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Introduction

Heart failure with a normal ejection fraction (HFNEF) is common as is associated with considerable morbidity and mortality.[1] While effective treatments and a widely accepted unifying understanding of pathophysiology exist for systolic heart failure, this is not the case for HFNEF. Though HFNEF has been historically attributed solely to diastolic dysfunction, numerous clinical observations and research findings suggest that the HFNEF may be physiologically diverse. Among many parameters measured by echocardiography in these (as in many other populations) patients is their ventricular geometry. Ventricular geometry may be important because it may predict different pathophysiologic mechanisms of disease and because different geometric patterns have been associated with morbidity and mortality in many populations including hypertensives, diabetics, and systolic heart failure patients.[2-4] Among systolic heart failure patients, those with concentric geometry have been found to have a worse prognosis that those with eccentric geometry.[4] However, less is known about geometry in patients with HFNEF. As newer and more accurate imaging techniques, such as cardiac MR and 3D echocardiography (3DE), become more commonly used clinically, research is needed on the clinical implications of measures of ventricular geometry using these more accurate assessments of geometry. Therefore, the research goal of this study is to test whether 3DE defined ventricular geometry is an important predictor of outcomes is patients with HFNEF. Also there is no data on frequent serial monitoring of patients with HFNEF, and the change in their geometry over time is unknown.

There are numerous clinical implications of this research. Having variables that provide prognostic information is important for risk stratification of patients. Additionally, if different geometric patterns can attributed to different pathophysiologic mechanisms, then stratification based on geometry and prognosis can be used to guide therapy.

Hypothesis

Ventricular geometry as measured by 3DE with affect outcomes (particularly a combined endpoint of overall mortality and hospitalization for heart failure at one year) in patients with HFNEF.

Methods

The primary outcome of this study will be a combined end point heart failure hospitalizations and all cause mortality. Secondary outcomes will include all-cause mortality and heart failure hospitalizations as individual end-points, mortality from a cardiovascular cause, and hospitalization for cardiovascular cause (heart failure, myocardial infarction, unstable angina, arrhythmia, or stroke). The patients will have 3DE done during their initial enrollment (preferably prior to discharge from their hospitalization or within a week of their hospitalization), at 6 months, and at one year

upon the conclusion of the study. A 3DE machine currently available at Columbia Presbyterian Medical Center will be used to conduct the studies. The geometry of patients will be defined based on their ratio of end-diastolic volume divided by their left ventricular mass (EDV/LVM).[5] A ratio of <0.5 will be used to define concentric geometry and > 0.5 will be used to define eccentric geometry.[5] Patients will also have routine labs, including core lab measures of CBC, BMP, and BNP done on the day of their 3DEs.

The study will be a prospective longitudinal case-control study where patients will have their ventricular geometry evaluated by 3DE on three occasions and then will be assessed at one year for the occurrence of primary and secondary outcomes. There will be no active intervention. It is expected that a subset of these patients will be on no medications or no cardiovascular medications during their initial HF hospitalization. These patients will be treated with currently accepted medications.

The study will recruit patients after a hospitalization for HFNEF from one large tertiary care center. Consecutive patients meeting the inclusion criteria will be approached to increase the external validity of the study. Patients will need to meet the diagnostic criteria HFNEF.[5] Additionally, inclusion criteria will include a history of hypertension (SBP>140) or treatment with antihypertensive medication. This inclusion criteria is necessary to reduce the known influence of hypertension on ventricular remodeling and to increase patient homogeneity. Exclusion criteria will include ESRD, significant valvular disease, and myocardial infarction within last three months. These exclusion criteria are needed because they may interfere with the ability to accurately relate geometry to heart failure. Also, those with a life expectancy from a different disease of less than one year will be excluded.

The statistical tests used in the study will include T-test and Chi-square. The T-test will be used to compare geometry among those who did have a primary endpoint within one year versus those who did not. A two by two chi-square can be set up to include those with/without the primary end-point and those with/without eccentric geometry. Among the whole cohort, the expected rate of combined end point of overall mortality and HF hospitalization rate at one year is approximately 30%.[1] Assuming a 10% absolute difference in the primary endpoint (25% vs 35% of patients with primary end-point), approximately 700 patients are needed for 80% power using p of<0.05 for statistical significance. Multiple groups can then be additionally analyzed, including those with certain eGFR (for example, above and below 60) and those who presented on no cardiovascular medications.

Miscellaneous Issues

There will be no additional study drugs or medical devices used in the study. Patients will not need to fill out questioners. The results of the 3DE will be provided to the patient and their physician if requested. Patients will be compensated financially for the time spent getting the three additional 3DEs which they would not otherwise receive.

The expected time spent by the patients will be There will be no substantial risks or benefits to the patients in the study.

Reference List

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