# EVALUATION OF LEFT VENTRICULAR SYSTOLIC FUNCTION IN PATIENTS WITH PRIMARY DIASTOLIC HEART FAILURE

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**Ahmed ElGuindy**

**ABSTRACT**

**Background:** Heart failure is a burgeoning problem worldwide with approximately one half of the affected patients having normal or near-normal left ventricular systolic function. Left ventricular diastolic dysfunction in an essential requirement for the diagnosis of this condition, but the extent of possible systolic function impairment remains enigmatic. Subtle systolic function abnormalities may not be reflected by estimation of conventional systolic function parameters including ejection fraction, fractional shortening, and mean circumferential fiber shortening rate.

**Objective:** Studying the status of left ventricular systolic function in patients with diastolic heart failure using novel parameters including mitral annular plane systolic excursion which reflects LV longitudinal axis systolic shortening, pre-ejection contraction time, isovolumic contraction time, systolic ejection time and myocardial performance index (MPI).

**Methods:** 30 patients with symptoms and/or signs of heart failure with echocardiographic evidence of diastolic dysfunction and normal left ventricular ejection fraction (> 50%) were recruited for the study, in addition to 10 age- and sex-matched healthy controls. All study subjects and controls had full clinical history, physical examination, 12-lead electrocardiogram and a comprehensive echocardiographic evaluation with measurement of a number of LV systolic function parameters (fractional shortening, ejection fraction, mitral annular plane systolic excursion, myocardial performance index, precontraction time, contraction time, mitral annular systolic velocity and time to peak mitral annular systolic velocity.

**Results:** There was no significant difference in LV systolic function parameters between patients and controls apart from minor (but statistically significant) reduction in mitral annular plane systolic excursion (14.08 ± 2.84 vs 16.1 ± 2.69, $p = 0.046$ for patients and controls respectively).

**Conclusion:** Our findings clearly show that patients with diastolic heart failure do not exhibit any significant impairment of left ventricular systolic function.

**Key Words:** Diastolic heart failure, left ventricular systolic function, mitral annular plane systolic excursion, long-axis function, myocardial performance index.

# LIST OF ABBREVIATIONS

| | |
|---|---|
| **A** | Late mitral inflow |
| **A'** | Peak late diastolic mitral annular velocity |
| **ACEI** | Angiotensin-converting enzyme inhibitors |
| **AF** | Atrial fibrillation |
| **ANP** | atrial natriuretic peptide |
| **ATP** | Adenosine triphosphate |
| **BNP** | Brain natriuretic peptide |
| **CAD** | Coronary artery disease |
| **cGMP** | cyclic Guanosine monophosphate |
| **CHARM** | Candesartan in Heart failure Assessment Reduction of Mortality and morbidity |
| **CHF** | Congestive heart failure |
| **CKD** | Chronic kidney disease |
| **CMR** | Cardiovascular megnetic resonance |
| **CNP** | C-type natriuretic peptide |
| **COPD** | Chronic obstructive lung disease |
| **CT** | Contraction time |
| **CVS** | Cerebrovascular stroke |
| **DIG** | Digitalis Investigators Group |
| **DM** | Diabetes mellitus |
| **DNP** | Dendroaspis natriuretic peptide |
| **E** | Early mitral inflow |
| **E'** | Peak early diastolic mitral annular velocity |
| **ECM** | Extracellular matrix |
| **EFECT** | Enhanced Feedback for Effective Cardiac Treatment |
| **ESC** | European Society of cardiology |
| **ESPVR** | End-systolic pressure-volume relationship |

| | |
|---|---|
| **ET** | Ejection time |
| **HTN** | Hypertension |
| **IVC** | Isovolumic contraction |
| **IVCT** | Isovolumic contraction time |
| **IVR** | Isovolumic relaxation |
| **IVRT** | Isovolumic relaxation time |
| **IVS** | Interventricular septum |
| **LAP** | Left atrial pressure |
| **LV** | Left ventricle |
| **LVEDD** | Left ventricular end-diastolic dimension |
| **LVEDV** | Left ventricular end-diastolic volume |
| **LVEF** | Left ventricular ejection fraction |
| **LVESD** | Left ventricular end-systolic dimension |
| **LVESV** | Left ventricular end-systolic volume |
| **MAPSE** | Mitral annular plane systolic excursion |
| **MRI** | Magnetic resonance imaging |
| **NEP** | Neutral endopeptidase |
| **NHF** | National Heart Failure project |
| **NPR** | Natriuretic peptide receptor |
| **NT** | N-terminal |
| **NYHA** | New York Heart Association |
| **PASP** | Pulmonary artery systolic pressure |
| **PCT** | Pre-contraction time |
| **PVd** | Pulmonary vein diastolic flow |
| **PVs** | Pulmonary vein systolic flow |
| **PWT** | Posterior wall thickness |
| **RV** | Right ventricle |
| **RVSP** | Right ventricular systolic pressure |
| **RyR** | Ryanodine receptor |

