The question of how best to treat patients with multivessel coronary artery disease and left ventricular dysfunction has challenged physicians for years. Although most clinicians are comfortable recommending revascularization when there is angina, extensive coronary disease, and a left ventricular ejection fraction of more than 35%, the benefits of such a strategy are less clear when the ejection fraction is substantially impaired.

The evidence base for the benefits of revascularization is even weaker when angina is not present in patients with ischemic cardiomyopathy. In such a situation, myocardial viability and hibernation (i.e., chronically hypoperfused myocardium resulting in a hypocontractile state) provide the rationale for revascularization — namely, that contractile function will improve with adequate blood flow. Ischemic left ventricular dysfunction is one of the few truly reversible causes of systolic heart failure. This reversible state has to be clearly distinguished from an irreversibly injured or infarcted ventricle, in which case the restoration of coronary blood flow would not be justified. Numerous nonrandomized clinical studies have supported this concept. Yet, clinical equipoise exists, since data from randomized, prospective trials have been lacking, and both surgical and nonsurgical therapies for coronary disease and heart failure have improved substantially. It is in this context that the Surgical Treatment for Ischemic Heart Failure (STICH) trial, sponsored by the National Heart, Lung, and Blood Institute, was designed and executed.

In this issue of the Journal, two studies — by Velazquez et al. and Bonow et al. — describe the respective findings of the overall STICH trial and of a substudy that was limited to patients who underwent assessment of myocardial viability. In the main study, 1212 patients with an ejection fraction of less than 35% and coronary disease amenable to coronary-artery bypass grafting (CABG) were randomly assigned to receive optimal medical therapy for heart failure and coronary disease (602 patients) or to receive optimal medical therapy plus CABG (610 patients). The original protocol called for the enrollment of 2000 patients who would be followed for 3 years. However, because of slower-than-expected recruitment, the study was modified to a target of 1200 patients with 5 years of follow-up, an enrollment that would still allow a sufficient number of events for the trial to be adequately powered. The primary end point was death from any cause. Important secondary end points included death from cardiovascular causes and hospitalization.

The results of the main study by Velazquez et al. were illuminating: there was no significant difference in the rate of death from any cause between the two study groups. As expected, there was an early hazard to CABG that abated over 2 years. CABG was effective in significantly reducing the major secondary end points of the rate of death from cardiovascular causes and the rate of a composite of death or hospitalization for cardiovascular causes. Perhaps surprisingly, in the substudy by Bonow et al., the investigators found that assessment of myocardial viability did not identify patients who might have selectively benefited from CABG.

Before we accept these findings and potential conclusions, what are the strengths and weaknesses of this trial? It was extremely well conducted. Both surgical and medical oversight com-
mittees were used to ensure that care with respect to both therapies was optimal. Surgical investigators were required to show previous surgical expertise (operative mortality, <5%) in patients with ischemic left ventricular dysfunction. More than 90% of the patients who were assigned to the CABG group actually underwent surgery, with a majority of patients undergoing the procedure within the protocol-specified window of 14 days after randomization (median interval, 10 days). Follow-up was ascertained in more than 99% of patients.

The authors appropriately acknowledge several limitations to the study. Although the crossover rate of 17% was well within the prespecified statistical limit (20%), crossovers may have diminished the benefits of CABG in the intention-to-treat analysis. It should be recognized that clinical equipoise may have also been lost in patients who crossed over, since the reasons for the selection of CABG in almost half of the cases were at the discretion of the physician, patient, or family. The authors also note that the relevance of a benefit for CABG with respect to secondary end points is uncertain when the primary end point was not met. In fact, the clinical relevance of a decrease in cardiovascular mortality is unclear when overall mortality is unaffected. Such was the case in the Defibrillator in Acute Myocardial Infarction Trial (DINAMIT), in which the use of implantable cardioverter–defibrillators in high-risk patients soon after myocardial infarction did not have a significant effect on the rate of death from any cause, although there was a significant decrease in the rate of sudden cardiac death. Finally, secondary end points that include a subjective outcome such as hospitalization are less robust in an unblinded trial.

Some other observations are worth noting. The trial was a study of ischemic heart disease rather than heart failure per se. The patients were younger (mean age, 60 years) and had more angina (>60%) and less severe heart failure symptoms (>60% with New York Heart Association functional class I or II) than in a typical group of patients with systolic heart failure. The presence of heart failure was not necessary for trial enrollment. In addition, the fate of patients who were screened but did not undergo randomization is not reported. It is possible that these patients, particularly those who were considered good surgical candidates, went on to have surgery, thus potentially biasing the randomized study against CABG.

In addition, the results of the substudy of myocardial viability should be interpreted cautiously. Viability testing was not mandated or performed in a randomized manner but, rather, at the discretion of the investigators, which may have introduced substantial bias. The authors note that there were clinical differences between patients who were tested and those who were not tested. However, the substudy’s findings do raise reasonable questions about the most appropriate method to assess myocardial viability. Since most of the patients had angina, one wonders whether this simple question is enough. The analysis is a strong reminder that in this era of cost-effectiveness, the role of expensive technologies should be accountable to a rigorous study of incremental benefit.

How should these trial results inform our clinical practice? Patients should continue to be evaluated for coronary artery disease when there is left ventricular dysfunction. In the STICH trial, patients with left main disease or severe angina were not eligible for randomization. In the absence of these conditions, aggressive medical therapy should be initiated and optimized, according to evidence-based guidelines. Decisions with respect to revascularization (including percutaneous approaches) should be carefully weighed but can be safely deferred as treatment plans are individualized and modified over time. For patients with persistent or progressive symptoms, revascularization can be offered. With the results of the STICH trial, we should be comfortable with the notion that in general, surgery is not superior to optimal medical therapy for ischemic left ventricular dysfunction.

Finally, the courage of the patients who consented to participate in this trial should be acknowledged. There are few more difficult choices in illness than selecting between two of the most extreme poles of modern-day therapeutics. These patients made such a decision on the basis of a coin flip, and none of them lost.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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