Ratio of Tricuspid Annular Plane Systolic Excursion to Systolic Pulmonary Artery Pressure in Patients with Heart Failure with Preserved Ejection Fraction

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ABSTRACT
Background: Tricuspid annular plane systolic excursion (TAPSE) connected to pulmonary artery systolic pressure (PASP) may enhance prognosis in heart failure with an adequate ejection fraction.
Objective: The aim of the current study is to evaluate the applicability of TAPSE in cases with heart failure and preserved ejection fraction (HFpEF), which is indexed to PASP.
Patients and methods: The present study included 75 patients with HFpEF. They were divided into 2 groups depend on the results of 6-minute walking test. *Group I* included 49 patients with good exercise tolerance and *Group II* included 36 patients with reduced exercise tolerance.
Results: The TAPSE/PASP ratio has a sensitivity of 83.5% and a specificity of 79.3% for detecting individuals with reduced exercise intolerance, with an area under the curve (AUC) of 0.834 (95%CI: 0.753-0.916, P <0.001).
Conclusion: A relevant clinical indicator of the length/force relation may be the correlation between longitudinal RV fibre shortening (TAPSE) and developed pressure (PASP), and the ratio of 2 variables may be more reliable than either of the two measures alone in predicting the severity of disease.
Keywords: TAPSE, Right ventricular function, Heart failure, Case control study, Zagazig University.

INTRODUCTION

A crucial indicator of prognosis for certain cardiovascular diseases, right ventricular (RV) malfunction is one of the heart failures that include the left side. Maladaptive RV remodelling is connected to RV myocardial dilatation, sarcomere changes, fibrosis, capillary rarefication, and metabolic problems, is a common complication of ischemia and non-ischemic cardiomyopathy. These alterations result in right side heart failure (HF) and progressive RV dysfunction [1].

With rising prevalence and morbidity, on a global level, a significant public health issue is HFpEF. Despite the fact that modern medicinal methods have increased life quality, mortality rates are still high [2]. Determinants of functional ability in individuals with HFpEF have not been thoroughly studied. The 6-minute walk test (6-MWT) has been utilized to objectively assess activity ability in the context of HF. For individuals with HFrEF, several resting echocardiographic indicators indicated limited exercise ability; however, none of these markers are related to functional ability in people with HFpEF [3].

People with HF and reduced left ventricular (LV) ejection fraction (HFrEF) as well as those with HF and retained LV ejection fraction (HFpEF) have revealed that the TAPSE/PASP ratios can predict serious adverse outcomes [4].

The aim of the current study is to evaluate the applicability of TAPSE in cases with heart failure and preserved ejection fraction (HFpEF), which is indexed to PASP.

PATIENTS AND METHODS

A cross-sectional study was conducted at Cardiology Department, Zagazig University Hospital, from Heart Failure Clinic. Included patients were diagnosed with HFpEF (EF more than 50%, Symptoms of HF, Signs of HF, Evidence of diastolic dysfunction) and functioning classes I through III of the New York Heart Association (NYHA) were included.

Cases with greater mild mitral regurgitation, severe arrhythmias, limited physical activity caused by conditions other than cardiac symptoms, such as arthritis, and those with clinical signs of cardiac decompensation were excluded from the study.

Every patient had a thorough *medical history* review and *physical assessment*. Thereafter, *laboratory tests* included lipid profile, kidney profile, hemoglobin, fasting blood glucose levels, brain natriuretic peptide. All patients underwent standard 12-lead *ECG* recordings during both rest and stress.

Echocardiography was performed for all participants: The apical 2 and 4 chamber photos were utilised to determine the LV volumes and EF utilizing a modified Simpson's technique. The M-mode cursor was placed at the lateral, septal, and tricuspid ring angles to track the movement of the ventricles along their long axis. Like I said previously, peaks from the inside to the outside were used to calculate the long axis motion's overall amplitude [5]. The M-mode cursor was put at the position of the aortic valve leaflets to estimate the left atrial diameter from recordings of the aortic root.

