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Original Article

Tissue Doppler Right Ventricle Myocardial Performance Index (TDI RV-MPI) Versus Tricuspid Annular Plane Systolic Excursion (TAPSE) in Evaluation of RV dysfunction in Patients with or without LV dysfunction

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Abstract:

Introduction: *Cardiovascular disease remains a leading cause of death. Right ventricular (RV) function is a strong predictor of outcome in many cardiovascular diseases, but its significance is often neglected. It has often been coined "the forgotten chamber. RV dysfunction may be secondary to left ventricle (LV) dysfunction as a consequence of "Ventricular Interdependence". As RV dysfunction is associated with high in-hospital morbidity and mortality, early reorganization of RV dysfunction is warranted; but until today it remains a challenging task because of complex structure and asymmetric shape of RV.*

Objective: *Our objective was to compare the efficacy of Tissue Doppler Right Ventricle Myocardial Performance Index (TDI RV-MPI) with Tricuspid Annular Plane Systolic Excursion (TAPSE), as a predictor of RV Systolic dysfunction.*

Methods: *This was a cross-sectional study in patients undergoing comprehensive Transthoracic Echocardiography for any indication. Our aim was to compare Tissue Doppler Right ventricle Myocardial Performance Index (TDI RV-MPI) with TAPSE to predict RV function in patients with or without LV dysfunction .The current study recruited 100 patients who presented to the Cardiology Clinic of Lab Aid Cardiac Hospital. In addition to calculation of conventional, quantitative LVEF done in 2D guided M-mode in Para-sternal long-axis view, RV function was assessed in all subjects by measurement of Tricuspid Annular Plane Systolic Excursion (TAPSE) & Tissue Doppler RV Myocardial Performance Index (TDI RV-MPI). Both were compared in prediction of RV dysfunction in patients with or without LV systolic dysfunction*

Results: *RV dysfunction was found in subjects with LV dysfunction by both TAPSE & TDI RV -MPI. RV dysfunction increased with reducing left ventricular ejection fraction. Normal TAPSE (~24 mm) was evidence of normal TDI RV-MPI (0.2594±0.03269, P<.001), consistent with normal RV function. Of note, reduced TAPSE (~12 mm) was at the same time was evidence of increased TDI RV-MPI (0.7550±0.06351, P<.001), suggestive of RV dysfunction. Simultaneously normal LVEF (~ 55%) was evidence of normal TAPSE (22±1.582 mm, P<.001) & normal TDI RV-MPI (0.25±.0509, P<.001). Reduced LVEF (~25%) was at the same time, evidence of reduced TAPSE (15.50±3.317 mm, P<.001) & increased TDI RV-MPI (0.66±.1150, P<.001). A statistically significant negative correlation of TDI RV-MPI (r=-0.927) was observed with TAPSE (p<0.001). Also statistically significant negative correlation of TDI RV-MPI (r=-0.798) and significant positive correlation of TAPSE (r=0.813) were observed with LVEF (p<0.001). In the analysis TDI RV-MPI maintained significant correlation with both LVEF & TAPSE. In linear regression analysis TAPSE & LVEF were significant independent predictor of TDI RV-MPI. Most important determinants of TDI RV-MPI was TAPSE (R=0.927, p<0.001) .*

Conclusion: *This study demonstrated that in patients with LV dysfunction there was RV dysfunction due to 'ventricular interdependence' as detected by both TAPSE & TDI RV-MPI. TDI RV-MPI is a simple, sensitive, reproducible, noninvasive, non-geometirc echocadiographic parameter to provide global assessment of systolic and diastolic function of RV. It has the ability to detect RV dysfunction at an early stage, so as to reduce morbidity and mortality in these patients. It is evident that TDI RV-MPI can be a surrogate of TAPSE even with superior efficacy in RV functional assessment maintaining close relation with LVEF. These observations could guide decision making in daily clinical practice.*

Keywords: *LVEF-Left Ventricular Ejection Function, TAPSE-Tricuspid Annular Plane Systolic Excursion, TDI-RV MPI -Tissue Doppler Right ventricle Myocardial Performance Index.*

