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Implication of right ventricular dysfunction on long-term outcome in patients with ischemic cardiomyopathy undergoing coronary artery bypass grafting with or without surgical ventricular reconstruction

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Objective: Whether right ventricular dysfunction affects clinical outcome after coronary artery bypass grafting with or without surgical ventricular reconstruction is still unknown. The aim of the study was to assess the impact of right ventricular dysfunction on clinical outcome in patients with ischemic cardiomyopathy undergoing coronary artery bypass grafting with or without surgical ventricular reconstruction.

Methods: Of 1000 patients in the Surgical Treatment for Ischemic Heart Failure with coronary artery disease, left ventricular ejection fraction 35% or less, and anterior dysfunction, who were randomized to undergo coronary artery bypass grafting or coronary artery bypass grafting + surgical ventricular reconstruction, baseline right ventricular function could be assessed by echocardiography in 866 patients. Patients were followed for a median of 48 months. All-cause mortality or cardiovascular hospitalization was the primary end point, and all-cause mortality alone was a secondary end point.

Results: Right ventricular dysfunction was mild in 102 patients (12%) and moderate or severe in 78 patients (9%). Moderate to severe right ventricular dysfunction was associated with a larger left ventricle, lower ejection fraction, more severe mitral regurgitation, higher filling pressure, and higher pulmonary artery systolic pressure (all $P < .0001$) compared with normal or mildly reduced right ventricular function. A significant interaction between right ventricular dysfunction and treatment allocation was observed. Patients with moderate or severe right ventricular dysfunction who received coronary artery bypass grafting + surgical ventricular reconstruction had significantly worse outcomes compared with patients who received coronary artery bypass grafting alone on both the primary (hazard ratio, 1.86; confidence interval, 1.06-3.26; $P = .028$) and the secondary (hazard ratio, 3.37; confidence interval, 1.36-8.37; $P = .005$) end points. After adjusting for all other prognostic clinical factors, the interaction remained significant with respect to all-cause mortality ($P = .022$).

Conclusions: Adding surgical ventricular reconstruction to coronary artery bypass grafting may worsen long-term survival in patients with ischemic cardiomyopathy with moderate to severe right ventricular dysfunction, which reflects advanced left ventricular remodeling. (J Thorac Cardiovasc Surg 2015;149:1312-21)

See related commentary pages 1322-3.

In patients with heart failure (HF), right ventricular (RV) systolic dysfunction has been associated with decreased exercise capacity[1,2] and a poor clinical outcome[3-7] when compared

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CAD = coronary artery disease
CV = cardiovascular
EF = ejection fraction
HF = heart failure
LV = left ventricular
RV = right ventricular
RVFAC = right ventricular fractional area change
STICH = Surgical Treatment for Ischemic Heart Failure
SVR = surgical ventricular reconstruction
TAPSE = tricuspid annular plane systolic excursion

with patients who have preserved RV function. However, the small numbers of patients described in previous studies of RV dysfunction severely limit an assessment of the prevalence of RV dysfunction in patients with HF. Moreover, the clinical implications of RV dysfunction in patients with ischemic cardiomyopathy who undergo coronary artery bypass grafting (CABG) with or without surgical ventricular reconstruction (SVR) have not been clearly defined. The Surgical Treatment for Ischemic Heart Failure (STICH) trial[8] provides a unique opportunity to assess the importance of RV dysfunction in this clinical situation. In the STICH trial, the Echocardiography Core Laboratory (Mayo Clinic, Rochester, Minn) provided a baseline echocardiographic evaluation of structural, functional, and hemodynamic parameters of both the left and right ventricles. The STICH trial tested 2 clinically unresolved and relevant hypotheses in patients with coronary artery disease (CAD) and reduced left ventricular (LV) ejection fraction (EF). The SVR hypothesis (Hypothesis 2) of STICH randomized 1000 patients with anteroapical dysfunction to CABG with SVR versus CABG alone to test the hypothesis that in patients with LV EF 35% or less, CAD amenable to CABG, and anterior LV dysfunction, the addition of SVR improves survival free of subsequent hospitalization for cardiac cause in comparison with CABG alone.[8] The concept and technique of surgical ventricular restoration have been well described by Dor and colleagues.[9] The primary outcome of this population has been reported by Jones and colleagues,[10] and the description of clinical characteristics has been reported by Zembala and colleagues.[11] Patients randomized to Hypothesis 2 were followed for a median of 48 months. Only 4 of the 1000 patients withdrew consent for follow-up, and 6 patients were lost to follow-up.