Area-length measurements of LA volumes were made from the apical four chamber images. Left atrial maximal volume (LAV max) and left atrial minimal volume (LAV min) were assessed at the conclusion of

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the LV systole and just prior the mitral valve opens, respectively. Using the formula, the LA empty fraction (LA EF) was determined. [6]:

LA total emptying fraction= LAVmax -LAVmin/ LAVmax ×100

Utilizing spectral pulsed wave Doppler with the sample volume placed at the tips of the mitral and tricuspid valve leaflets, respectively, the diastolic LV and RV function were evaluated during a brief apnoea. E/A ratios were calculated using the peak early (E wave) and late (A wave) diastolic velocities for the LV and RV. Each study participant's E wave deceleration time (DT) was assessed as the interval between the E wave's peak and its decline.

The transmitral E wave, combined with the normal lateral and septal segmental e' wave velocities, were used to calculate the E/e' ratio. On the Doppler monitoring of pulsed waves, the isovolumic relaxation interval between mitral valve opening and aortic valve closure was also discovered. When the E/A ratio is greater than 2.0, the E wave DT is less than 140 ms, and over than 40 mm in transverse dimensions of the left atrium are dilated, the left atrium is considered to have a "restrictive" filling pattern. Both the length of the aortic Doppler flow velocity from beginning to end and the length of the complete LV filling period were noted. As per to the standards of Echocardiography's American and European Society, the degree of mitral regurgitation was classified as mild, intermediate, or utilizing the flow velocity profile and the left atrium's relative jet area in a serious manner [7].

Additionally, tricuspid regurgitation was evaluated utilizing continuous-wave Doppler and colour Doppler. Pneumotension was believed to exist when the retrograde trans-tricuspid pressure reduction was more than 35 mmHg [7]. The ECG was recorded over all M-mode and Doppler data at a quick pace of 100 mm/s (lead II). The maximum tricuspid annulus excursion from the end of diastole to the end of systole was used to compute TAPSE. Right atrial pressure (RAP), which was calculated from right atrial pressure (PASP), which was determined as the pressure differential between the right atrium and the right ventricle from the TR jet peak velocity, was used to measure the size and collapsibility of the inferior vena cava.

Six-minute walk test (6-MWT)**:** A 6-MWT was carried out within 24 hours of the echocardiographic test using the Gyattetal method on a level hallway surface [8]. Patients were directed to walk as far as they could along a 15-m level, obstacle-free hallway during the allotted 6-min period before turning 180 degrees and continuing. At the conclusion, the distance travelled overall was calculated.

Ethical Consideration:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University. Written informed consent was obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical Analysis

The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (SPSS) version 20 for windows. Qualitative data were defined as numbers and percentages. Chi-Square test and Fisher's exact test were used for comparison between categorical variables as appropriate. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as means and standard deviation (SD), and independent sample t-test was used for comparison between groups. Spearman's correlation was utilized to examine the relationship between two variables. P value ≤ 0.05 was considered to be statistically significant.

RESULTS

There is substantial variation between the studied groups as regard 6-minute walking distance and brain natriuretic peptide **(Table 1).**

Table (1): Demographic and baseline data in patients with decreased versus good exercise tolerance.

Variable	Group I N= 49	Group II N= 36	P-value
Age (years)	57 ± 8.5	61 ± 8.7	0.18
BMI (kg/m2)	27 ± 3.3	27 ± 3.7	0.21
6 MWT distance, m	549 ± 46	251 ± 25	<0.001*
Waist/hip ratio	0.92 ± 0.35	0.93 ± 0.51	0.25
Hypertension, n (%)	37 (75.5)	27 (745)	0.69
Diabetes, n (%)	25 (51)	19 (53)	0.75
Coronary artery disease (%)	12 (24.5)	9 (25)	0.65
SBP (mmHg)	137 ± 16	143 ± 21	0.35
DBP (mmHg)	82 ± 9	85 ± 11	0.20
NYHA class	1.1 ± 0.9	1.4 ± 0.5	0.15
DD grade	1.1 ± 0.75	1.2 ± 0.68	0.35
HR (bpm)	81 ± 14	82 ± 15	0.49
Fasting glucose (mmol/l)	6.4 ± 1.8	6.1 ± 1.1	0.55
Urea (mmol/l)	7.5 ± 1.3	6.9 ± 1.5	0.57
Total cholesterol (mmol/l)	5.7 ± 1.3	5.6 ± 1.4	0.58
Urea (mmol/l)	7.5 ± 1.3	6.9 ± 1.5	0.57
Triglycerides (mmol/l)	1.7 ± 0.2	1.8 ± 0.3	0.61
Creatinine (mmol/l)	89 ± 3	85 ± 8	0.20
Brain natriuretic peptide (pg/mL)	95 ± 15	269 ± 45	<0.0.01*
ACE-I, n (%)	30 (61)	21 (58)	0.71
ARB, n (%)	12 (24.4)	10 (27.7)	0.57
Diuretic, n (%)	18 (36.7)	15 (41.7)	0.28
Beta-blocker, n (%)	22 (44.8)	14 (39)	0.63
CCB, n (%)	5 (10.29)	4 (9)	0.89
Nitrates, n (%)	8 (16.3)	6 (16.7)	0.65

