced in the previous viability substudy of STICH, and thus the results are not completely unexpected, as they are derived from the same data. The various reasons for such findings have been discussed extensively by the investigators and in previous debates (8,9) and may be related to the select population in STICH that underwent viability testing, the high degree of OMT achieved, the use of implantable cardioverter-defibrillators, and the characteristics of the overall population in STICH (including less severe angina, higher prevalence of single-vessel disease, difficult patient enrollment in the study and thus a more select cohort, fewer comorbidities, the requirement for coronary anatomy amenable to revascularization and the more severe LV function at entry).

Do LV size and viability matter? Indeed, both LV size and viability matter. The present study and earlier ones have shown worse outcomes in patients with more reduced LV function, excessively enlarged ventricles, and no viability. The major question to be answered is whether there is a threshold of LV size or viability extent beyond which the relative benefits of revascularization in relation to OMT are modified. The present investigation, although not designed to address this question prospectively and in a randomized fashion, gives the most robust data so far. However, it is not a definite answer. Patients in this substudy had a wide range of LV sizes within the select clinical characteristics of STICH, and there was no interaction between LV size and mode of therapy. However, the same cannot be said conclusively about viability, as the vast majority of patients in this substudy had viability (81%), and the pre-specified viability cutoff definition in STICH is quite high (>11 of 17 segments by nuclear imaging, >5 of 16 segments by dobutamine echocardiography), increasing even further the prevalence and specificity of viability in the population studied. Thus the prognostic impact of a true lack of viability (or a smaller extent) and its interaction with LV remodeling and treatment modality cannot be fully assessed. Of interest, there was a trend toward better outcomes in patients with less viability and larger ventricles who underwent CABG compared with OMT; the number of patients in this category, however, was small (3).

Patients with ischemic LV dysfunction face a significant challenge. Although the present study cannot fully address the issue of the significance of viability in its total spectrum, it adds important data to our knowledge in patients with ischemic LV dysfunction. Patients with moderate or large extent of viability who have clinical characteristics similar to those in STICH appear to fare equally well in the long term with CABG and OMT, and there is no threshold effect of LV volumes within this range of viability, welcome news for patients. Ideally, one would like to see the clinical importance of viability tested in its full spectrum, prospectively, in a randomized design, using uniform imaging methodology, inclusive of magnetic resonance. However, this has proved to be a daunting task from past experience, partly because of entrenched clinical practices. In the interim, decisions on the management of individual patients with coronary artery disease and LV dysfunction will always have to take into consideration a multitude of factors, including symptoms and severity of angina and/or heart failure, degree of LV dysfunction, coronary anatomy, correlation of coronary disease to regional dysfunction and viability, the presence and extent of ischemia, comorbidities inclusive of age, feasibility and type of revascularization, and patient preference. As medical options and revascularization procedures continue to evolve and improve, the complexity of such management decisions is palpable and thus mandates that cardiologists, surgeons, and patients navigate this wide array of options together.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Jagat Narula, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, New York, New York 10029. E-mail: narula@mountsinai.org.
REFERENCES


