Original Research

Retrospective Study of Pulmonary Hypertensive Patients: Is Right Ventricular Myocardial Performance Index a Vital Prognostic Factor?

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Introduction: Right ventricular function is a determinant of prognosis and survival in patients with pulmonary hypertension. The pulmonary hypertensive right ventricle has a complex shape. Transthoracic two-dimensional echocardiography is the primary examination for demonstrating right ventricular impairment. Nowadays, many indices have been linked with pulmonary hypertension. The myocardial performance index (MPI), which may be determined by both conventional Doppler and tissue Doppler imaging (TDI), is one of these.

Methods: Ninety-three patients with pulmonary hypertension were examined retrospectively over 3 years' treatment. The relationship between MPI and right ventricular impairment was studied, as well as the correlation with various echocardiographic determinants. In addition, we examined the correlation between conventional echocardiography and tissue Doppler imaging with reference to the MPI.

Results: MPI had a statistically significant relationship with the visual estimation of right ventricular impairment ($r=0.714$, $p=0.001$), the degree of pulmonary regurgitation ($r=0.155$, $p=0.048$), left ventricular eccentricity index ($r=0.299$, $p=0.001$ in systole) and the presence of pericardial effusion ($r=0.199$, $p=0.008$), while it was inversely correlated with left ventricular fractional shortening ($r=-0.284$, $p=0.001$). However, the index had no correlation with tricuspid regurgitant velocity, right ventricular acceleration time or right atrial volume. There was significant agreement between the MPI measured by conventional Doppler echocardiography and by TDI ($r=0.83$, $p<0.001$; mean value -0.10, SD 0.2). Finally, some patients showed a significant decrease in tricuspid regurgitant velocity and MPI during their treatment.

Conclusion: Right ventricular MPI has a good correlation with several parameters and can be a good prognostic factor for right ventricular impairment in patients with pulmonary hypertension.

Pulmonary hypertension has various causes and exerts a significant effect on the right heart chambers.[1-4] The main alterations in ventricular function as a result of pulmonary hypertension include elevated pulmonary artery pressures, right ventricular hypertrophy and dilatation[5] (due to adaptation of the right ventricle to chronic pressure overload), progressive volume overload (due to further right ventricular dilatation and functional tricuspid valve incompetence), as well as right ventricular systolic dysfunction. Furthermore, in severe cases, there is diastolic dysfunction of the left ventricle, due to the marked impairment of the geometry.[6-8]

Patients and methods

Ninety three patients with pulmonary hypertension from different causes, classified as primary (idiopathic), thromboembolic, portal (liver disease), systemic disease, heart disease (repair of congenital heart disease, hypertension and other causes) and chronic pulmonary disease[9,10] were studied. The diagnosis of pulmonary hypertension was established with a combination of two-dimensional echocardiography and right heart catheterisation (tricuspid regurgitant velocity >2.8 m/s, pulmonary capillary wedge pressure <15 mmHg, peripheral vascular resistance >3 Wood units). The patients' age was 49.8 ± 15.74 (age range 24-84 years, Table 1). Patients with an irregular heart rhythm, such as atrial fibrillation, previous myocardial infarction, resting wall motion abnormalities, cardiomyopathy or the presence of a pacemaker or defibrillator lead in the right ventricle were excluded.

Treatment initiation was considered a determinant factor for the study of many parameters concerning right ventricular function and the patients' prognosis. All participants were followed for 3 years with an echocardiographic examination every six months. The follow-up studies comprised a transthoracic echocardiogram (Philips Sonos 7500, transducer S3 1.8-3 MHz), including a parasternal long and short axis, apical chamber view, subcostal and suprasternal views, as well as the use of colour Doppler in all projections, pulsed and continuous wave Doppler.

Among various Doppler parameters, peak tricuspid regurgitation velocity, measured in the apical four-chamber view, is considered to be the most robust measurement for screening patients with suspected pulmonary hypertension. It is clinically important for the estimation of the pulmonary artery systolic pressure using the modified Bernoulli equation. Pulmonary regurgitation was estimated quantitatively and qualitatively (Table 2). Visual estimation of right ventricular impairment (Table 3) can be achieved from all views, according to the degree of trabeculation, dilatation of the chamber and interventricular septal flattening. Pulmonary artery flow acceleration time is another haemodynamic parameter[11] that has been related to mean pulmonary artery pressure. It is measured by pulsed wave Doppler when the sample volume is placed within the right ventricular outflow tract or proximal main pulmonary artery.

