Revascularization in Systolic Heart Failure
A Difficult Decision

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Clinicians frequently face difficult decisions regarding coronary revascularization in patients with left ventricular systolic dysfunction and heart failure. Their ability to balance the potential, although somewhat uncertain, benefits of revascularization with the greater-than-usual periprocedural risks in this population is complicated by the lack of completed randomized trials and the limitations of the existing scientific literature. In this issue, Tarakji et al report on 765 consecutive patients with ejection fraction $\leq 35\%$ and heart failure who underwent positron emission tomography (PET), including fluorodeoxyglucose (FDG) imaging. From a propensity analysis matching 153 patients who underwent early intervention with 153 patients who did not, they conclude that “early intervention may be associated with improved survival regardless of the degree of viability.”

The authors acquired 3 separate PET images: A resting rubidium-82 perfusion image, a dipyridamole stress rubidium-82 perfusion image, and an FDG metabolic image after an oral glucose load. This approach allows comprehensive assessment of both stress-induced ischemia and viability, which is an advantage compared with most previous studies. However, it may be difficult to compare the results to the previous literature because resting rubidium-82 images were used in only 2 previous studies, and other studies have used different viability thresholds (50% and 65%) compared with the 70% used by Tarakji et al. Differences in imaging protocols, metabolic conditions during FDG imaging, image analyses, and viability definitions can change the diagnostic performance of PET and further confound its application to clinical practice.

Rather than restricting their study to patients who underwent coronary artery bypass grafting (CABG) alone, the authors included patients who underwent valve surgery and CABG, surgical ventricular restoration (the DOR procedure), and heart transplantation. They thereby avoided the selection bias inherent in the (unbalanced) inclusion of patients who did not undergo revascularization because they were thought not to be candidates for some other kind of procedure. This inclusive design is much more representative of patient populations in tertiary centers with expert cardiac surgeons.

Tarakji et al have accounted for the deaths of patients waiting to undergo intervention by excluding 8 patients who died before the median time (8 days) at which intervention was performed. By using an end point of all-cause mortality, they avoided the inherent difficulties of the review of death certificates or clinical records for cause of death.

Through the use of a propensity score, the authors have attempted to rigorously account for the differences in baseline parameters between those patients who underwent early intervention and those patients who were treated with medical therapy. This analysis was complemented by a secondary analysis of all 765 patients incorporating the propensity score and a more familiar multivariable regression analysis that did not include the propensity score. The results of all 3 analyses showed that early intervention was predictive of improved survival, with an adjusted hazard ratio of $\approx 0.5$. Given the similarity between the results of propensity analysis and those of the conventional multivariable regression analysis, propensity analysis seemed to offer little advantage in this study.

In addition to these noteworthy strengths, this study has several limitations that are inherent in such observational studies and generally beyond the authors’ control. Several of these are noted by the authors. The authors’ propensity analysis can account only for the impact of the variables listed in their Table 2 on the decision to proceed with revascularization. Confounding of treatment assignment with prognosis is present if these variables have an additional effect on patient outcome, which seems to be true for PET ischemia. Because these variables were well matched, other variables not recorded presumably accounted for the choice of therapy. Experienced clinicians recognize that the complex decision of whether to proceed with revascularization in a patient with left ventricular systolic dysfunction and heart failure is not fully captured by the variables listed in Table 2. The most important omission from this table is the presence and severity of angina, which may coexist with heart failure.

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Circulation is available at http://www.circulationaha.org DOI: 10.1161/CIRCULATIONAHA.105.595462

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and often determine the decision to proceed with revascularization independently of the presence or amount of viable myocardium. Other important omissions (presumably because not all patients underwent coronary angiography) are the extent of coronary artery disease and the perceived ability to revascularize the viable region. Finally, clinicians recognize that their estimate of the risk of revascularization, although influenced by age, previous CABG, and renal function, must also include their perception of the patient’s overall vitality and ability to withstand the stress of CABG.

