The Effect of Coronary Artery Plaque Burden on Left Ventricular Diastolic Function in Asymptomatic Adults with Normal Ejection Fraction

Thesis

Submitted for Partial Fulfillment
of Master Degree in ***Cardiology***

Presented

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DEDICATION

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Protocol

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INTRODUCTION

Left ventricular (LV) diastolic dysfunction is a common condition associated with increased risk of morbidity and mortality even when it is asymptomatic or “preclinical” (1, 2).

The earliest manifestation of LV diastolic dysfunction is characterized by delayed LV relaxation and is most commonly seen with hypertension or LV hypertrophy. Symptomatic diastolic heart failure occurs when LV stiffness increases and an elevation in mean left atrial (LA) pressure is superimposed on the impaired LV relaxation (3, 4).

CAD in the form of angina, previous myocardial infarction, or previous coronary artery bypass surgery is commonly cited as a mechanism underlying diastolic dysfunction. However, the association of LV diastolic dysfunction with stable or non-flow-limiting asymptomatic CAD, independent of other known risk factors, has not been established (5, 6).

Coronary artery calcium is only present in atherosclerotic arteries and can be quantified quickly and noninvasively with electron-beam computed tomography (EBCT). (7)Computed tomographic coronary artery calcium score (CACS) is a surrogate for coronary atherosclerosis burden and independently predicts future cardiovascular (CV) risk (8-10).

Over the past 20 years, the survival of patients with systolic heart failure has improved, whereas the prognosis of diastolic heart failure has not changed. Diagnostic echocardiographic and Doppler techniques have improved, and criteria for the diagnosis of diastolic heart failure have been developed, but the evolution of therapeutic strategies has not kept pace with this growing public health problem. Improved therapy will depend on basic research directed at mechanisms

of disease, coupled with clinical investigations directed at diagnosis and therapy (11-14).

If a strong association between CACS and LV diastolic dysfunction exists, this would have important implications for the use of this test in the risk stratification of individuals not only for CAD but also for diastolic dysfunction. Therefore the objective of this study is to determine if a meaningful relation between CACS and LV diastolic function exists using a study group of asymptomatic adults with normal ejection fractions and a low probability of obstructive CAD on the basis of negative cardiac stress test results.

AIM OF THE WORK

This study aims at assessing the relationship between CAD without ischemia and left ventricular (LV) diastolic dysfunction using coronary artery calcium score (CACS) as a surrogate for coronary atherosclerosis burden.

PATIENTS AND METHODS

PATIENTS:

This study will include 60 asymptomatic patients aged from 45 to 65 years who underwent stress testing with negative results for obstructive CAD within three month of the study, referred to cardiology department-Kobry El Koba military hospital for routine checkup including CACS assessment, and echocardiography.

Inclusion criteria:

- Age range: 45 - 65 *years*.
- Only males will be included.
- Asymptomatic adults with normal LV ejection fraction who underwent stress testing with negative results for obstructive CAD within three month of the study.

Exclusion criteria:

Patients were excluded if they were known to have:

- Personal history of CAD, defined as a history of acute coronary syndrome, percutaneous coronary intervention, or coronary artery bypass surgery.
- Cerebrovascular disease.
- Stress testing with positive results for ischemia.
- Any form of arrhythmia at time of the study.

Ethical consent:

Verbal informed consent will be obtained from the patients after explanation of the aim of the study and its benefits.

METHODS:

The 60 patients enrolled in the study will be divided into 2 equal groups based on whether or not the patients have any degree of diastolic dysfunction by echocardiogram.

A comparison will be made between the two groups regarding the plaque burden (CACS), and the two groups will be matched regarding the other risk factor.

All patients will be subjected to the following:

1. ***History and clinical examination:***
   Proper history taking and clinical examination with special emphasis on past history of CAD or cerebrovascular disease.

2. ***ECG:***
   To detect signs of ischemia or rhythm abnormalities.

3. ***CACS assessment:***
   Multidetector computed tomography will be performed to determine CACS on the basis of the x-ray attenuation coefficient, or computed tomographic number measured in Hounsfield units, and the area of calcium deposits (Agatston score) (15) in a non-contrast-enhanced scan.

4. ***Echocardiographic examination:***
   Full Echocardiographic study will be done using current recommendations of the American Society of Echocardiography and the European Society of Echocardiography (16). With special attention toward assessment of diastolic function as follows:

- **Doppler measurements:**

Mitral inflow will be assessed using pulsed-wave Doppler from the apical four-chamber view. The Doppler beam will be aligned parallel to the direction of flow, and a 1-mm to 2-mm sample volume will be placed between the tips of mitral leaflets during diastole. From the mitral inflow profile E-wave and A-wave peak velocities, mitral deceleration time (DT) and the E/A ratio will be determined.

- **Tissue Doppler measurements:**

Mitral annular motion lateral and septal velocity obtained using the tissue Doppler technique will be measured, and e' and the E/e' ratio will be calculated.

Diastolic function grade will be assessed using the methods and criteria recommended in the American Society of Echocardiography guidelines. This method integrates Doppler measurements of mitral inflow and Doppler tissue imaging of the mitral annulus with estimations of LV filling pressures.

Diastolic function will be divided into five categories:

(1) Normal diastolic function

(2) Mild diastolic dysfunction (impaired relaxation without evidence of increased filling pressures)

(3) Moderate diastolic dysfunction (impaired relaxation or pseudonormal with moderate elevation of filling pressures)

(4) Severe diastolic dysfunction (advanced reduction in compliance)

(5) Indeterminate diastolic function.

Normal diastolic function will include subjects with septal e' ≥ 8, lateral e' ≥10 and LA volume <34 mL/m^2. Those with one or more elevated values for these variables will be considered abnormal, and additional measurements will be used to determine the grade of diastolic dysfunction.

- Mild diastolic dysfunction (grade I) will be classified as a mitral E/A ratio <0.8, DT >200 msec, and an E/e' ratio <8 (septal and lateral).
- Moderate diastolic dysfunction (grade II) will be classified as a mitral E/A ratio of 0.8 to 1.5, DT of 160 to 200 msec, and average E/e' ratio of 9 to 12
- Severe diastolic dysfunction (grade III) characterized by restrictive filling with an E/A ratio ≥2, DT <160 msec, and average E/e' ratio >13 or septal E/e' ratio ≥15 and lateral E/e' ratio >12.

Subjects are required to meet two Doppler criteria for moderate or severe diastolic dysfunction to be so classified. Subjects meeting one criterion for moderate or severe diastolic dysfunction or those with borderline parameters will be classified as indeterminate rather than normal.

N.B. Maximal LA volume will be measured in all patients using a modified biplane area-length method (17). LA volume will be indexed according to body surface area**.**

STATISTICS:

All data will be gathered, tabulated, and statistically analyzed on a PC computer using a commercially available statistical software package.

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