Right atrial volume was calculated from the area and long axis length of the atrium as $0.85 \times A^2/L$ (Figure 1). The eccentricity index was estimated from the parasternal short axis projection, at the level of the papillary muscles. It is calculated as the ratio of the major axis of the left ventricle to the minor axis at the level of the *chordae*, at end-diastole and end-systole (Figure 2). Myocardial performance index[12] (MPI or Tei-index) was measured with Doppler echocardiography, using the apical four-chamber and parasternal axis views of the right ventricular outflow tract. MPI was also measured with tissue Doppler imaging, in which pulsed wave Doppler was applied to the right ventricular free wall (Figure 3). MPI is calculated by dividing

Table 1. Demographic data of 93 patients, N (%).

Sex	
Women	50 (53.7%)
Men	43 (46.3%)
Aetiology	
Primary	46 (49.5%)
Heart disease (shunt)	20 (21.5%)
Chronic thromboembolic disease	11 (11.8%)
Systemic disease	7 (7.5%)
Portal hypertension	5 (5.3%)
Pulmonary cause	4 (4.3%)
Therapy	
Bosentan	54 (58%)
Sildenafil	7 (7.5%)
Bosentan & sildenafil	16 (17.2%)
Treprostinil	9 (9.6%)
Iloprost & bosentan	3 (3.2%)
Iloprost & sildenafil	2 (2%)
Iloprost & treprostinil	2 (2%)

Table 2. Classification of pulmonary regurgitation.

1	No evidence
2	Mild
3	Moderate
4	Severe

Table 3. Classification of right ventricular impairment.

1	Good function
2	Mild impairment
3	Moderate impairment
4	Moderate to severe impairment
5	Severe impairment

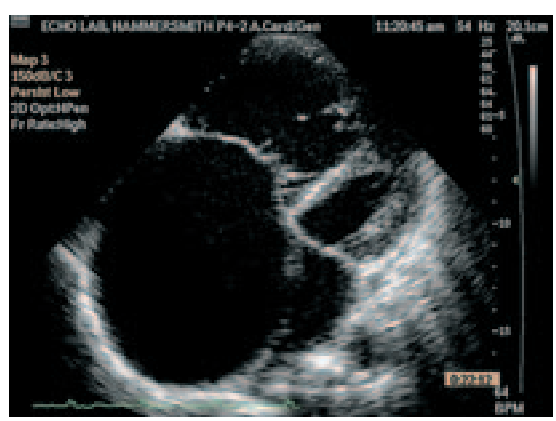


Figure 1. Primary pulmonary hypertension. Right atrial volume: 550 ml.

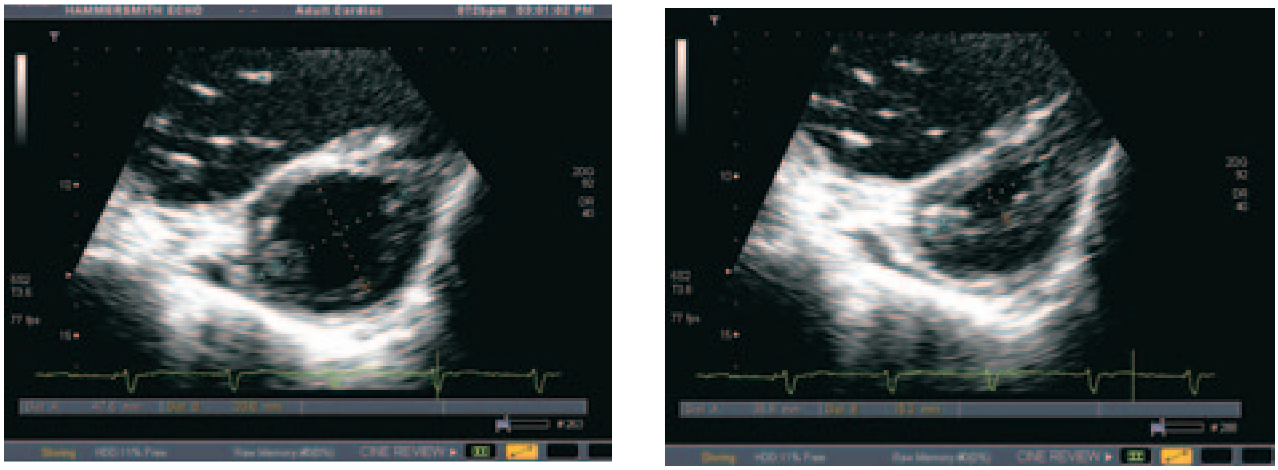
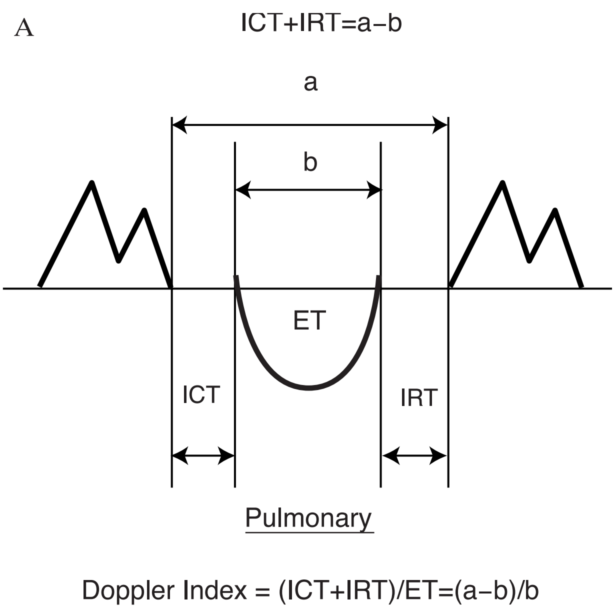


