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Right Ventricular Function in Patients with Pulmonary Hypertension: Correlation between Myocardial Performance Index measured by Conventional Pulsed Wave Doppler and Tissue Doppler Imaging

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Abstract: ***Background and aim**: Myocardial performance index (MPI) measured by conventional pulse-wave Doppler is invariably used to evaluate right ventricular (RV) systolic function in patients with pulmonary hypertension (PH). The primary objective of this study was to assess the degree of agreement between MPI measured by conventional pulsed-wave Doppler (PWMPI) and tissue Doppler imaging (TDMPI) in patients with PH. Secondary objective was to correlate MPI measured by these two methods with other RV systolic function related echocardiographic measures. **Methods**: It was a hospital-based, cross-sectional, observational study involving 100 consecutive patients with PH. Different echocardiographic parameters were used to evaluate RV systolic function. In all patients, conventional pulsed-wave Doppler and tissue Doppler imaging were used as a tool to calculate MPI. **Results**: Bland–Altman analysis showed moderate agreement between PWMPI and TDMPI (the mean difference was-0.14 at 95% intervals of agreement, absolute difference =-0.39 to 0.11; 95% intervals of agreement, percentage of average =-32.6 to 27.7). We found significant correlation of PWMPI with S'-wave velocity (r =-0.57, p = <0.0001), RVEF (r =-0.245, p = 0.013), RVFAC (r =-0.385, p = 0.0001), RV dp/dt (r =-0.295, p = 0.002), and TAPSE (r =-0.39, p = 0.0001). With regards to TDMPI, we found significant correlation with RVEF (r =-0.527, p = <0.0001), RVFAC (r =-0.53, p = <0.0001), RV dp/dt (r =-0.557, p = <0.0001), TAPSE (r =-0.50, p = <0.0001), and S'-wave velocity (r =-0.583, p = <0.0001). **Conclusion**: Our findings proved that MPI measured by tissue Doppler is a safe, effective, and accurate method to evaluate global RV function in patients with chronic PH.*

Keywords: Agreement, Doppler, Pulmonary hypertension, Right ventricle, Two-dimensional echocardiography

1. Introduction

The term pulmonary hypertension (PH) is described as mean pulmonary artery pressure ≥20 mm Hg at rest confirmed by right heart catheterization, the "gold standard" for the diagnosis of PH (1). PH affects approximately 10–20% of global population (2). While there are many causes of PH like pulmonary vascular diseases and thromboembolic diseases, it is almost always associated with left-sided heart diseases and chronic lung diseases. However, patients presenting with chronic PH are more susceptible to develop right-sided heart failure as well. About two-thirds of deaths in patients with chronic PH are attributable to right ventricular (RV) failure in the general population (3). In chronic PH, the heart responds to high resistance by raising pulmonary arterial pressure to preserve the cardiac output. Since RV function is greatly dependent on small changes in afterload, this may cause RV hypertrophy and dilatation eventually resulting in RV failure and death. Altogether, RV function is a critical determinant of clinical presentation, prognosis, and long-term outcomes of PH (4); hence early detection of RV dysfunction is a quintessential aspect of the diagnosis.

Among various invasive and non-invasive diagnostic tools to assess cardiac morphology and functions, echocardiography is a revolutionary imaging modality in clinical practice to screen PH patients. Nonetheless, RV assessment by echocardiography is vulnerable to the complex geometry of the RV (5). Myocardial performance index (MPI) or Tei index is a crucial prognostic and progression marker for evaluation of systolic and diastolic functions in both ventricles at the same time for patients with PH (6). MPI is an established ratio of isovolumic time to ventricular ejection time [MPI = (isovolumic contraction time (IVCT) + isovolumic relaxation time (IVRT)) /ejection time] (7). Conventionally, pulsed-wave Doppler has been used in defining PH. With the advent of technology, tissue Doppler imaging (TDI) has also emerged for the screening of PH patients. It has been stated that MPI measured by TDI (TDMPI) correlated better with other RV dysfunction related echocardiographic measures in the setting of idiopathic PH than conventional pulsed-wave Doppler MPI (PWMPI) (8). Nevertheless, there remains a scarcity of evidence to validate TDI as a method for measuring RV MPI. Towards this end, we attempted to give our dedication to this interesting matter by conducting this study. The aim of this study was twofold. The first was to assess the degree of agreement between conventional pulsed-wave Doppler and TDI methods for measuring MPI in patients with PH. The second was to correlate MPI measured by these two methods with other RV systolic function related echocardiographic measures.