Introduction:

Cardiovascular disease remains a leading cause of death. Right ventricular (RV) function is a strong predictor of outcome in many cardiovascular diseases, but its significance is often neglected. The right ventricle (RV) has often been coined "the forgotten chamber.[1] RV dysfunction is an established predictor of morbidity and mortality in both cardiovascular and respiratory diseases, including heart failure (HF),[2] myocardial infarction,[3] primary pulmonary

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hypertension,[4] chronic obstructive pulmonary disease,[5] pulmonary embolism .[6]

Hence early recognition of RV dysfunction is warranted; but until today it remains a challenging task because of complex structure and asymmetric shape of RV.[7] Standard 2-dimensional echocardiographic evaluation of RV volumes and ejection fraction is cumbersome due to difficulty in exact delineation of RV endocardial borders because of prominent trabeculations and crescentric shape of the RV.[8]

Right ventricular ejection fraction (RVEF) derived from cardiac magnetic resonance imaging (MRI) remains the gold standard for functional RV assessment. Several parameters have been suggested for echocardiographic evaluation of the RV. Several studies have demonstrated the value of tricuspid annular plane systolic excursion (TAPSE), [9, 10] tissue Doppler imaging of the basal free lateral wall of the RV (S′),[11] longitudinal strain of the free lateral wall of the right ventricle (RV-GLS),[12] fractional area change (FAC), [13] right ventricular myocardial performance index (RIMP) ,[11, 14] and the rate of pressure rise in the RV (dp/dt).[15] Furthermore, three-dimensional echocardiography allows an exact and reproducible estimation of volume and ejection fraction of the RV. [16]

TAPSE is measured using M-mode echocardiography. It directly measures the displacement of the lateral annulus of the tricuspid valve during the cardiac cycle (Figure 1). In 2015, a number <17 mm was designated as abnormal.[17] However, this method is limited. TAPSE evaluates only 1 small segment of the RV. In patients with regional wall-motion abnormalities, the TAPSE can be misleading.

The RIMP/ MPI is a calculation based on tissue Doppler velocities or pulse wave velocities from the RV: (isovolumic relaxation time + isovolumic contraction time)/RV ejection time. These variables are measured during flow and do not require complete visualization of the RV.[17] The MPI is a Doppler derived time interval index that combines both systolic and diastolic cardiac performances.[19] Many studies documented that MPI is simple, noninvasive, easy to estimate and reproducible.[20, 21] Using PWD-MPI is limited because both the mitral inflow or tricuspid inflow and the ejection time are not acquired in the same cycle. Using tissue Doppler imaging (TDI) overcomes this limitation since all the parameters are acquired simultaneously.[18] TDI-MPI for the RV is shown to be superior to PWD-MPI.[22.] An abnormal RIMP is >0.43 if measured by pulsed-wave Doppler or >0.54 if measured by tissue Doppler.[17]

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The advent of reliable and reproducible Echocardiographic measures of RV has made the assessment of RV function in cardiac diseases easier and helped to identify the important role of RV in HF subjects.

Objective:

Our objective in the present study was to compare the efficacy of Tissue Doppler Right Ventricle Myocardial Performance Index (TDI RV-MPI) with Tricuspid Annular Plane Systolic Excursion (TAPSE), as a predictor of RV Systolic dysfunction in patients with or without LV systolic dysfunction.

Material & Methods:

This was a cross-sectional study in patients undergoing comprehensive Transthoracic Echocardiography for any indication. From April 2022 to March 2023, we prospectively enrolled 100 adult (from 30 to age 103 years) of both sexes who had been referred to the Cardiology service of LABAID Cardiac Hospital for routine health check up. We performed a complete Transthoracic Echocardiography study. Echocardiograms were recorded on a Vivid ™ E 95 with cSound™ ultrasound system (GE Medical System) with M5sc-D (GE) multifrequency transducer.