There is statistically **substantial** variation between the research groups regarding left ventricular mass index, E/e´ ratio, LAV min, and PASP, lateral, septal e´, TAPSE and TAPSE/PASP LAEF **(Table 2).**

Table (2): Echocardiographic measures in cases with decreased versus good exercise tolerance

Variable	Group I N= 49	Group II N= 36	P-value
LV mass index (g/m$^{2.7}$)	43 ± 10	60 ± 18	**<0.001***
IVSd (cm)	1.1 ± 0.2	1.2 ± 0.2	0.05
LVEDD(cm)	4.8 ± 0.6	5.0 ± 0.5	0.17
LVEF (%)	63 ± 5.3	62.8 ± 5.1	0.46
LVPWd (cm)	0.99 ± 0.1	1.1 ± 0.1	0.29
LVESD(cm)	3.1 ± 0.5	3.2 ± 0.3	0.22
LV shortening fraction (%)	35.2 ± 3.3	35.8 ± 3.9	0.87
Septal s′(cm/s)	5.5 ± 1.6	5.1 ± 1.1	0.15
Lateral s′(cm)	6.1 ± 1.5	5.7 ± 1.6	0.28
E/e′ ratio	8.2 ± 1.9	9.9 ± 4.0	**0.005***
E-wave velocity (cm/s)	61 ± 16	59 ± 17	0.53
E-wave DT (ms)	197 ± 45	208 ± 45	0.45
Septal e′ (cm/s)	7.5 ± 2.7	5.2 ± 1.9	**0.005***
Lateral e′ (cm/s)	8.9 ± 3.0	6.4 ± 2.5	**0.005***
LA diameter (cm)	4.0 ± 0.4	4.2 ± 0.5	0.21
LAVmax (ml)	51 ± 13	53 ± 17	0.53
LAVmin (ml)	17.5 ± 6.7	23 ± 9.2	**0.005***
LAEF (%)	64 ± 10	55 ± 8.5	**<0.001***
Tricuspid E (cm/s)	52 ± 13	45 ± 11	0.05
Right s′ (cm/s)	9.8 ± 2.6	8.6 ± 2.9	0.11
Right e′ (cm/s)	10.8 ± 3.5	9.5 ± 3.1	0.05
TAPSE (mm)	19.9 ± 5.7	15.6 ± 4.7	**<0.001***
PASP (mmHg)	32.8 ± 10.2	39.5 ± 11.5	**0.01***
TAPSE/PASP (mm/mmHg)	0.62 (0.51, 0.83)	0.40 (0.30, 0.54)	**<0.001***

There is significant positive connection between TAPSE and LAEF, right e′ and mean e′. There is statistically significant negative connection between TAPSE and all of BNP, 6 minute walking distance, LV masse, E/e′ ratio, TAPSE and LAV min **(Table 3).**

Table (3): Clinical and echocardiographic parameters and TAPSE correlations.

Variable	*r*	*P-value*
BNP	−0.34	0.03*
6 MWTD	−0.59	<0.001*
LV-Masse	−0.32	<0.01*
E/e′ ratio	−0.29	<0.03*
Right e′(cm/s)	0.22	<0.05*
Mean e′(cm/s)	0.28	<0.05*
LAVmin (ml)	−0.32	<0.01*
TAPSE(cm)	0.30	<0.03*
LAEF (%)	0.35	<0.01*

It was found that higher BNP significantly increase hazard by 4.18 folds. Higher LV masse, E/e′ ratio, mean e′ and LAV min significantly increase hazard by 1.42, 2.19, 1.49 and 1.76 folds, respectively. Also, higher right e′, TAPSE, TAPSE/PASP significantly increase hazard by 1.25, 1.73 and 5.16 folds, respectively **(Table 4).**

Table (4): Univariate analysis for prediction of reduced exercise tolerance in HFpEF patients.