2. Materials and Methods

2.1 Participants

In this hospital-based, cross-sectional, observational study, we enrolled 100 consecutive patients with PH who were referred to our institution between June, 2021 and June 2022. The study was approved by the local institutional ethical committee, and all patients gave written informed consent. Patients with moderate to severe PH and age >18 years irrespective of any gender bias were enrolled in this study. Criteria for excluding the subjects were: patients with no sinus rhythm, history of myocardial infarction, presence of pacemaker lead in the right ventricle, PH associated with conduction disorders, patients with valvular heart diseases, and patients with co-existing left heart diseases (both systolic and diastolic dysfunction).

2.2 Echocardiography

All patients were subjected to echocardiography in order to assess RV systolic function related measures. MPI was measured by both conventional Doppler and TDI as per standard procedures. Two-dimensional echocardiography was carried out using M/sPhilips-IE33, equipped with the transducer of 5 MHZ, tissue Doppler and simultaneous echocardiography. The following parameters were used to evaluate RV functions: a) RV ejection fraction (RVEF), b) RV fractional area change (RVFAC), c) RV contractility dP/dt, d) tricuspid free wall annular plane systolic excursion (TAPSE) or e) peak myocardial systolic velocity (S'-wave velocity). Pulmonary artery systolic pressure (PASP) was estimated on the basis of the Doppler assessment of peak tricuspid regurgitant jet velocity (TRV). This calculation takes into account the right atrial pressure (RAP) with a simplified Bernoulli equation: PASP = (4 x TRV^2) + RAP (9). RVEF was calculated by Simpson's method, subtracting end-systolic volume (ESV) from end-diastolic volume (EDV) divided by EDV: RVEF% = 100 × (EDV-ESV) /EDV. For estimation of RVFAC, the RV free wall and septum were traced from base to apex, and the respective RV areas (end-diastolic area (EDA), end-systolic area (ESA)) were determined. RVFAC can be calculated using this formula: (EDA-ESA) / EDA.

2.3 Data analysis

All continuous data were presented as mean ± standard deviation and categorical data were expressed as numbers and percentages. A two-tailed *p*-value of less than 0.05 was considered statistically significant. The Bland Altman analysis was performed to evaluate the degree of agreement between PWMPI and TDMPI. Pearson's correlation analysis was done to determine linear correlation of PWMPI and TDMPI with other echocardiographic variables. The software applications used to analyse the data were Statistical Package for the Social Sciences, version 13 (SPSS Inc., Chicago, IL, USA) and MedCalc for Windows, version 9.5.0.0 (MedCalc Software, Mariakerke, Belgium).

3. Results

3.1 Clinical characteristics of study populations

The study involved a total of 100 PH patients with mean PASP of 50.3 ± 21.2 mmHg. The mean age of the study population was 40.65 ± 13.49 years. The main aetiologies associated with the genesis of PH were lung diseases (74%), followed by primary PH (23%) and chronic thromboembolic PH (3%). **Table 1** illustrates the baseline demographic and echocardiographic characteristics of the enrolled patients.

3.2 Bland–Altman Analysis

The Bland–Altman plot demonstrated moderate agreement between PWMPI and TDMPI (*n* = 100, the mean difference was-0.14 at 95% intervals of agreement, absolute difference =-0.39 to 0.11; 95% intervals of agreement, percentage of average =-32.6 to 27.7) (**Figure 1).**