In addition to calculation of conventional, quantitative LVEF done in 2D guided M-mode in Para-sternal long-axis view**,** RV systolic function was assessed in all subjects using different methods. It was based on the American Society of Echocardiography guidelines for Echocardiographic assessment of the right heart in adults. This included Tricuspid Annular Plane Systolic Excursion (TAPSE) & Right Ventricle Myocardial Performance Index (RV-MPI) using Tissue Doppler imaging (TDI).

TAPSE**:** We measured TAPSE in 2-dimensional M-mode echocardiograms from the apical 4- chamber view, positioning the cursor on the lateral tricuspid annulus near the free RV wall and aligning it as close as possible to the apex of the heart (Fig-1). TAPSE Values <17 mm was designated as abnormal[17] and indicated RV dysfunction.

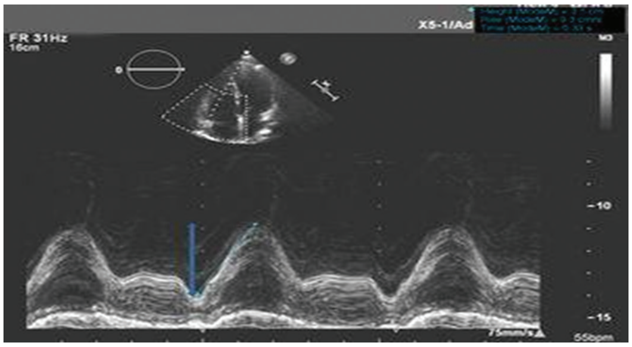


Fig 1: Standard technique for measuring tricuspid annular plane systolic excursion using one-dimensional mode echocardiography

Tissue Doppler RV-MPI: Right Ventricle Myocardial Performance Index (RV-MPI) using tissue Doppler imaging (TDI) is an index of global RV function and was obtained in the apical four-chamber view in Tissue Doppler mode. Pulsed Doppler sample volume was placed on the Tricuspid annulus level of RV free wall in apical −4 chamber view (Figure 2). The Tissue Doppler RV -MPI was calculated as follows using formula

Tissue Doppler RV-MPI = IVCT+IVRT/ET [36]

RV MPI values >0.54 implied RV dysfunction when measured by Tissue Doppler.[17]

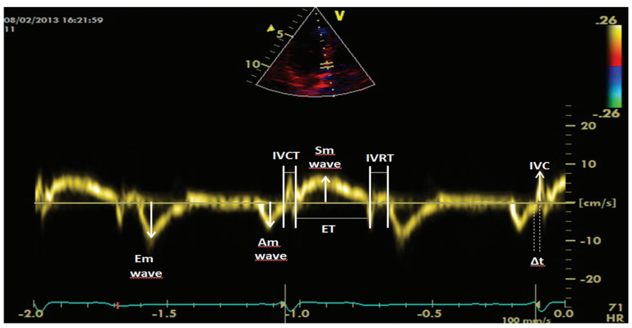


Fig 2: Evaluation of **Tissue Doppler RV-MPI.** Abbreviations: MPI- myocardial performance index; IVCT- Isovolumic Contraction time. IVRT-Isovolumic Relaxation time. ET- Ejection time.

An LVEF > 50% was considered as normal, an LVEF between 40% and 49% was considered heart failure with a midrange ejection fraction (HFmrEF), an LVEF<40% was classified as Heart failure with a reduced ejection fraction HFrEF, and an LVEF≤30% was defined as advanced Heart failure (AHF).

The mean values were taken by at least 2 measurements for reducing inter-observer and intra-observer variability's. To prevent systematic errors in obtaining or interpreting the Echocardiograms, 2 noninvasive Cardiologists obtained the Echocardiograms. Both TAPSE & TDI RV-MPI were compared with each other and with LVEF in various groups. Patient with, chronic obstructive lung disease, confirmed congenital & valvular heart disease were excluded.