The present study sought to examine the prevalence of RV dysfunction in those 1000 patients to determine the relationship between RV dysfunction and other parameters of cardiac structure and function measured by echocardiography. We also examined the interaction of RV dysfunction with treatment on short- and long-term survival in these patients.

MATERIALS AND METHODS

Study Population and Patient Selection

Among the 2136 patients enrolled in the STICH trial with an LV EF 35% or less and CAD amenable to CABG, 1000 patients with anteroapical dysfunction for whom adding an SVR operation to CABG was reasonable but not required were randomized to CABG versus CABG + SVR. Of the 1000 patients enrolled, 866 had a baseline echocardiogram rated as fair to excellent quality (excellent for textbook quality, good for clear definition of RV walls from multiple views, and fair for good definition of RV walls from limited views) for qualitative assessment of RV function by the Echocardiography Core Laboratory (Figure 1).

Echocardiography Study

Baseline echocardiography was obtained within 3 months before enrollment by clinical sites and sent to the Echocardiography Core Laboratory, where each study was initially analyzed by a research sonographer blinded to randomized treatment assignment and clinical outcomes using American Society of Echocardiography guidelines[12] and with a second over-read by a physician. Details of the methodology used for echocardiographic analysis have been published.[13]

Right Ventricular Function Assessment

RV function was assessed prospectively by visual interpretation and categorized as normal, mild, moderate, or severe dysfunction. The appreciation of the overall mechanical function of the RV was mainly based on the extent of RV free wall segmental motion, wall thickening, RV cavity size, and subjective assessment of RV area change (normal >50%, mild 30%-50%, moderate 20%-30%, and severe <20% from diastole to systole). RV assessment was derived from the parasternal long-axis, apical 4-chamber, and subcostal views. This assessment was based on visual assessment by an experienced Echocardiography Core Laboratory physician.[14]

Once the results of the impact of RV function by visual assessment were known, 40 patients in each group (normal, mild, and moderate dysfunction) and all 21 patients with severe RV dysfunction were sent for blinded post hoc calculation of RV fractional area change (RVFAC). RVFAC was calculated from apical 4-chamber views as ([RV end-diastolic area − RV end-systolic area]/RV end-diastolic area) by a research sonographer with no knowledge of the patients' clinical or other echocardiography data.

Statistics

Clinical and echocardiographic characteristics were described using means and standard deviations for continuous variables and frequencies and percentages for categoric variables. Because of the limited number of patients with moderate and severe RV dysfunction, these 2 groups have been combined and analyzed as 1 moderate/severe subgroup. Comparisons of patients across 3 different levels of RV dysfunction (ie, normal, mild, or moderate/severe) were performed using Kruskal–Wallis nonparametric analysis of variance on continuous and ordinal variables. Group comparisons of nominal categoric variables were performed using the conventional chi-square test or Fisher exact test. The prognostic effect of RV dysfunction on the short-term end point of death within 30 days after surgery was tested using the logistic regression model. The effects of the 3 levels of RV dysfunction on the long-term end points of (a) death or cardiovascular (CV) hospitalization and (b) all-cause mortality and relative risks were assessed using the Cox regression model. Event-rate estimates in each RV dysfunction group for each long-term end point were calculated using the Kaplan–Meier method. The logistic regression model and Cox regression model were also used to assess the interaction of RV dysfunction and treatment (CABG vs CABG + SVR). Testing of the independent prognostic effect of RV dysfunction and testing of the interactive effect of RV dysfunction and treatment were performed after adjusting for LV EF and other key prognostic factors identified from previous modeling analyses of the STICH SVR hypothesis patient data.