3.3 Correlation of PWMPI and TDMPI with other RV systolic function related echocardiographic measures

Figure 2, 3, 4, 5, 6 depict scattered plot for correlation of MPI measured by conventional pulsed-wave Doppler and TDI with other RV systolic function related echocardiographic measures. Our results demonstrated that there was a moderate negative correlation between S'-wave velocity and PWMPI (r =-0.57, n = 100, p = <0.0001). Moreover, a weak negative correlation of PWMPI with RVEF (r =-0.245, n = 100, p = 0.013), RVFAC (r =-0.385, n = 100, p = 0.0001), RV dp/dt (r =-0.295, n = 100, p = 0.002), and TAPSE (r =-0.39, n = 100, p = 0.0001) were also found. In relation to TDMPI, we found a moderate significant negative correlation with RVEF (r =-0.527, n = 100, p = <0.0001), RVFAC (r =-0.53, n = 100, p = <0.0001), RV dp/dt (r =-0.557, n = 100, p = <0.0001), TAPSE (r =-0.50, n = 100, p = <0.0001), and S'-wave velocity (r =-0.583, n = 100, p = <0.0001).

4. Discussion

PH is becoming an increasingly major global health problem. The development of PH is associated with worsened symptoms and increased risk of mortality. In certain clinical scenarios, for example, suspected thromboembolic disease, ascites and peripheral edema of unknown origin, and unexplained dyspnea, identification of the presence of PH is of utmost importance (10). As already mentioned, RV function is a primary determinant of outcomes in patients with PH (11, 12). However, comprehensive assessment of RV function by echocardiography remains a great challenge. RV function has been conventionally estimated by TAPSE, S'-wave velocity, RV fractional area change (FACecho), and myocardial strain derived from the RV lateral free wall (FWSecho) (13). These measures only consider longitudinal RV shortening. In the recent era, RVFAC and RVEF are fair and accurate candidates to estimate RV systolic function. (14). In agreement with Hoette *et al.* (15), RVFAC is a better index for the determination of RV ejection fraction than TAPSE in patients with pulmonary artery hypertension as it includes the transverse component of RV function.

With conventional MPI Doppler, it is essential to measure transtricuspid inflow velocities and RV outflow during separate cardiac cycles. Due to the necessity to average the measurements of the intervals of many cardiac cycles, there may be a decrement in reproducibility of MPI Doppler. Besides, the velocity ratio of E-and A-waves have proven to be a potent predictor for the assessment of diastolic function in the RV. However, measurement of these velocities may be of great challenge during tachycardia (16).

TDI has recently been introduced in echocardiography to measure the velocity of the myocardial tissue. TDI eliminates the problem of variability based upon changing heart rate, which is inherent in the pulsed Doppler as the RV inflow and outflow are not measured simultaneously. Unlike conventional MPI Doppler, in which many measurements are needed to overcome beat-to-beat variation (16), TDMPI allows simultaneous measurement of both the diastolic and systolic intervals in the same cardiac cycle with high diagnostic accuracy (17, 18). Furthermore, it is less subjected to background noise.

In our study, Bland-Altman analysis showed moderate agreement (the mean difference was-0.14 at 95% intervals of agreement, absolute difference =-0.39 to 0.11; 95% intervals of agreement, percentage of average =-32.6 to 27.7) between PWMPI and TDMPI in patients with the PH of diverse aetiology. Cabrita *et al.* [2010] (19), reported moderate agreement (the mean difference was-0.02, absolute difference =-0.32 to 0.29; 95% intervals of agreement, percentage of average =-46.6 to 40.8%) between PWMPI and TDMPI. These values correlate favourably well with our findings. Controversially, it has been reported significant agreement between the PWMPI and TDMPI (r = 0.83, p < 0.001; mean value-0.10, *SD* 0.2) (20). Considering many discrepancies in the agreement between two methods of MPI measuring, in this regard, more compelling studies are warranted to draw the final conclusion. Thus, the authors enlighten to report the method applied to calculate MPI in echocardiographic studies.

In our study, both TDMPI and PWMPI were significantly correlated with RVFAC, RVEF, S‘, TAPSE, and RV dP/dT. Moreover, good correlation in terms of highly significant p-value was found in TDMPI than PWMPI for all RV systolic function related measures including, RVEF, FAC, RV dp/dt, and TAPSE, except for S’-wave velocity, indicating superiority of MPI measured by TDI over conventional MPI Doppler. In the same vein, Cabrita *et al.* (19) also proved the superiority of TDI over conventional MPI Doppler.

