STUDY OF DIASTOLIC DYSSYNCHRONY IN PATIENTS WITH STAGE C AND D HEART FAILURE WITH AND WITHOUT PROLONGED QRS DURATION

A thesis submitted in partial fulfillment of the Medical Doctorate (MD) Degree in Cardiology

By

Ahmed Mohamed ElGuindy

MSc, MRCP (UK)

Under the supervision of Professors

Hussein H. Rizk, MD

Professor of Cardiology, CairoUniversity

Wafaa A. El Aroussy, MD

Chair and Professor of Cardiology, Cairo University

Azza A. Farrag, MD

Professor of Cardiology, CairoUniversity

Faculty of Medicine

CairoUniversity

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ABSTRACT

Diastolic dyssynchrony has rscently beenrecognized as a common feature in both Systolic and diastolic heart failure. This study aims to identifly the prevalence of diastolic Dyccynchrony in heart failure with preserved and with reduced ejection fraction as well As correlate the degree of diastolic dyssynchrony with various indices of systolic and Diastolc function. The currentstudy concluded that L V diastolic dyssynchrony is Common (occurring in 42.5% of patients with satges C and D heart failure) and shows Significant correlation with the myocardial performace index and pulmonary artery artery Systolic pressur.

Key words:

Diastolic dyssynchrony

Heart failure with preserved ejection fraction

Heart failure with reduced ejection fraction

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Ahmed ElGuindy

LIST OF ABBREVIATIONS

6MWT	6-minute walk test
A	Late mitral inflow
A'	Peak late diastolic mitral annular velocity
ACC	American College of Cardiology
ACEI	Angiotensin-converting enzyme inhibitors
AF	Atrial fibrillation
AHA	American Heart Association
ANP	Atrial natriuretic peptide
APD	Action potential duration
AS	Atrial sensed
AS-VP	Atrial sensed-to-ventricular paced
ATP	Adenosine triphosphate
AV	Atrioventricular
AVD	Atrioventricular delay
BiVP	Biventricular pacing
BNP	Brain natriuretic peptide
CAD	Coronary artery disease
cGMP	cyclic Guanosine monophosphate
CHF	Congestive heart failure
CKD	Chronic kidney disease
CMR	Cardiac magnetic resonance
COMPANION	Comparison of Medical Therapy Pacing and Defibrillation in Heart Failure
COPD	Chronic obstructive lung disease

CRT	Cardiac resynchronization therapy
CT	Contraction time
CVS	Cerebrovascular stroke
DM	Diabetes mellitus
E	Early mitral inflow
E'	Peak early diastolic mitral annular velocity
ECG	Electrocardiogram
ECM	Extracellular matrix
EF	Ejection fraction
EGM	Electrogram
ESC	European Society of cardiology
ESPVR	End-systolic pressure-volume relationship
ET	Ejection time
FDA	Food and Drug Agency
FDG	Fluorodeoxyglucose
HTN	Hypertension
ICD	Implantable cardioverter defibrillator
IVC	Isovolumic contraction
IVCD	Intraventricular conduction delay
IVCT	Isovolumic contraction time
IVR	Isovolumic relaxation
IVRT	Isovolumic relaxation time
IVS	Interventricular septum
LA	Left atrium
LAP	Left atrial pressure
LBBB	Left bundle branch block
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
MADIT-CRT	Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy
MAP	Mitogen-activated protein
MIRACLE	Multicenter InSync Randomized Clinical Evaluation
MLWHF	Minnesota Living With Heart Failure
MR	Mitral regurgitation
MRI	Magnetic resonance imaging
MUSTIC	Multisite Stimulation in Cardiomyopathy
NT	N-terminal
NYHA	New York Heart Association
PASP	Pulmonary artery systolic pressure
PATH-CHF	Pacing Therapies in Congestive Heart Failure
PCT	Pre-contraction time
PET	Positron emission tomography
PROSPECT	Predictors of Response to Cardiac Resynchronization Therapy
PVd	Pulmonary vein diastolic flow
PVs	Pulmonary vein systolic flow
PWT	Posterior wall thickness
QOL	Quality of life
QTc	Corrected QT interval
RBBB	Right bundle branch block
REVERSE	Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction
RV	Right ventricle
RVSP	Right ventricular systolic pressure
RyR	Ryanodine receptor

S'	Peak mitral annular systolic velocity
SD	Standard deviation
SERCA	Sarcoplasmic endoplasmic reticulum Ca^{2+} ATPase
SPECT	Single-photon emission computed tomography
SPWMD	Septal-to-posterior wall motion delay
SR	Sarcoplasmic reticulum
SV	Stroke volume
TAPSE	Tricuspid annular plane systolic excursion
TDI	Tissue Doppler imaging
TNF	Tumor necrosis factor
TST	Total systolic time
VCF	Velocity of circumferential fiber shortening
VF	Ventricular fibrillation
VS	Ventricular sensed
VT	Ventricular tachycardia
VTI	Velocity time integral
VV	Ventriculo-ventricular / interventricular
Vp	Propagation velocity