Only a limited range of patients were matched by propensity analysis. Viability by PET/FDG imaging was strongly associated with early intervention. Not surprisingly, only 34 patients (8% of the 230 undergoing early intervention) had early intervention without any viability on PET/FDG. Thus, as the authors acknowledge, the results do not address the value of intervention in patients without viability. The results also have limitations at the other end of the spectrum, i.e., patients who underwent early intervention with a large amount of ischemia and hibernation. The authors indicate that they were able to match only a subset of early intervention patients. They did not systematically compare the 153 patients with early intervention who were matched (Table 2) with the cohort of patients who could not be matched (77 patients). However, comparison of the PET/FDG findings in the total cohort of 230 patients undergoing early intervention (Table 1) with those who were matched is revealing. The 153 matched patients had a median value of combined ischemia and hibernation of only 17% and a median value of ischemia of only 4%. With the addition of the 77 patients who could not be matched, the median value for total combined ischemia and hibernation increased from 17% to 28%, and the median for ischemia increased from 4% to 13%. A detailed understanding of the unmatched patients is not possible from these limited data, but we can infer that they were more likely to have larger areas of ischemia and hibernation than those who were matched. Because the patients with larger amounts of ischemia and hibernation appear to have been underrepresented in the matched population, the effects of early intervention in patients with large amounts of ischemia are unknown. Given the absence of patients at the “extreme,” the authors’ inability to detect any statistical interaction between the effect of revascularization and the magnitude of ischemia is not surprising and must be cautiously interpreted. Therefore, the final clause of their conclusion in the abstract—“regardless of the degree of viability”—does not appear well supported; perhaps a more appropriate conclusion is simply that “early intervention may be associated with improved survival.”

The impact of arrhythmias and/or defibrillators on the results is uncertain. The authors indicate that the mechanism of benefit from early revascularization is unknown but may include stabilization of arrhythmic substrate. An early study from the Coronary Artery Surgical Study (CASS) registry showed that revascularization in patients with extensive coronary artery disease and left ventricular dysfunction reduced the subsequent risk of sudden death. Most of the patients studied by Tarakji et al would currently be considered candidates for implantable cardioverter defibrillators (ICDs) under Medicare criteria. The authors do not provide the number of patients who underwent ICD implantation, but it was presumably modest at the beginning of this study (1997) because compelling randomized trial data showing the value of ICDs were not yet available. Implantation of ICDs in appropriate candidates according to current standards may influence the results.

Medical therapy was not optimal in either the early intervention and the no-intervention groups. In these patients with coronary artery disease and left ventricular dysfunction, only approximately one half were taking aspirin, β-blockers, or statins, which are generally indicated (class I) in ACC/AHA guidelines. About two thirds were taking angiotensin-converting enzyme inhibitors, which also are generally indicated. The scientific evidence indicating that these medical therapies improve outcomes is far stronger than the available evidence for revascularization. This study is not unique in this regard. This is yet another example of the apparent gap between existing clinical practice guidelines and everyday care. More uniform use of these medications could have altered the results.

The patient population was primarily white men. The percentage of women was <20% and of blacks was <10%, which may limit the application of the results to these important groups.

What are the implications of this study for clinical practice? First, the authors have added a sizable new study to the existing literature that suggests that early revascularization may benefit patients with systolic heart failure and viable myocardium. Second, although early intervention may benefit such patients, their overall outcomes remain relatively poor. Their Figure 1 shows that the average annual mortality over the next 5 years of the patients undergoing early intervention was >6%, which is twice the 3% annual mortality used to define high-risk patients among unselected patients with coronary artery disease.

Appropriate medical therapy according to existing ACC/AHA practice guidelines should be administered to all patients with left ventricular dysfunction and heart failure. In patients with coronary artery disease and systolic heart failure, aspirin, β-blockers, angiotensin-converting enzyme inhibitors, and lipid-lowering therapy are all generally indicated.

The poor outcomes of all the patients in this study demonstrate the need for prevention. The ACC/AHA guidelines on heart failure highlighted the importance of identifying patients with stage A and B heart failure. Such patients should receive appropriate risk factor modification and medical therapy (including angiotensin-converting enzyme inhibitors and β-blockers) to avoid progression to stage C or D heart failure, which was present in all the patients in this study.

Finally, as indicated by the authors, more randomized trial data are needed to provide definitive answers. Patients should be considered for ongoing trials whenever possible. Careful observational studies such as the one by Tarakji et al can suggest when improved outcomes are possible.

Disclosures

Drs Gibbons and Chareonthaitawee have received research grants from King Pharmaceuticals and Boston Scientific. Dr Bailey reports no conflicts.
References


KEY WORDS: Editorials • heart failure • revascularization
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Circulation. 2006;113:180-182
doi: 10.1161/CIRCULATIONAHA.105.595462

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