Variable	Hazard Ratio	95%CI	*P*-value
BNP	4.18	1.69-7.85	0.03*
LV-Masse	1.42	1.09–1.62	< 0.05*
E/e′ ratio	2.19	1.46–3.71	<0.01*
Mean e′(cm/s)	1.49	0.92–1.83	<0.05*
MAPSE	0.29	0.11–0.57	0.06
LAVmin (ml)	1.76	0.91–1.89	< 0.01*
LAEF (%)	1.99	0.98–2.53	<0.05*
Right e′(cm/s)	1.25	0.80–1.76	< 0.05*
TAPSE (cm)	1.73	1.15–2.88	<0.03*
TAPSE/PASP	5.16	2.01-8.35	<0.001*

It was found that higher LAV min, TAPSE, TAPSE/PASP significantly independently increase hazard by 1.18, 1.42, and 4.29 folds, respectively. Higher right and mean e′ non-significantly reduce hazard (hazard ratios 0.52 and 0.65, respectively) **(Table 5).**

Table (5): Multivariate analysis for prediction of reduced exercise tolerance in HFpEF patients.

Variable	Hazard Ratio	95%CI	*P*-value
BNP	1.38	0.91-2.15	0.22
LV-Masse	1.02	0.30–1.42	0.25
E/e′ ratio	1.21	0.52–1.98	0.13
Mean e′ (cm/s)	0.65	0.45–1.37	0.17
LAVmin (ml)	1.18	0.85–1.67	**<0.05***
LAEF (%)	1.07	0.75–1.50	0.09
Right e′ (cm/s)	0.52	0.39–0.75	0.12
TAPSE (cm)	1.42	0.93–1.89	**<0.05***
TAPSE/PASP	4.29	2.11-6.50	**<0.001***

Patients' ROC curves were assessed in order to establish the best cut-off level for the TAPSE/PASP ratio in the predicting of impaired exercise tolerance in HFpEF (**Table 6 and Figure 5**). The TAPSE/best PASP's cut-off level was ≤ 0.48 mm/mmHg. The TAPSE/PASP ratio has a sensitivity of 83.5% and a specificity of 79.3% for detect individuals with reduced exercise intolerance, with an AUC of 0.834 (95%CI: 0.753-0.916, P <0.001) **(Table 6).**

Table (6): TAPSE/PASP ratio ROC analysis in predicting HFpEF patients' lower exercise tolerance.

TAPE/PASP Optimal value	AUC	95%CI	P-value	Sensitivity	Specificity
0.48	0.834	0.753–0.916	<0.001	83.5%	79.3%

DISCUSSION

Respecting *Group I*, the mean LV mass index was 43, the mean LVEDD, LVESD, IVSd, LVPWd, and LVWF were 4.8, 3.1, 1.1, 0.99, and 63, respectively.

The mean LV shortening fraction was 35.2%, Lateral S' was 6.1, Septal S' was 5.5, and E/e' ratio was 8.2. The mean E-wave velocity, E-wave DT, lateral e', and septal e' were 61, 197, 8.9, and 7.5, respectively.

The mean LA diameters, LAV max, and LAV min was 4, 51, and 17.5, respectively.

The mean LAEF was 64%. The mean tricuspid E was 53 cm/s. The mean right e' and right s' were 10.8 and 9.8, respectively.

The mean TAPSE was 19.9 mm, and mean PASP was 32.8 mmHg. The mean TAPSE/PASP ratio was 0.62.

While concerning *Group II*, the mean LV mass index was 60, the mean LVEDD, LVESD, IVSd, LVPWd, and LVWF were 5, 3.2, 1.2, 1.1, and 62.8, respectively.

The mean LV shortening fraction was 35.8%, Lateral S' was 5.7, Septal S' was 5.1, and E/e' ratio was 9.9.