Among all echocardiographic parameters, RVEF is a crude and more subtle measure for the evaluation of PH patients. With regards to the correlation between PWMPI and RVEF, we found a weak negative correlation (r =-0.245, n = 100, p = 0.013). By the same token, Miller *et al.* (21) found a weak negative correlation (r =-0.38, n = 100, p = 0.006) between PWMPI and RVEF. Another important finding is moderate significant correlation (r =-0.527, n = 100, p = <0.0001) between TDMPI and RVEF. This result was consistent with Sato *et al.* ’s (22) finding (r =-0.59, n = 100, p < 0.0001).

Our study did have some limitations. First of all, we did not include patients with PH due to left heart disease might be a potential for bias as RV dysfunction might be affected by LV performance due to ventricular interdependence (23). Moreover, we did not use angle correction to estimate RV function by either tissue Doppler or pulse Doppler. Also, cardiac magnetic resonance, the gold standard for accurate determination of RV function, was not used as a comparator for the estimation of RV function. Besides, invasive methods were not used to assess PASP and systolic function in the study population.

5. Conclusions

One of the most significant findings emerged from this study was moderate agreement between PWMPI and TDMPI for measuring MPI in PH patients. Good correlation was found in TDMPI as compared to PWMPI for all RV systolic function related measures, except for S’-wave velocity. Moreover, TDMPI was a parameter uninfluenced by RV geometry and importantly has the benefit of simultaneously recording the time intervals from the same cardiac cycle. In brief, existing facts and our findings altogether revealed the superiority of TDA as a marker of disease as compared to conventional Doppler. Nonetheless, results may be biased due to the smaller sample size. Future studies with larger sample sizes should be warranted to validate the use of simple PWMPI and TDMPI in clinical practice.

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Tables

Table 1: Demographic and echocardiographic characteristics of study population

Characteristics	PH patients (n=100)
Age (years)	40.65 ± 13.49
Male[a]	62
Aetiology[a]	
Lung diseases	74
Primary PH	23
Chronic thromboembolic PH	3
TRV (m/s)	3.4 ± 1.2
PASP (mmHg)	50.3 ± 21.2
PWMPI	0.426 ± 0.12
TDMPI	0.56 ± 0.14
RVEF (%)	38.09 ± 10.1
RVFAC (%)	31.39 ± 9.84
RV dP/dt (mmHg/s)	407.20 ± 81.54
S'-wave velocity (cm/s)	9.88 ± 2.47
TAPSE (cm)	1.61 ± 0.32

‡PH, Pulmonary hypertension; TRV, Tricuspid regurgitant velocity; PASP,
Pulmonary artery systolic pressure; MPI, Myocardial performance index; PW,
Pulsed-wave; TD, Tissue Doppler; RVEF, Right ventricular ejection fraction;
RVFAC, Right ventricular fractional area change; TAPSE, Tricuspid annular plane systolic excursion.
Data are mean ± standard deviation. [a] Value is percentage

Table 2: Demonstrates correlation of MPI measured by conventional Doppler echocardiography and tissue Doppler imaging with echocardiographic measures

MPI Method	RVEF	RVFAC	RV dP/dt	TAPSE	S' (cm/s)
PWMPI	r =-0.245, p = 0.013	r =-0.385, p = 0.0001	r =-0.295, p = 0.002	r =-0.39, p = 0.0001	r =-0.57, p = <0.0001
TDMPI	r =-0.527, p = <0.0001	r =-0.53, p = <0.0001	R =-0.557, p = <0.0001	r =-0.50, p = <0.0001	r =-0.583, p = <0.0001

‡ MPI, Myocardial performance index; PW, Pulsed-Wave; TD, Tissue Doppler; RVEF, Right ventricular ejection fraction; RVFAC, Right ventricular fractional area change; TAPSE, Tricuspid annular plane systolic excursion; S', Peak myocardial systolic velocity