Statistical Analysis: Numerical data obtained from the study were analyzed and significance of difference was estimated by using statistical method. The statistical data were analyzed using IBM SPSS 25.0. The continuous data were expressed as frequency, the mean ± standard deviation, and the categorical data were expressed as percentages. Significance of difference between groups was evaluated by unpaired student t test. Graphical representation, Correlation test & Pearson correlation coefficient were used to measure the relationship between TAPSE &

TDI RV–MPI with each other and with LVEF. Stepwise simple linear regression analysis was used to estimate the relation between Echocardiographic variables and also to identify best predictor of RV- MPI. Probability values (P<0.05) were considered statistically significant in the analyses.

Results:

In total, 100 patients were enrolled in the study. We examined 53 males (53%) and 47 females (47%). Echocardiography tracings of sufficient quality for analysis were obtained in all patients.

Fig- 3 showed age & sex distribution of study patients. Some summary result of age and sex distribution is as follows: Age ranged from 30 years to 103 years. Majority of the cases (>60%), were in between 41 to 70 years of age. Mean age ±SD was 58.7±11.66 yrs. Male and Female ratio was 1.1:1. Majority male patients were in between 51-70 yrs of age and majority of female patient were in between 61 to 70 yrs of age.

Table I showed Distribution of Echocardiography parameters. The LVEF ranged from 20% to 68% (mean ± SD = 47.14 ± 15.77%), the EPSS ranged from 4 to 28 mm (mean ± SD = 9.26 ± 5.60mm), the LVIDd ranged from 30 to 72 mm (mean ± SD = 50.43 ± 8.97mm), LVIDs ranged from 12 to 62 mm (mean ± SD = 34.77 ± 12.32mm), RV Dimension ranged from 17 to 34 mm (mean ± SD = 24.28 ± 3.975mm), TAPSE ranged from 12 to 25 mm (mean ± SD = 19.15 ± 3.878mm), TDI RV-MPI ranged from 0.20 to 0.81 (mean ± SD = 0.42± 0.176) and S wave ranged from 6 to 18 mm (mean ± SD = 12.62 ± 3.8mm).

Table II showed correlation of mean TDI RV-MPI, LVEF & TAPSE. A statistically significant negative correlation of TDI RV-MPI (r = -0.927) was observed with TAPSE (p<0.001). Simultaneously a statistically significant negative correlation of TDI RV-MPI (r = -0.798) and significant positive correlation of TAPSE (r = 0.813) were observed with LVEF (p<0.001). Table III showed that normal LVEF (~ 55%) is evidence of normal TAPSE (22 ± 1.582 mm, P<.001) & normal TDI RV-MPI (0.25 ± 0.0509, P<.001), consistent with normal RV function. Of note, reduced LVEF (~25%) is at the same time, is evidence of reduced TAPSE (15.50 ± 3,317 mm, P<0.001) & increased TDI RV-MPI (0.6650 ± 0.1150, P<.001), both are suggestive of RV dysfunction.

Table IV showed that normal TAPSE (~24 mm) is evidence of normal TDI RV-MPI (0.2594 ± 0.0326, P<.001), consistent with normal RV function. Of note, reduced TAPSE (~12 mm) is at the same time, is evidence of increased TDI RV-MPI (0.7550 ± 0.0635, P<.001), both are suggestive of RV dysfunction.

Fig 4 showed that normal TAPSE is evidence of normal TDI RV-MPI, consistent with normal RV function. Of note, reduced TAPSE is at the same time, evidence of increased TDI RV-MPI both are suggestive of RV dysfunction. Fig 5 showed measurement of TDI RV-MPI in Fig 5a, 5c & TAPSE in Fig 5b, 5d. When TDI RV-MPI was 0.4, TAPSE was 22 mm indicative of normal RV function & when TDI RV-MPI was 0.6, TAPSE was 15 mm, both indicating RV dysfunction.

