Correlation between Tricuspid Annular Plane Systolic Excursion to Pulmonary Artery Systolic Pressure Ratio and Atrial Dyssynchrony in Heart Failure with Preserved Ejection Fraction

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Abstract

Introduction: Heart failure with preserved ejection fraction (HFpEF) is still unresolved problem. Interatrial dyssynchrony was associated with worse clinical status in such patients. Tricuspid Annular Plane Systolic Excursion to Pulmonary Artery Systolic Pressure (TAPSE/PASP) Ratio could be correlated with intra- and interatrial conduction time in patients with HFpEF. **Methods:** In 73 consecutive patients with HFpEF, we measured of right ventricular TAPSE, PASP, and parameters of atrial dyssynchrony. We assessed atrial dyssynchrony by measuring the difference between the times from the electrocardiogram P wave onset to the tissue doppler A′ wave onset (PA′ interval) at the levels of lateral mitral, septal mitral, and tricuspid annuli. We studied the association of such dyssynchrony with TAPSE/PASP ratio in patients with HFpEF. **Results:** Based on the median of TAPSE/PASP ratio, 73 patients were categorized into two groups as having TAPSE/PASP ≤0.48 (group I) or having TAPSE/PASP >0.48 (group II). Group I patients had higher NYHA class ($p<0.05$), higher brain natriuretic peptide (<0.01), higher left ventricular mass index ($p<0.01$), greater left atrial volume index ($p<0.003$), reduced left atrial ejection fraction ($p<0.01$), and higher E/e′ ratio ($p<0.01$). Furthermore, group I patients had prolonged mitral and tricuspid PA′ intervals ($p<0.001$) and significantly increased left and right atrial dyssynchrony ($p<0.001$) compared with group II patient. TAPSE/PASP ratio correlated with left atrial dyssynchrony ($r=-0.53$, $p<0.001$), right atrial dyssynchrony ($r=-0.55$, $p<0.001$) and with interatrial dyssynchrony ($r=-0.48$, $p<0.005$). **Conclusion:** In patients with HFpEF with TAPSE/PASP < 0.48, had prolonged right atrial, left atrial, and interatrial dyssynchrony which is a risk marker for arrhythmia. Therefore, TAPSE/PASP ratio might help to improve risk stratification to predict outcome in HFpEF patients.

Key Words: TAPSE, atrial dyssynchrony, Heart failure with preserved ejection fraction.

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Introduction

Heart failure with preserved ejection fraction (HFpEF) is still unresolved clinical syndrome in which treatment is ineffective. The main pathophysiological point is elevated left ventricular (LV) filling pressures which in turns will elevate left atrial (LA) pressure [1]. Chronic elevation of LA pressure is responsible for LA remodeling, pulmonary hypertension, and secondary right ventricular (RV) systolic dysfunction which are poor prognostic parameters in HFpEF [2].

Mechanical LA remodeling leads to electrophysiological LA remodeling which increases the risk of atrial fibrillation (AF) and subsequently the risk of clinical deterioration and thrombo-embolic stroke [3]. Previous research tried to pick up predictors of AF in patients with HFpEF for better improvement in both screening and protection against thromboembolic stroke. Among the studied predictors, atrial dyssynchrony was a fair predictor of atrial arrythmias and AF [4]. However, right atrial (RA) remodeling is linked to increased RV filling pressures after development of pulmonary hypertension [5]. Therefore, interatrial dyssynchrony could be a potential marker of the HFpEF severity [6].

Interatrial dyssynchrony, the delay between right atrial (RA) and left atrial (LA) contraction, could be assessed with simple bed side echocardiography. Interatrial dyssynchrony could be assessed by calculating the difference between the time from the onset of P wave on electrocardiogram (ECG) and A' wave (PA' interval) of both mitral annulus and tricuspid annulus tissue Doppler imaging (TDI) [7].

Tricuspid annular plane systolic excursion to pulmonary artery systolic pressure (TAPSE/PASP) ratio is a good marker of RV deterioration in patients with heart failure (HF). With more advanced HF, the PASP rises and RV systemic function, as assessed with TAPSE, decreases with subsequent decrease in TAPSE/PASP ratio [8]. There is a paucity of data about the association between TAPSE/PASP ratio and interatrial dyssynchrony in patients with HFpEF and this was the main objective of our study.

Methods

We performed a cross sectional study in Zagazig university hospitals in the duration between March 2022 and July 2022. Institutional research board (IRB) committee of faculty of medicine, Zagazig university, Egypt has reviewed and accepted the study protocol with reference number (**ZU.IRB #93779-3-2022**). An informed consent was obtained from all human adult participants.