Figures

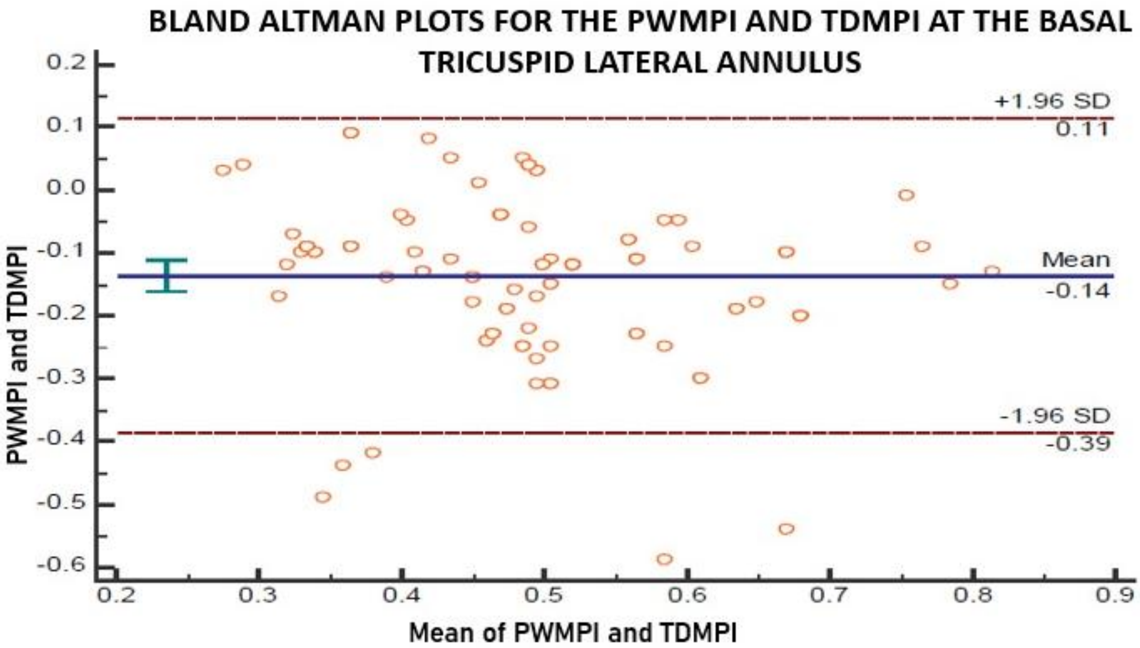

Figure 1: Bland Altman plots for the PWMPI and TDMPI at the basal tricuspid lateral annulus. The differences between both methods are displayed against the average of both measures. The lines denote the mean difference and 95% interval of agreement in the absolute value of the differences

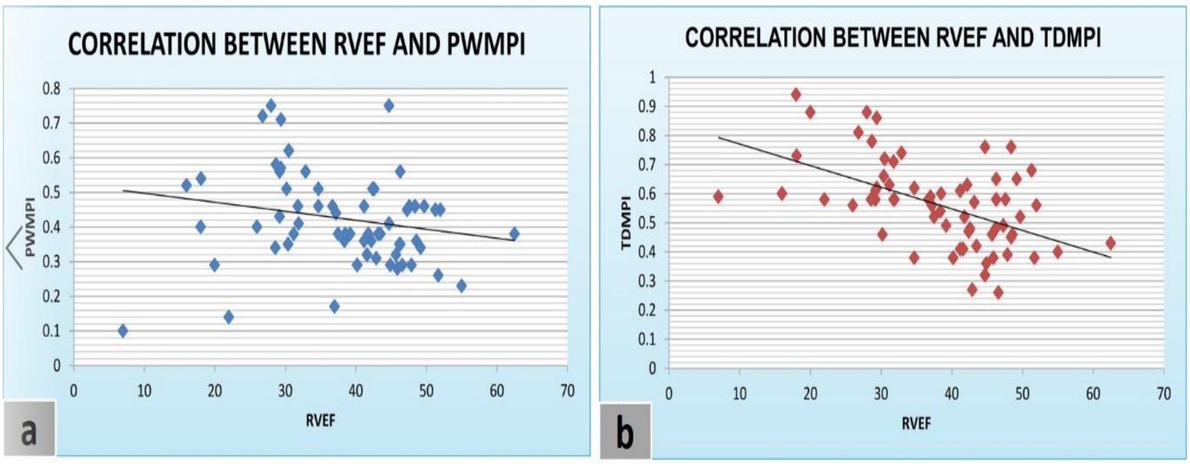

Figure 2: Correlation between (a) PWMPI and right ventricular ejection fraction (b) TDMPI and right ventricular ejection fraction