The mean E-wave velocity, E-wave DT, lateral e', and septal e' were 59, 208, 6.4, and 5.2, respectively. The mean LA diameters, LAV max, and LAV min was 4.2, 53, and 23, respectively. The mean LAEF was 55%. The mean tricuspid E was 45 cm/s. The mean right e' and right s' were 9.5 and 8.6, respectively. The median TAPSE was 15.6 mm, and median PASP was 39.5 mmHg. The median TAPSE/PASP ratio was 0.4. There was substantial variation between the two groups respecting LV mass index, E/e' ratio, lateral e', septal e', LAV min, LAEF, TAPSE, PASP, and TAPSE/PASP ratio.

Fossati *et al.* [9] found the mean E-wave was 88, the mean LVEDD, LVESD were 71, and 32.4, respectively. The mean TAPSE and PASP were 19.8 mm and 39.5 mmHg, respectively. TAPSE/PASP ratio and 6MWT distance had a substantial correlation (r= 0.46; P= 0.007).

Guazzi *et al.* [10] in their study on 46 cases with HFpEF, showed that the mean LVEF was 55%, the mean E/e' ratio was 11.5, the mean PASP was 40.1 mmHg, the mean TAPSE was 17.5mm, and the TAPSE/PASP ratio was 0.51.

The present findings showed significant correlations between TAPSE and BNP, 6METD, LV mass index, E/e' ratio, Mean e', right e', LAV min, and LAEF.

Guazzi *et al.* [10] show that the connection between TAPSE/PASP and NYHA functional class was inverse and that the prognostic resolution was slightly improved when the two variables were combined. As a result, TAPSE/PASP was considered and recommended as a thorough technique for determining how the right heart's contractile function and clinical functional state are related.

The current results showed that BNP, LV-Masse, E/e' ratio, Mean e', LAV min, LAEF, Right e', TAPSE, and TAPSE/PASP ratio had the ability to predict reduced exercise tolerance in HFpEF.

Guazzi *et al.* [10] cox regression analysis findings for both single- and multivariate cases were provided. Age, NYHA class, all tissue Doppler echocardiography findings, and NT-pro-BNP were meaningful univariate predictions when measurements were analyzed as continuous variables. It indicates that TAPSE/PASP enhances univariate prediction. TAPSE had the greatest X^2 value, but NYHA class and E/e' were preserved in the multivariate analysis. TAPSE/PASP showed the greatest X2 in the second multivariate analysis, despite the fact that only NYHA class was kept in the analysis as a supplementary predictive indicator. The second multivariate analysis predictive model showed a slight improvement, as indicated by the concordance index. They strengthened the case for the conclusion that TAPSE had a good predictive value by analysing a heterogeneous sample with varying severity and HFpEF.

The cut-off level for the TAPSE/best PASP was ≤0.48 mm/mmHg. The TAPSE/PASP ratio had an AUC of 0.834 (95% CI: 0.753-0.916, P <0.001), a sensitivity of 83.5%, and a specificity of 79.3% for detecting individuals with reduced exercise intolerance.

The optimum dichotomous threshold for TAPSE/PASP was determined to be </≥ 0.36 mm/mmHg by **Guazzi *et al.*** [10] (Sensitivity: 83%, specificity: 72%, AUC: 0.78, 95% CI: 0.75- 0.86, P <0.001).

Bosch *et al.* [8] revealed that There were no distinctions in the subjects' baseline clinical features between those with and without PASP metrics for age (P= 0.06, 66 vs. 65 years,), sex (50% female for both groups), incidence of hypertension (P= 0.06, 64 vs. 72), or level of coronary artery disorder (29 vs. 33, P= 0.37). Non-measurable patients exhibited lower rates of AF (9% versus 20%, P= 0.012), greater rates of diabetes (P= 0.006, 52% vs. 40.5%), and a median BMI (P= 0.002 for 27.2 vs. 25.7 kg/m2) as compared to those who had PASP measures. In survival studies limited to patients with quantifiable PASP, similar predictive correlations for TAPSE/PASP and RVLS/PASP (modified HR 2.96; 95% CI 1.34-6.56, P= 0.007) were discovered.

CONCLUSION

RV systolic function-related non-invasive echo-derived variables are fundamentally clinically significant in HF. The correlation between longitudinal RV fibre shortening (TAPSE) and generated pressure (PASP) may be regarded as an effective clinical indicator of the length/force connection. The ratio of the two factors may be more accurate in determining the degree of the illness than either of the two measures by itself. For HF patients who arrive with maintained ejection function, this strategy appears to be worthwhile of attention.

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