Table V showed Pearson Correlation between different variables. A statistically significant negative correlation of TDI RV-MPI (r = -0.927) was observed with TAPSE (p<0.001). Simultaneously a statistically significant negative correlation of TDI RV-MPI (r = -0.798) and significant positive correlation of TAPSE (r = 0.813) were observed with LVEF (p<0.001). In the analysis TDI RV-MPI maintained significant correlation with both LVEF & TAPSE. But correlation was much higher with TAPSE. Table VI showed Simple Linear Regression analysis. In linear regression analysis TAPSE & LVEF were significant independent predictor of TDI RV-MPI. Most important determinants of TDI RV-MPI was TAPSE (R=.927, p<0.001) followed by LVEF (R=.798, p<0.001).

Table VII showed Pearson Correlation between TAPSE and TDI RV-MPI. It was found that TDI RV-MPI has highly significant negative correlation with TAPSE (r =-.927, p<0.001). In Fig 6 Scatter plots showed the relationships of TDI RV-MPI with TAPSE (Fig 6a) & LVEF (Fig 6b) indicating their sample distribution. Plots showed TDI RV-MPI is inversely proportionate to both TAPSE & LVEF.

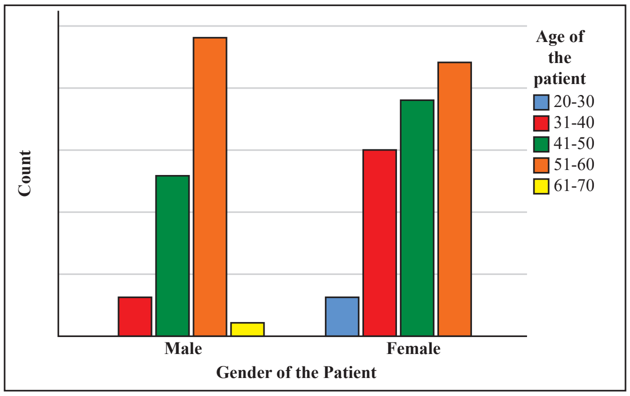


Fig 3: Age and sex distribution of the study patients

Table I: Distribution of Echocardiography parameters

Echocardiography Parameters	N	Minimum	Maximum	Mean	Std Deviation
Left Ventricle Diastolic Dimension (mm)	100	30	72	50.43	8.976
Left Ventricle Systolic Dimension(mm)	100	12	62	34.77	12.321
Left Ventricular Ejection Fraction (%)	100	20	68	47.14	15.777
E Point Septal Seperation (mm)	100	4	28	9.26	5.601
Right Ventricle Dimension(mm)	100	17	34	24.28	3.975
Tricuspid Annular Plane Systolic Excursion (mm)	100	12	25	19.15	3.878
TDI Right Ventricle Myocardial Performance Index (TDI-RV MPI)	100	.20	.81	.42	.176
S wave (mm)	100	6	18	12.62	3.8

Data presented as Mean± SD

Table II: Correlation of mean TDI RV-MPI, LVEF & TAPSE

		Mean	N	Std. Deviation	Correlation (r value)	Significance (p value)
Pair 1	Left Ventricular Ejection Fraction (%)	47.14	100	15.777		
	Tricuspid Annular Plane Systolic Excursion(mm)	19.15	100	3.878	.813	.000^{s}
Pair 2	Left Ventricular Ejection Fraction(%)	47.14	100	15.777		
	TDI Right Ventricular Myocardial Performance Index	.4243	100	.17686	-.798	.000^{s}
Pair 3	Tricuspid Annular Plane Systolic Excursion (mm)	19.15	100	3.878		
	TDI Right Ventricular Myocardial Performance Index	.4243	100	.17686	-.927	.000^{s}

*P value reached from Paired sample t test, *p*- value significant at<0.05.