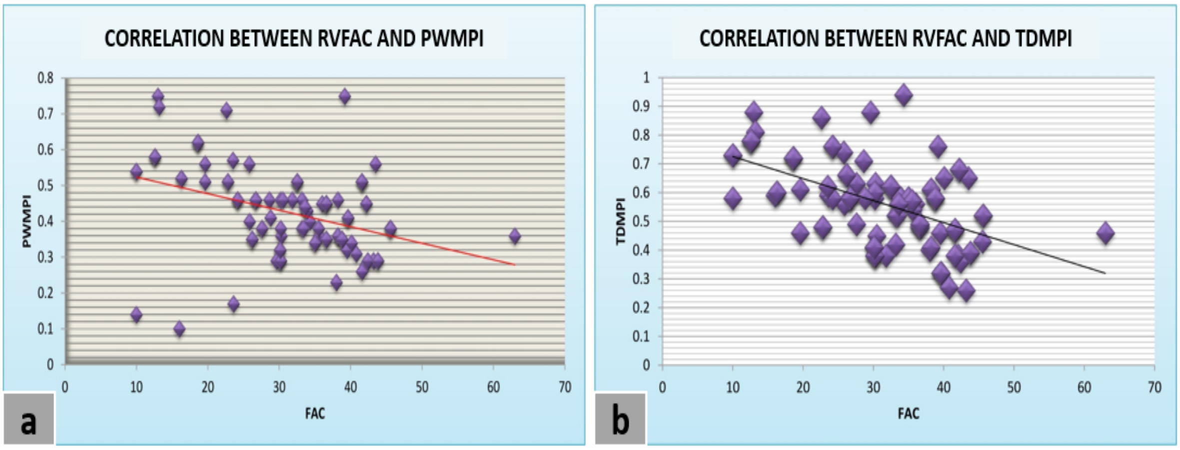

Figure 3: Correlation between (a) PWMPI and right ventricular fractional area change **(**b) TDMPI and right ventricular fractional area change

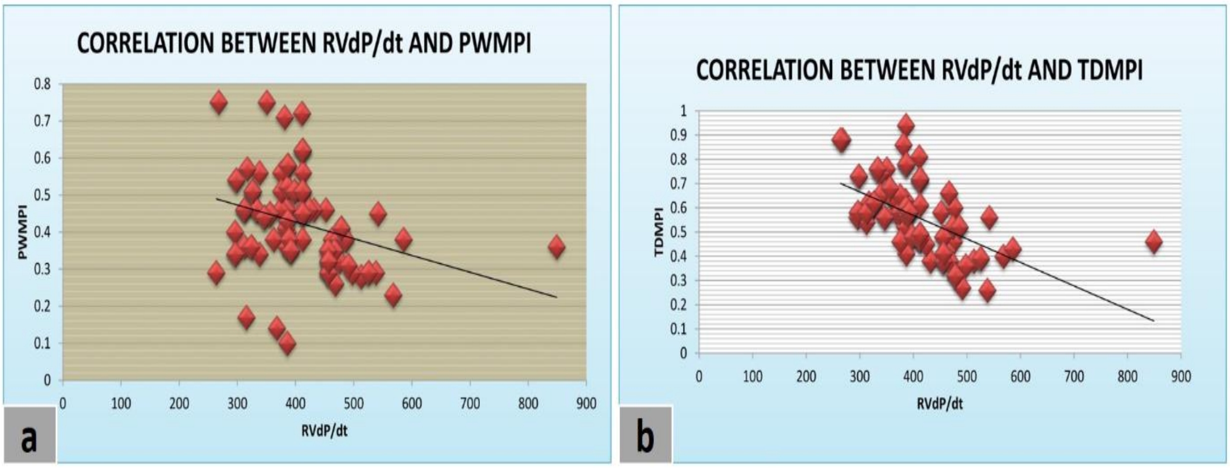

Figure 4: Correlation between (a) PWMPI and right ventricular RV contractility dP/dt **(**b) TDMPI and right ventricular RV contractility dP/dt