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INTRODUCTION

Cardiac resynchronization therapy (CRT) is an established therapy for patients with advanced heart failure (HF). The basic premise is that cardiac dyssynchrony complicates or causes myocardial dysfunction and that retiming of the sequence of contraction can improve cardiac function, thereby improving symptoms and reducing cardiovascular morbidity and mortality. Conceptually, cardiac dyssynchrony includes altered sequence of both cardiac contraction and relaxation. It encompasses AV dyssynchrony, interventricular dyssynchrony and intraventricular dyssynchrony. Whether interatrial dyssynchrony or dyssynchronous contraction within the thickness of the myocardial wall has an important effect on cardiac function remains uncertain.[1]

Diastolic dyssynchrony is at least as common as systolic dyssynchrony in patients with systolic heart failure and frequently exists without concurrent systolic dyssynchrony in this patient population [2–4]. In diastolic heart failure, diastolic dyssynchrony occurs in more than half of such patients and is more frequent than systolic dyssynchrony [5]. Several pathophysiological mechanisms have been proposed to account for diastolic dyssynchrony in patients with systolic or diastolic heart failure. The most obvious explanation is that it occurs secondary to systolic dyssynchrony; the segments with delayed contraction also show delayed relaxation [6,7]. Another potential reason is the presence of coronary artery disease which results in asynchronous regional diastolic function that improves after coronary revascularization [8–10]. Additionally, diastolic function and ventricular filling pattern appear to be important components of the underlying pathophysiology of diastolic dyssynchrony. The degree of diastolic but not systolic dysfunction has been shown to predict diastolic dyssynchrony [11]. Moreover, LV filling abnormalities related to ventricular interaction in diastole are of crucial importance. Left ventricular filling may be impeded in up to one-half of HF patients due to ventricular interaction from raised right ventricular diastolic pressure and by external compression from the pericardium. This diastolic interaction could explain the delayed onset of mechanical diastolic motion in the left ventricle even in patients without concurrent systolic dyssynchrony [12].

There is powerful evidence from a series of randomized controlled trials that CRT is an effective treatment of patients with heart failure who fulfilled their entry criteria which universally included patients with left ventricular dilatation, systolic dysfunction, wide QRS duration (≥ 120 ms) and in sinus rhythm. Nevertheless, only limited information on the pathophysiology of diastolic dyssynchrony and its affection by CRT is available. In small cohort studies, either no improvement in diastolic dyssynchrony [13] or less improvement than in systolic dyssynchrony [12]has been demonstrated shortly after the initiation of biventricular pacing. A mid-term follow up study showed improvement in diastolic dyssynchrony only in patients with nonischemic cardiomyopathy, whereas systolic dyssynchrony improved regardless of the heart failure etiology [3]. Recently, a large cohort study of heart failure patients, demonstrated significant improvement of both systolic and diastolic dyssynchrony acutely and at 6 months after CRT, with no difference between patients with ischemic and nonischemic HF. [14]

Despite significant shortening of QRS duration with CRT, there is only a weak correlation between the reduction QRS duration and improvement in systolic dyssynchrony. No such correlation was observed for diastolic dyssynchrony, suggesting that the improved coordination of LV myocardial relaxation with CRT is independent of electrical activation.[14]

The lack of response to CRT in up to 30% of patients remains one of the greates challenges of such therapy. This has been variously attributed to lack of mechanical dyssynchrony in some patients with broad QRS, suboptimal lead placement or incorrect device setup. The myocardial scar burden and its location have also been incriminated, with nonresponders to CRT having 3 or more scar segments and delivery of pacing over the scarred segments [15]. The role of uncorrected diastolic dyssynchrony in CRT nonresponders has also been proposed, but not adequately addressed and may turn out to be a significant contributor to such phenomenon.

In addition to providing better understanding of cardiac diastolic function, identifying the prevalence of diastolic dyssynchrony in patients with both systolic and diastolic heart failure as well as the variables that affect diastolic resynchronization is paramount in selecting the appropriate candidates for the invasive and expensive procedure of CRT.

AIM OF WORK

This study has three primary objectives:

1. Study the prevalence and magnitude of diastolic dyssyncrony in patients with both heart failure with preserved ejection fraction and heart failure with reduced ejection fraction.
2. Identify whether the degree of diastolic dyssynchrony is related to the severity of
    a. Diastolic dysfunction
    b. Systolic dysfunction
    c. Systolic dyssynchrony
    d. QRS width and QT interval
3. Correlate the degree of diastolic dyssynchrony with various echocardiographic indices of left ventricular systolic and diastolic function.

REVIEW OF LITERATURE