Table III : Prediction of RV dysfunction by TDI RV-MPI & TAPSE in comparison to LVEF

	Left Ventricular Ejection Fraction (%)	N	Mean	Std. Deviation	Significance
Tricuspid Annular Plane Systolic Excursion (mm)	25	4	15.50	3.317	.000^{s}
	55	5	22.00	1.582	.000^{s}
TDI Right Ventricular Myocardial Performance Index	25	4	.6650	.11504	.000^{s}
	55	5	.2500	.05099	.000^{s}*

P value reached from unpaired student t test, S = significant, P 0<.01

Table IV : Prediction of TDI RV-MPI in comparison of TAPSE

	Tricuspid Annular Plane Systolic Excursion(mm)	N	Mean	Std. Deviation	Significance (P value)
TDI Right Ventricular Myocardial Performance Index	12	4	.7550	.06351	.000s
	15	20	.6300	.05351	.000s
	20	14	.3379	.07748	.000s
	24	17	.2594	.03269	.000s

*P value reached from unpaired student t test, S = significant

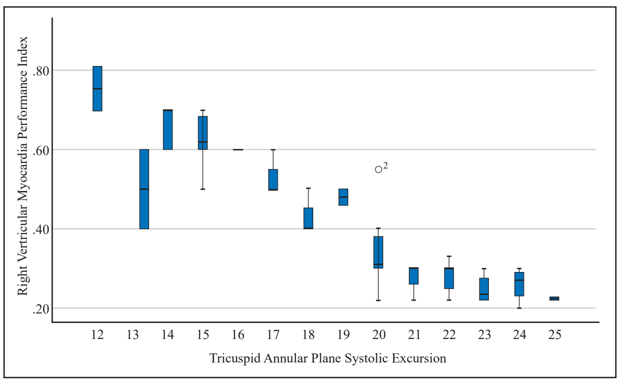
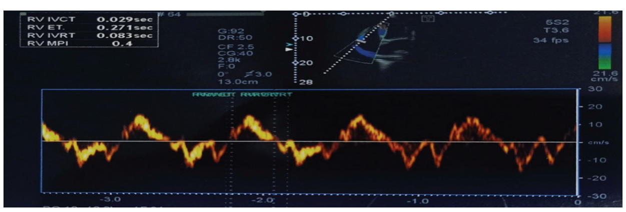


Fig 4: TDI Right Ventricular Myocardial Performance Index & TAPSE Stem-and-Leaf Plots



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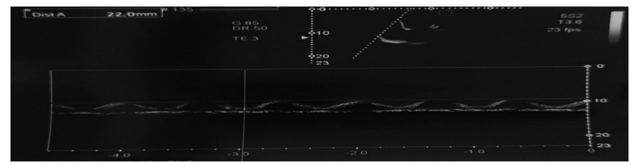

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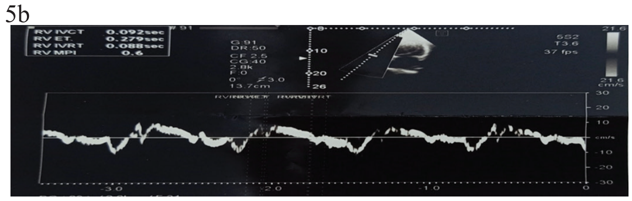

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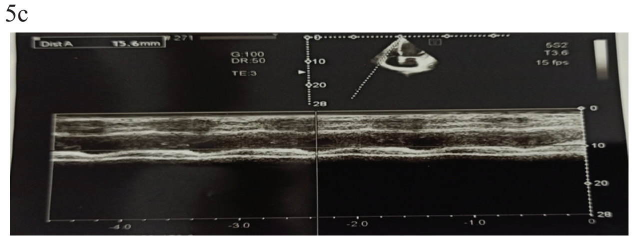

5d

Fig 5: Measurement of TDI RV-MPI in Fig 5a, 5c & **TAPSE** in Fig 5b, 5d. When TDI RV-MPI was 0.4, TAPSE was 22 mm indicative of normal RV function & when TDI RV-MPI was 0.6, TAPSE was 15 mm, both indicating RV dysfunction.