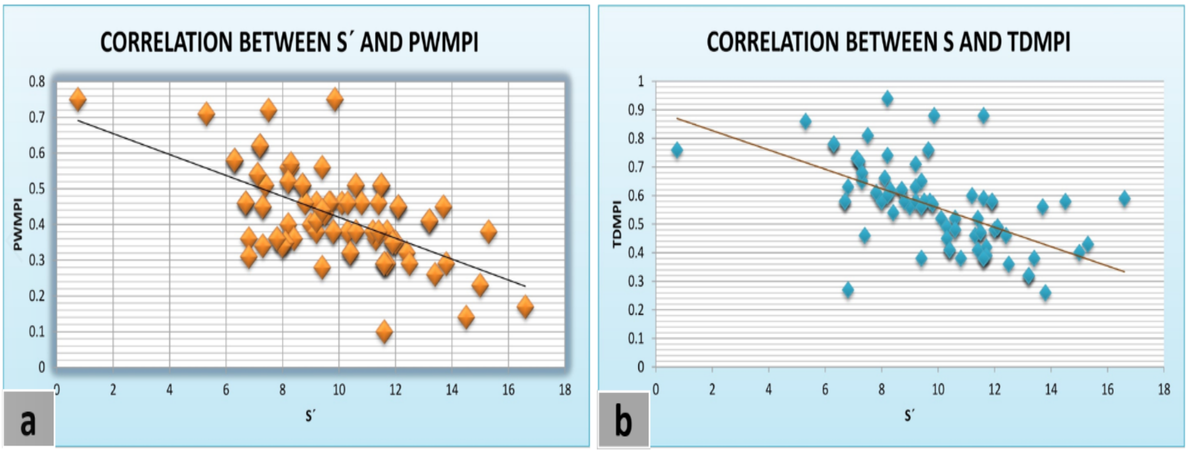

Figure 5: Correlation between (a) PWMPI and tricuspid annular plane systolic excursion (b) TDMPI and tricuspid annular plane systolic excursion

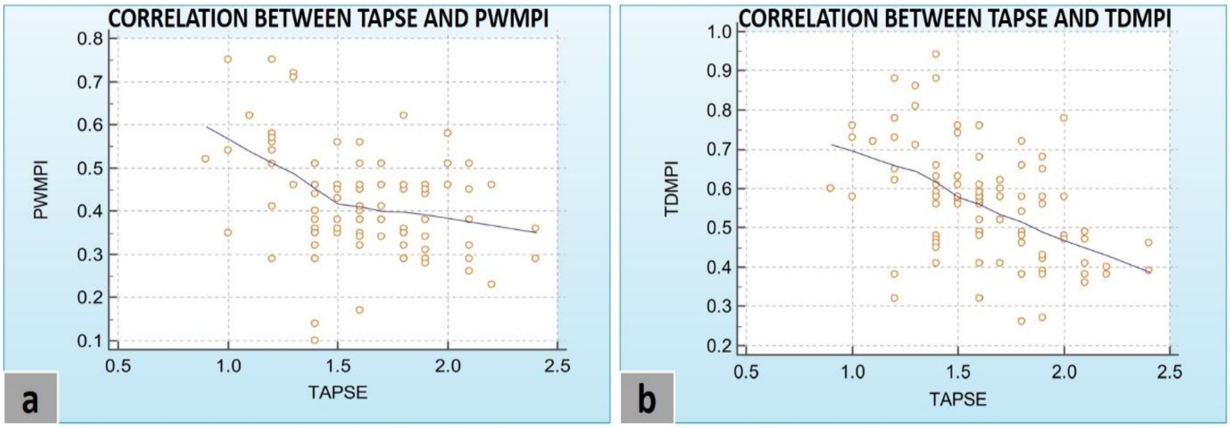

Figure 6: Correlation between (a) PWMPI and S'-wave velocity (b) TDMPI and S'-wave velocity