Study population

We included patients with HFpEF with New York heart association (NYHA) function class I-III. HFpEF is defined as the combination of all the following: clinical symptoms and signs of HF, ejection fraction (EF) more than 50%, and evidence of diastolic dysfunction more than grade I by echocardiography [9].

We excluded patients with heart failure with election fraction below 50%, acute heart failure, NYHA class IV, atrial fibrillation, frequent atrial or ventricular ectopics, mitral stenosis, more than moderate mitral regurgitation, chronic obstructive pulmonary disease, stroke, acute coronary syndrome, and anemia.

Study variables and clinical assessment

We collected basic characteristics and risk factors for all patients including age, gender, body mass index, waist/hip ratio, history of hypertension, history of diabetes mellitus, history of coronary artery disease, heart rate, blood pressure, NYHA class, fasting blood sugar, lipid profile, kidney function tests, and brain natriuretic peptide.

Echocardiographic assessment

For all patients we calculated LV end diastolic volume (LVEDV), LV end systolic volume (LVESV), LV end diastolic diameter (LVEDD), end diastolic posterior wall thickness (PWTD), end diastolic interventricular septal thickness (IVSTD), LVEF as following [LVEDV – LVESV / LVEDV] in both apical 2 and apical 4 chambers views, LV mass (LVM) as following [1.04 ([LVEDD + PWTD + IVSTD]3-[LVEDD]3) -13,6 g] [10], and LVM index calculated as [LVM/ body surface area (BSA)[11]. We measured LA diameter from the M mode recording at the level of the aortic valve leaflets. LA volumes were assessed from the modified apical 4 chamber view using area-length method. Furthermore, we measured LA maximal volume (LAV max) at the LV

end systolic frame and LA minimal volume (LAV min) at the LV end diastolic frame. Based on that, we measured LA emptying fraction (LAEF) as following: [(LAV max – LAV min) / LAV max x 100][12].

From the apical 4 chamber view, we obtained pulsed wave doppler (PWD) study of both mitral inflow and tricuspid inflow for assessment of early diastolic (E) wave peak velocity, late diastolic (A) wave peak velocity, E/A ratio, and E wave deceleration time (DT). DT was measured from the pean of E wave to the end of its deceleration [13]. We performed M mode assessment of mitral annular plane systolic excursion (MAPSE) and tricuspid annulus plane systolic excursion (TAPSE) by measuring the total amplitude of longitudinal wall motion from M mode assessment of lateral mitral, septal mitral, and lateral tricuspid annuli [14, 15]. We measured pulmonary artery systolic pressure (PASP) as the summation of the pressure gradient between the right atrium and the right ventricle, acquired from the tricuspid regurge jet peak velocity at continuous wave doppler study, and the right atrial pressure estimation, which was based on the size of the inferior vena cava and its collapsibility [16]. TAPSE/PASP ratio was calculated by dividing TAPSE by PASP [17].

Tissue doppler imaging was performed with assessment of longitudinal velocities of the basal part of lateral and septal LV segments and RV free wall. We recorded systolic (S'), early diastolic (e'), and late diastolic (a') waves for all patients. We calculated with mean value of lateral and septal e' velocities and calculated E/e' ratio [13].

Assessment of atrial dyssynchrony

The time from the P wave onset of on the surface ECG to the start of the A′ wave on TDI (PA′ interval) was calculated from the lateral (PA′ lateral) and septal (PA′ septal) mitral annuli as well as the lateral tricuspid annulus (PA′ tricuspid).10,11 The average of PA′ interval values was calculated form three consecutive beats. LA dyssynchrony was assessed by measuring the difference between PA′ lateral and PA′ septal intervals. In the same manner, RA dyssynchrony was assessed by measuring the difference between PA′ septal and PA′ tricuspid. However, interatrial dyssynchrony was assessed by measuring the difference between PA′ lateral and PA′ tricuspid [7].

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD), while the categorical variables are expressed as numbers and percentages. Continuous variables were compared using independent-sample t- test. Chi-square test was used to compare categorical variables. Pearson correlation analysis was used to find out the correlation of clinical and echo parameters with TAPSE/PASP in patients with HFpEF.

Results

We collected 73 consecutive patients with HFpEF with mean age 58±10 years. Patients were divided into two groups according TAPSE/PASP ratio median value which was 0.48. Group I involved patients with poor TAPSE/PASP ratio (≤0.48) and group II involved patients with better TAPSE/PASP ratio (>0.48).

Basic characteristics analysis **(table 1)** showed that the two groups did not differ regarding age, body mass index, waist/hip ratio, hypertension, diabetes, coronary artery disease, blood pressure, heart rate, blood sugar level, kidney functions, and lipid profile. However, group I patients had higher NYHA class (1.5±0.6 vs 1.1±0.3; P <0.05) and higher brain natriuretic peptide levels (275±43 vs 89±18; P <0.01).