Table V: Pearson Correlation between different variables

		Left Ventricular Ejection Fraction Excursion	Tricuspid Annular Plane Systolic Performance Index	TDI Right Ventricular Myocardial
Left Ventricular	Pearson Correlation	1	.813**	-.798**
Ejection Fraction (%)	Sig. (2-tailed)		.000 s	.000 s
	N	100	100	100
Tricuspid Annular Plane	Pearson Correlation	.813**	1	-.927**
Systolic Excursion(mm)	Sig. (2-tailed)	.000 s		.000 s
	N	100	100	100
TDI Right Ventricular	Pearson Correlation	-.798**	-.927**	1
Myocardial Performance Index	Sig. (2-tailed)	.000 s	.000 s	
	N	100	100	100

P value reached from Correlation test

**. Correlation is significant at the 0.01 level (2-tailed). S=significant

Table VI: Simple Linear Regression analysis.

Simple Linear Regression analysis			
(TDI-RV MPI)	R value	R Square	P value
TAPSE	.927	.860	.000[s]
LVEF	.798	.636	.000[s]

Dependent Variable: TDI RV-MPI, Predictor: TAPSE & LVEF, P value derived from Pearson correlation, S= significant, **. Correlation is significant at the 0.01 level (2-tailed).

Table VII: Pearson Correlation between TAPSE and TDI RV-MPI

TAPSE	Pearson Correlation Co –efficient (r value) (N=100)	P value
TDI RV-MPI	-.927**	. 000[s]

P value derived from Pearson correlation, S= significant, **. Correlation is significant at the 0.01 level (2- tailed).

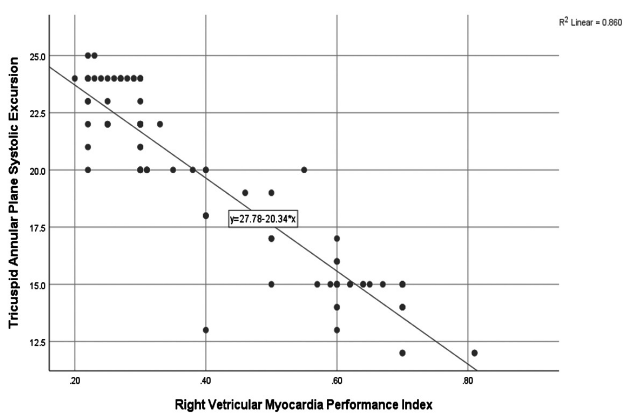

Fig 6a. Scatter plot (BIVAR) = TDI RV-MPI with TAPSE

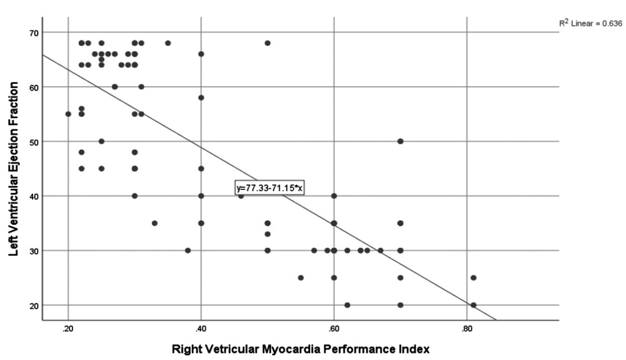

Fig 6b Scatter plot (BIVAR) = TDI RV-MPI with LVEF

Discussion:

RV dysfunction may be secondary to LV dysfunction, as a consequence of “Ventricular Interdependence”. There is close anatomic association between the two ventricles, as they are encircled by common muscle fibers, share a common septal wall and are enclosed within a common pericardium. So forces are transmitted from one ventricle to the other ventricle through myocardium and pericardium, independent of neural, humoral, and circulatory effects.

This study showed that RV systolic dysfunction is common in subjects with LV systolic dysfunction. In addition to TAPSE which is mostly routinely used to assess RV function in Echocardiographic studies, we investigated RV systolic function using alternative Echocardiographic parameter TDI RV- MPI. It showed that TDI RV- MPI can also be reliably used to assess RV systolic function in both normal & HF subjects. TAPSE is simple and easily reproducible and has been found to correlate with the radionuclide angiographic estimate of RV global systolic function.[23] However, TAPSE assumes that the longitudinal displacement of a single segment represents the function of a three-dimensional (3D) structure and is found to be angle and load dependent.[24]

Another study[25] of RV function in HF subjects using TAPSE found that although TAPSE is reduced with LV dysfunction in HF, the absolute reduction is small and seemed to be of minor importance in the clinical utilization of TAPSE as a measure of RV systolic function or as a prognostic factor.