**S'** Peak mitral annular systolic velocity

**SERCA** Sarcoplasmic endoplasmic reticulum $Ca^{2+}$ ATPase

**SR** Sarcoplasmic reticulum

**TAPSE** Tricuspid annular plane systolic excursion

**TDI** Tissue Doppler imaging

**TST** Total systolic time

**VCF** Velocity of circumferential fiber shortening

**Vp** Propagation velocity

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# INTRODUCTION

Heart failure due to primary diastolic dysfunction has been variously termed as diastolic heart failure, heart failure with preserved (or mildly abnormal) left ventricular systolic function and heart failure with normal (or mildly reduced) left ventricular ejection fraction. This reflects the uncertainty about the accepted magnitude of systolic dysfunction associated with this disorder. Such uncertainty stems essentially from the limitations of the various parameters of left ventricular systolic function. The most commonly used index of global ventricular systolic function is the left ventricular ejection fraction (LVEF). However, many pitfalls may contribute to misleading LVEF estimation. These include poor visualization of the left ventricular endocardium, various arrhythmias, acute ischemia, myocardial depressants, asynchrony of left ventricular contraction and foreshortening of left ventricular images. The use of Doppler echocardiography to determine the stroke volume and rate of rise of left ventricular systolic pressure is also limited by the mathematical assumption implied in calculating the left ventricular outflow, the variability in angle of incidence of the Doppler beam and the requirement for adequate recording of mitral regurgitation. Even newer echocardiography modalities including tissue Doppler and three-dimensional echocardiography have their own limitations in detecting and quantitating left ventricular systolic dysfunction. Although strain and strain rate imaging have the advantage of being less affected by motion or tethering, they are limited by their signal to noise ratio. Three-dimensional echocardiography provides tomographic cuts for evaluation of regional function and calculation of volume from any window but still imaging resolution is inferior to that of two-dimensional echocardiography.

Estimating the degree of systolic dysfunction in patients with primary diastolic heart failure is not only required for appropriate diagnosis of this condition, but it also has both therapeutic and prognostic implications. The prognosis of heart failure patients with normal systolic function is generally thought to be less ominous than that of patients with systolic dysfunction. This advantage will obviously be lost if prominent systolic dysfunction is associated with diastolic dysfunction. From the therapeutic standpoint, positive inotropic agents are often avoided in conditions of diastolic dysfunction since they have the potential to worsen pathophysiological processes such as myocardial ischemia that is a frequent cause of diastolic dysfunction. However, such agents may be of salutary value if associated systolic dysfunction is a prominent feature and conversely, negative inotropic agents should be cautiously utilized in such circumstances.

A new and relatively simple method of estimating left ventricular systolic function relies on the measurement of ventricular long axis velocities and amplitude using M-mode and tissue Doppler imaging of the mitral annulus. The left ventricular long axis is claimed to be a particularly sensitive measure of ventricular systolic function reflecting the subendocardial position of the longitudinal fibers which makes them more vulnerable to ischemia, left ventricular hypertrophy and other abnormalities of activation and relaxation. The technique of measuring atrioventricular plane displacement as a result of systolic long axis shortening is readily mastered and lacks most of the disadvantages associated with traditional echocardiographic techniques.

The intricate relationship between systole and diastole is supported by a substantial body of experimental evidence. Conceptually myocardial contraction and relaxation should be considered as a continuous cycle. The energy generated during systole is stored within the myocardium particularly in coiled collagen fibers and with the onset of diastole the ventricle uncoils creating left ventricular suction. As myocyte contractile function declines, recoil will also decline in parallel. This decline may be exacerbated by independent changes in extracellular matrix.

# AIM OF WORK

This study has four primary objectives:

1. Study the status of left ventricular systolic function in patients presenting with primary diastolic heart failure using novel parameters that may prove more sensitive than the commonly used ejection fraction.
2. Evaluating the value of mitral annular plane systolic excursion in detecting subtle changes in left ventricular systolic function that are undetectable by estimates of global systolic function in this cohort of heart failure patients.
3. Confirming or refuting the concept that systolic and diastolic heart failure are a continuum of pathophysiological changes as opposed to being two separate disorders with different morphological and physiological features.
4. Discussing the potential impact of our findings on the prognosis and therapy of patients with diastolic heart failure, a condition that still suffers from the scarcity of evidence-based management strategies.

# REVIEW OF LITERATURE

**CHAPTER 1**

# EPIDEMIOLOGY OF DIASTOLIC HEART FAILURE

Heart failure is a major public health problem. Given the data showing a significant increase in the number of heart failure related hospitalizations, it can be regarded as an emerging epidemic [1]. Recently, consistent figures regarding the incidence and prevalence of heart failure with normal left ventricular ejection fraction (LVEF) became available despite different definitions, diagnostic modalities and populations included. [2]

## Incidence

Data from the Olmsted County, Minnesota cohort-based study revealed that 43% of patients with newly diagnosed heart failure had normal LVEF. The group of patients with heart failure with normal LVEF was characterized by a higher proportion of women (69%), more advanced age (mean age 77 years), higher prevalence of atrial fibrillation (29%), lower prevalence of coronary artery disease (31%) and previous myocardial infarction (15%) compared with patients with heart failure and LVEF < 50% (women 41%, mean age 74 years, atrial fibrillation 24%, coronary artery disease 53% and previous myocardial infarction 42%). Interestingly, there was no difference between the two populations in the prevalence of hypertension and chronic obstructive pulmonary disease. In logistic regression analysis, two factors were independently associated with LVEF in patients with newly diagnosed heart failure: female sex and age > 90. [3]

## Prevalence *(Figure 1)*

Recently published data derived from consecutive patients hospitalized with decompensated heart failure in Olmsted County, Minnesota showed that prevalence of heart failure with normal LVEF significantly increased over the 15-year observation period (1987-2001) at a rate of 1% per year. Over the same period, there was no change in the prevalence of heart failure with reduced LVEF. There were more women and obese patients in the groups with normal