As compared to group II, echocardiographic assessment revealed that group I had higher LVMI (61±14 vs 44±12; P <0.01), lower mean e' (7±1.7 vs 9±2.5; P 0.005), higher E/e' ratio (10.9±4.5 vs 7.7±2.3; P <0.01), bigger LAVI (39.5±8.3 vs 27.5±5.1; P <0.03), and lower LAEF (51.3±7.1 vs 66.5±9; P <0.01) **(table 2).**

Regarding atrial dyssynchrony **parameters (table 3)**, group I patients had longer PA' interval (msec) at level of sepal (58.9±11.5 vs 41.6±7.3) and lateral mitral annulus (69.5±15.1 vs 47.5±9.6; P <0.01). Furthermore, group I patients had longer RA dyssynchrony parameter (msec) (34.5±8.6 vs 17.9±8.1: P <0.001), longer LA dyssynchrony parameter (msec) (27.3±6.2 vs 11.7±3.3; P <0.001), and longer interatrial dyssynchrony parameter (msec) (33.8±11.5 vs 21.5±7.8; P <0.003).

Correlation analysis revealed that TAPSE/PASP had significant positive correlation with LAEF and MAPSE but significant negative correlation with NYHA class, LVMI, E/e' ratio, LA dyssynchrony, RA dyssynchrony, and interatrial dyssynchrony **(table 4).**

Table (1): Comparison of clinical and biochemical data between patient groups.

	Group I n=36	Group II n=37	*P*-value
Age (years)	62±8.1	57±10	0.21
BMI (kg/m^2)	27.5±4.3	29.5±4.1	0.18
Waist/hip ratio	0.92±0.5	0.94±0.4	0.25
Hypertension, n(%)	28(77.8)	30(81.08)	0.69
Diabetes, n(%)	16(44.4)	18(48.6)	0.75
Coronary artery disease (%)	9(25)	10(27)	0.65
SBP (mmHg)	145±21	139±15	0.28
DBP (mmHg)	85±10	81±10	0.13
NYHA class	1.5±0.6	1.1±0.3	<0.05
HR (bpm)	83±10	80±13	0.28
Fasting glucose (mmol/l)	6.5±1.6	6.5±2.1	0.69
Total cholesterol (mmol/l)	5.9±1.5	5.7±1.7	0.63
Triglycerides (mmol/l)	1.8±0.5	1.7±0.7	0.70
Urea (mmol/l)	6.8±3.9	7.5±4.6	0.46
Creatinine (mmol/l)	75±19	83±22	0.25
Brain natriuretic peptide(pg/mL)	275±43	89±18	<0.01

BMI: Body mass index, **SBP:** Systolic blood pressure, **DBP:** Diastolic blood pressure

Table (2): Comparison of echocardiographic data between patient groups.

	Group I n=36	Group II n=37	*P*-value
LV mass index (g/m$^{2.7}$)	61±14	44±12	<0.01
LVEF (%)	63±8.0	64±8.2	0.76
E/A ratio	0.82±0.41	0.91±0.35	0.25
E-wave DT (ms)	219±49	19±42	0.33
mean e' (cm/s)	7.0±1.7	9.0±2.5	0.005
E/e' ratio	10.9±4.5	7.7±2.3	<0.01
MAPSE (cm)	2.2±0.4	2.3±0.4	0.27
TAPSE (cm)	1.4±0.4	1.9±0.5	<0.001
PASP	39.9±12.7	32.3±10.5	<0.01
TAPSE/PASP ratio	0.35±0.08	0.64±0.08	<0.001
LA diameter (cm)	4.1±0.5	3.8±0.3	0.19
LAVindex (ml/m2)	39.5±8.3	27.5±5.1	<0.03
LAEF (%)	51.3±7.1	66.5±9.0	<0.01

LV: Left ventricle, **EF:** Ejection fraction, **DT:** Deceleration time, **MAPSE:** Mitral annular plane excursion, **TAPSE:** Tricuspid annular plane excursion, **PASP:** Pulmonary artery systolic pressure, LA: Left atrial.