The right sided MPI also known as the Tei index is a global estimate of both systolic and diastolic function of the right ventricle. We found RV systolic dysfunction in subjects with LV systolic dysfunction by using both TAPSE & TDI RV-MPI. TDI RV-MPI was shown to correlate with radionuclide-derived RVEF.[26] Tei et al found that RV-MPI was a strong predictor of clinical status and survival in subjects with pulmonary hypertension.[27]

We assessed RV function in subjects with or without LV systolic dysfunction using both TAPSE and TDI RV-MPI. A statistically significant negative correlation of TDI RV-MPI (r= -.927) was observed with TAPSE ($p<0.001$). Simultaneously a statistically significant negative correlation of TDI RV-MPI (r= -.798) and significant positive correlation of TAPSE (r=.813) were observed with LVEF ($p<0.001$). In the analysis TDI RV-MPI maintained significant correlation with both LVEF & TAPSE. But correlation was much higher with TAPSE. Prevalence of RV dysfunction was increased with decreasing LVEF in this study.

Several studies[28, 29] have reported positive correlations between echocardiographic variables of RV systolic function and LVEF and LV chamber dimensions. A study noted that RV systolic dysfunction correlated positively with LVEDD in HF subjects[29]. Another study also reported that LVEF was the best correlate of TAPSE and RV S′; however, this was in a cohort of hypertensive subjects without features of HF[30]. In this study, subjects with reduced EF had the highest prevalence of RV systolic dysfunction (61.9% and 63% by TAPSE and RV MPI, respectively). This observation was also reported in other studies (52%)[31] and (63%–76%)[32].

Millar et .al.[7] reported that RV-MPI value >0.40 has 100% sensitivity and 100% positive predictive value to diagnose RV dysfunction. In accordance with another study[17] TAPSE values <17 mm was designated as abnormal and indicated RV dysfunction. An abnormal RIMP is >0.43 if measured by pulsed-wave Doppler or >0.54 if measured by tissue Doppler[17.] RV MPI values >0.54 implied RV dysfunction when measured by Tissue Doppler.[17]

In another study they found that in spite Simpson's RVEF being normal, RV-MPI was significantly prolonged in subgroups of LV-AMI suggesting RV-MPI is a simpler, sensitive, and accurate parameter contrary to RVEF to assess RV functions.[33] It requires no geometric assumptions.

RV function worsens with increasing severity of LV dysfunction and this may result from the concept of ventricular interdependence.[34] HF subjects with reduced EF but normal RV function have better prognosis compared to those with impaired RV systolic function.[35] Subjects with HF with preserved EF may also have RV dysfunction and this has been found to be associated with clinical and echocardiographic evidence of more advanced HF and is predictive of poorer outcomes.[35]

Conclusion:

This study demonstrated that in patients with LV dysfunction there is RV dysfunction due to 'ventricular interdependence' as detected by both TAPSE & TDI RV-MPI. TDI RV-MPI is a Doppler derived time interval index that combines both systolic and diastolic cardiac performances and provides global assessment of systolic and diastolic function of RV. It is a simple, reproducible, noninvasive, non-geometirc echocadiographic parameter to assess RV functions. Adequate Doppler images can be acquired even when 2D image quality is suboptimal. Since RV-MPI integrates both isovolumic and ejection phase indices, it becomes abnormal before an ejection phase measure such as Simpson's RVEF indicates an abnormality. TDI RV-MPI is a sensitive, accurate echocardiographic parameter with less variability & ability to detect RV dysfunction at an early stage, so as to reduce morbidity and mortality in theses patients. It is evident that TDI RV-MPI can be a surrogate of TAPSE even with superior efficacy in RV functional assessment maintaining close relation with LVEF. These observations could guide decision making in daily clinical practice.

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