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ORIGINAL RESEARCH

Severity of Remodeling, Myocardial Viability, and Survival in Ischemic LV Dysfunction After Surgical Revascularization

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ABSTRACT

OBJECTIVES This study sought to test the hypothesis that end-systolic volume (ESV), as a marker of severity of left ventricular (LV) remodeling, influences the relationship between myocardial viability and survival in patients with coronary artery disease and LV systolic dysfunction.

BACKGROUND Retrospective studies of ischemic LV dysfunction suggest that the severity of LV remodeling determines whether myocardial viability predicts improved survival with surgical compared with medical therapy, with coronary artery bypass grafting (CABG) only benefitting patients with viable myocardium who have smaller ESV. However, this has not been tested prospectively.

METHODS Interactions of end-systolic volume index (ESVI), myocardial viability, and treatment with respect to survival were assessed in patients in the prospective randomized STICH (Comparison of Surgical and Medical Treatment for Congestive Heart Failure and Coronary Artery Disease) trial of CABG versus medical therapy who underwent viability assessment (n = 601; age 61 ± 9 years; ejection fraction ≤35%), with a median follow-up of 5.1 years. Median ESVI was 84 ml/m^2. Viability was assessed by single-photon emission computed tomography or dobutamine echocardiography using pre-specified criteria.

RESULTS Mortality was highest among patients with larger ESVI and nonviability ($p < 0.001$), but no interaction was observed between ESVI, viability status, and treatment assignment ($p = 0.491$). Specifically, the effect of CABG versus medical therapy in patients with viable myocardium and ESVI ≤84 ml/m^2 (hazard ratio [HR]: 0.85; 95% confidence interval [CI]: 0.56 to 1.29) was no different than in patients with viability and ESVI >84 ml/m^2 (HR: 0.87; 95% CI: 0.57 to 1.31). Other ESVI thresholds yielded similar results, including ESVI ≤60 ml/m^2 (HR: 0.87; 95% CI: 0.44 to 1.74). ESVI and viability assessed as continuous rather than dichotomous variables yielded similar results ($p = 0.562$).

CONCLUSIONS Among patients with ischemic cardiomyopathy, those with greater LV ESVI and no substantial viability had worse prognosis. However, the effect of CABG relative to medical therapy was not differentially influenced by the combination of these 2 factors. Lower ESVI did not identify patients in whom myocardial viability predicted better outcome with CABG relative to medical therapy. (Comparison of Surgical and Medical Treatment for Congestive Heart Failure and Coronary Artery Disease [STICH]; NCT00023595) (J Am Coll Cardiol Img 2015;8:1121-9)

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ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass graft

CAD = coronary artery disease

EF = ejection fraction

ESV = end-systolic volume

ESVI = end-systolic volume index

FDG = ^{18}F-fluorodeoxyglucose

LV = left ventricular

PET = positron emission tomography

SPECT = single-photon emission computed tomography

Despite advances in diagnosis and treatment, heart failure remains a substantial cause of death and disability (1,2), driven importantly by the causal role of coronary artery disease (CAD) in the development of left ventricular (LV) dysfunction (3). LV systolic dysfunction in the setting of CAD is not always an irreversible process because LV function may improve substantially with beta-blocker therapy, cardiac resynchronization, and revascularization (3–7). LV function is most likely to improve with medical, device, or surgical therapies in patients with viable myocardium identified using noninvasive imaging (4,8–14). Many previous studies, primarily retrospective and performed before the advent of beta-blockers for LV systolic dysfunction, suggested that myocardial viability also identified patients in whom survival is enhanced with revascularization compared with medical management (8,15,16). In contradistinction, the prospective STICH (Comparison of Surgical and Medical Treatment for Congestive Heart Failure and Coronary Artery Disease) trial, which randomized patients with CAD and LV dysfunction to evidence-based medical therapy or coronary artery bypass graft (CABG) surgery plus medical therapy, demonstrated no interaction between myocardial viability and treatment strategy with respect to survival (17).

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Previous retrospective studies of patients with ischemic LV dysfunction have suggested that the severity of LV remodeling affects the relation between myocardial viability and survival with CABG, such that patients with marked LV dilation (i.e., large end-systolic volume [ESV]) develop irreversible remodeling to the extent that viable myocardium, if present, does not contribute to improved LV function or improved survival with revascularization. According to this concept, the beneficial effect of CABG on LV functional recovery and survival would thus be limited to patients with viable myocardium and smaller ESV (18–21). This theory is plausible but has not been tested prospectively with random allocation of treatment strategies. The current study investigated the impact of LV remodeling on the relationship between myocardial viability, treatment with revascularization versus medical management, and survival in patients enrolled in the STICH trial.

METHODS

PATIENT ENROLLMENT. Design and enrollment criteria for the STICH study and STICH viability substudy have been reported in detail (17,22,23). The STICH study is a multicenter, nonblinded, randomized trial funded by the National Heart, Lung, and Blood Institute (NHLBI). The study of revascularization versus medical therapy was conducted at 99 sites in 22 countries. Patients with angiographic documentation of CAD amenable to surgical revascularization and LV ejection fraction (EF) ≤35% were eligible for enrollment. Exclusion criteria included left main coronary stenosis >50%, cardiogenic shock, myocardial infarction within 3 months, and need for aortic valve surgery. All participants provided written informed consent. Patients were randomized to receive medical therapy alone or medical therapy plus CABG. A "risk at randomization" score was calculated for each patient using a statistical model derived in an independent dataset from multiple variables with known power to predict 5-year risk of death without CABG (24). Medical therapy was excellent, with ≥90% of patients receiving statins, beta-blockers, and either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers at 1 year and 88% receiving aspirin (≥92% received either aspirin or warfarin) (23).

VIABILITY TESTING. Of the 1,212 enrolled patients, 601 underwent viability testing. Details regarding patient selection for imaging have been reported previously (17). Viability was assessed using single-photon computed tomography (SPECT) in 471 patients or dobutamine echocardiography in 280 patients;

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