Table (3): Atrial dyssynchrony parameters among patients with in group I vs group II

	Group I n=36	Group II n=37	*P*-value
P-RA (ms)	29.6 ± 5.7	27.5 ± 3.2	0.31
P-IAS (ms)	58.9 ± 11.5	41.6 ± 7.3	<0.01
P-LA(ms)	69.5 ± 15.1	47.5 ± 9.6	<0.03
LA dyssynchrony(ms)	27.3 ± 6.2	11.7 ± 3.3	<0.001
RA dyssynchrony (ms)	34.5 ± 8.6	17.9 ± 8.1	<0.001
Interatrial dyssynchrony (ms)	33.8 ± 11.5	21.5 ± 7.8	<0.003

P-RA= onset of P-wave to onset of A-wave at the right atrium;
P-IAS= onset of P-wave to onset of A-wave at the interatrial septum;
P-LA= onset of P-wave to onset of A-wave at the LA; RA = right atrium;
LA = left atrium.

Table (4): Correlations of clinical and echocardiographic variables with TAPSE/PASP ratio.

	r	P value
NYHA class	−0.30	<0.05
LV mass index (g/m$^{2.7}$)	−0.23	<0.09
E/e' ratio	−0.32	<0.05
LAEF (%)	0.39	<0.01
MAPSE (CM)	0.22	0.07
LA dyssynchrony (ms)	−0.53	<0.001
RA dyssynchrony (ms)	−0.55	<0.001
Interatrial dyssynchrony (ms)	−0.49	<0.005

MAPSE: Mitral annular plane excursion, **LAEF:** Left atrial ejection fraction, **LV:** left ventricle, **RA:** Right atrium

Discussion:

Heart failure with preserved ejection fraction (HFpEF) is still unresolved clinical syndrome in which prediction of outcome is deficient and treatment is ineffective [1]. Among predictors of outcome in patients with HFpEF, low TAPSE/PASP ratio is good independent predictor of poor prognosis. Low TAPSE/PASP ratio reflects more increase in pulmonary artery pressure and more decrease in RV systolic function [17]. Furthermore, intra- and inter-atrial dyssynchrony, as a result in increase in atrial pressures, could predict poor cardiovascular outcome in patients with HFpEF[6]. We studied the correlation between atrial dyssynchrony and TAPSE/PASP in patients with HFpEF.

Clinically, our study revealed that patients with HFpEF and low TAPSE/PASP ratio (<0.48) had worse symptoms and higher BNP levels. Echocardiographic evaluation revealed that such category of patients had larger LVMI and LAVI, more advanced diastolic dysfunction, lower LA function, and more intra- and interatrial dyssynchrony.

TAPSE/SPAP ratio is rapid, easy, and reliable method that was studied in different clinical scenarios with different cut off values. In patients with systemic sclerosis, low TAPSE/SPAP ratio was correlated with poor functional capacity as a result of advanced RV dysfunction [18]. TAPSE/SPAP ratio below 0.35 predicted high all cause morality in patients undergoing mitral clipping [19]. In patients with acute pulmonary embolism, TAPSE/SPAP ratio below 0.6 predicted high incidence of adverse events [20]. Furthermore, TAPSE/SPAP ratio below 0.38 predicted poor cardiovascular outcomes in patients with ischemic and non-ischemic cardiomyopathy [21].

Echocardiographic assessment of atrial dyssynchrony in a novel and valid way that could help in prediction of cardiovascular outcomes. Fuenmayor and colleagues demonstrated that echocardiographic assessment of interatrial dyssynchrony was well correlated with interatrial conduction time that was measured during electrophysiology study [22]. Furthermore, Merckx and colleagues concluded that left atrial doppler tissue imaging could be a trusted estimation of the total atrial electrical activation, and potential predictor of atrial fibrillation [23]. Acar and colleagues studied tissue doppler based atrial electromechanical delays in patients with type I diabetes mellitus and demonstrated a significant

association with impairment of ventricular and atrial functions [24].

LA dyssynchrony occurs on top of LA remodeling which is independent predictor of stroke even in patients with sinus rhythm. This could be due to blood stasis in dilated LA with dysfunction and subsequent thrombus formation[3]. Furthermore, LA dyssynchrony predicted recurrence of AF even with catheter ablation[25]. In concordance, interatrial dyssynchrony predicted postoperative AF in patients underwent open heart surgery [26]. In patients with paroxysmal AF, longer atrial electromechanical coupling was associated with more frequent and longer episodes of AF [27]. However, LA dyssynchrony did not have any prognostic value in general population regarding major adverse cardiovascular outcomes [28].

Our study had few limitations; the study was observational study. We did not perform follow up to detect the impact on cardiovascular outcomes. Further research is warranted to test the impact of TAPSE/SPAP and atrial dyssynchrony on different cardiovascular outcome parameters in patients with HFpEF.

Conclusion:

In patients with HFpEF with TAPSE/PASP < 0.48, had prolonged right atrial, left atrial, and interatrial dyssynchrony which is a risk marker for arrhythmia. Therefore, TAPSE/PASP ratio might help to improve risk stratification to predict outcome in HFpEF patients.

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