A Comparison of Echocardiographic LV Diastolic Parameters and Structural Properties in Individuals with Diastolic Heart Failure

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A. Study Purpose and Rationale

Congestive heart failure (CHF) is a major public health problem that affects 4.6 million people in the United States, Various epidemiological studies have shown that 20 to 40% of patients with CHF have a normal left ventricular ejection fraction. In this subgroup of patients, CBF is usually due to left ventricular diastolic dysfunction. Diastolic heart failure (DBF), however, remains difficult to characterize diagnostically because interpretation of the various measured indices of LV diastolic function is complex as they vary for multiple reasons making their predictive value not very useful, There is a need for a better understanding of the physiologic properties of the heart during diastole and how they are affected by the structural properties of the heart in diastolic failure.

The purpose of this study is to compare certain echocardiographic LV diastolic parameters and structural properties in people with diastolic heart failure and people without cardiovascular disease. The aim is to elucidate significant differences between the two groups that may aid in further defining the diagnosis of DBF.

B. Study Design and Statistical Analysis Design

The study will be an observational study with two study groups. The study group will be patients with diastolic heart failure, defined as patients with CBF and a LV EF >=50%, presenting to the CPMC ER with pulmonary edema. The clinical criteria for CBF are symptoms (dyspnea with exercise), signs (distended neck veins, peripheral edema, rales) and laboratory evidence (chest x-ray with pulmonary vascular congestion or pulmonary edema). Patients will be recruited by physician referral, ER physicians will be informed of the purpose of the study and the inclusion/excluision criteria and will be invited to refer patients to be screened, Detailed inclusion/exclusion criteria are listed in Section G.

The control group will be people with no history or evidence of cardiac disease that will be matched for age, gender, and ethnicity. They will be recruited by physician referral from the AIM clinic. AIM physicians will be informed of the purpose of the study and the inclusion/exclusion criteria and will be invited to refer patients to be screened. Detailed inclusion/exclusion criteria are listed in Section G.

After initial screening (history and physical), the following information will be obtained from patients: weight, height, and systolic and diastolic blood pressure. The patients will then have a 2D echo done to measure LV diastolic function (E peak wave, A peak wave, E/A ratio, deceleration time of the E wave, isovolumic relaxation time) and a 3D echo to measure LV cavity end diastolic volume and LV mass. The echos will be read by two separate echocardiographers that will be blinded to the study group of the subject. The reported results will be means of the measurements of each reader.

The number of subjects to be enrolled in each group is 20, which is the calculated number of subjects needed to see a difference of 30% with 80% power.

Statistical Analysis The unpaired Student's t test will be used to compare the mean values. Relations between LV diastolic function indices and ventricular mass and volume will be assessed with linear regression,

C. Study Procedures

Doppler Echocardiographic Examination: Two-Dimensional pulse wave Doppler echocardiography will be performed for the left ventricle. Mitral inflow velocities in the apical four-chamber view with the sampling window placed at the mitral annulus will be recorded. Measurements to be taken include: peak early mitral wave filling velocity (E wave), peak atrial filling velocity (A wave), ratio of peak early and atrial-filling velocity (E/A), and the deceleration time of the E wave (DT). The isbvolumic relaxation time (IVRT) will be measured by moving the sampling window to a position between the anterior mitral leaflet and left ventricular outflow tract. Measurement of left ventricular end diastolic volume and mass will be done using the three-dimensional echocardiography method developed by King DL et al (JACC 1994, 24:504-13).

All data acquisition will be done at one session. Cardiac echocardiography is not an invasive procedure and the subjects should not experience any pain or discomfort.

D. Study Drugs

No study drugs will be used.

E. Medical Devices

The devices used in this study are accepted as standard medical care and commercially available.

F. Study Questionnaire

The document to be used to record baseline information for each subject is currently being developed.

G. Study Subjects

a. Study Subject Inclusion Criteria

1. CHF
   - Symptoms at least once within last six months: dyspnea on exertion
   - Signs documented on ER presentation: distended neck veins, peripheral edema, rales,
   - Lab: chest x-ray done in ER with PVC or pulmonary edema
2. Normal systolic function
   - EF >=50% on echo done within 72 hours of ER presentation

3 Age > 18

b. Study Subjects Exclusion Criteria

1. Valvular Heart Disease

- MS, any degree
- AS, any degree
- MR, moderate to severe
- AI, moderate to severe

2. Renal failure

- Renal replacement (hemodialysis, peritoneal dialysis, renal transplant)
- Creatinine > 2

3. Pulmonary Disease
4. Atrial fibrillation

c. Control Subjects Exclusion Criteria

1. Cardiovascular disease defined as angina pectoris, myocardial infarction, CABG, PTCA, hypertension, CHF as defined above, valvular heart disease as defined above, atrial fibrillation, left bundle branch block, right bundle branch block

2. Renal failure as above
3. Pulmonary Disease
4. Age < 18

H. Recruitment of Subjects

All subjects will be recruited by physician referrals. ER staff physicians will be informed about the study and entry criteria and encouraged to refer study patients. Medicine staff on cardiology service will also be informed and invited to refer study patients that are admitted that meet the entry criteria. Physicians in the AIM clinic, in turn, will be informed of the entry criteria for control subjects and will be invited to refer patients.

I. Confidentiality of Study Data

Identifying patient data will be matched with a study ID # so that all information will be tracked by this ID#. The key to the ID #'s will be stored in a location yet to be designated.

J. Potential Conflict of Interest

No proprietary interest in the procedures and devices to be used on behalf of the investigators exists at this time.

K. Location of the Study

All study procedures will be done in a CPMC echo laboratory.

L. Potential Risks

No treatment risks are involved in this non-interventional study. Study subjects will enter the study already knowing their diagnosis. A potential risk may arise from a healthy control volunteer being diagnosed with a cardiac abnormality not known a priori as this may cause the subject emotional stress. However, referral for further medical evaluation and management will be offered.

M. Potential Benefit

The potential benefit to the subject is confirmation of normal cardiac function. No therapeutic benefit is offered or expected by participating in this study, however. The benefit to society will hopefully be a better understanding of a prevalent disease process.

N. Alternative Therapy

Does not apply.

O. Compensation to Subjects

Patients will not be compensated for participating in the study. They will be reimbursed for travel expenses to and from the study site.

P. Costs to Subjects

None anticipated.

Q. Minors as Research Subjects

Does not apply.

R. Radiation or Radioactive Substances

Does not apply.