Figure 2. Eccentricity index of the left ventricle, as measured at end-diastole and end-systole.

A



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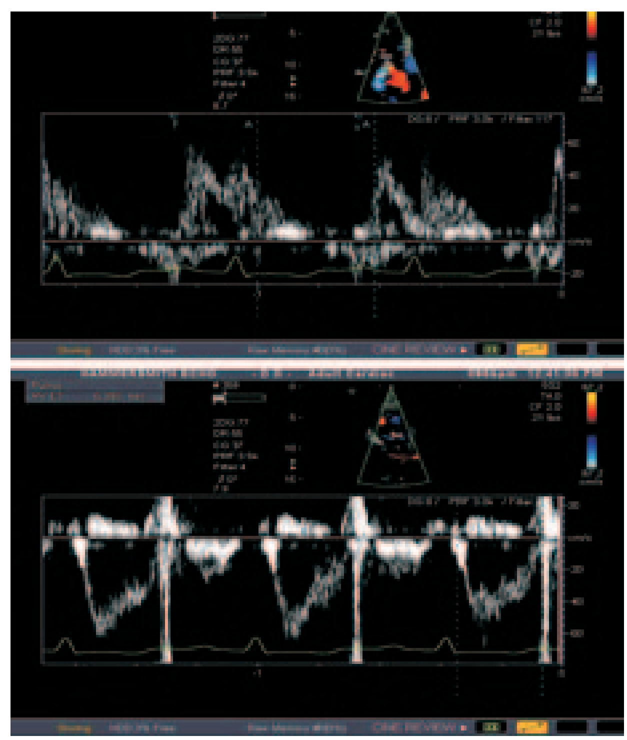

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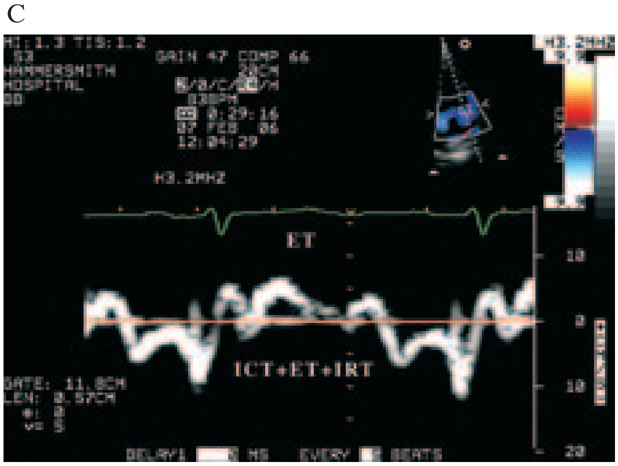

Figure 3. Measurement of myocardial performance index. A: Schematic representation. B: Using Doppler echocardiography (pulsed wave Doppler at tricuspid inflow and right ventricular outflow tract). C: Using tissue Doppler imaging at the right ventricular lateral wall. ICT – isovolumic contraction time; IRT – isovolumic relaxation time; ET – ejection time.

the sum of the isovolumic contraction time and isovolumic relaxation time by the ejection time.

The status of the left ventricle was estimated by the E and A waves of mitral inflow, measured with Doppler echocardiography, aortic flow velocity, as well as left ventricular outflow tract velocity. Fractional shortening of the left ventricle was also estimated from the parasternal long-axis view. Finally, the evidence of pericardial effusion was estimated from all projections (Table 4), and the diameter of the inferior *vena cava* was measured from the subcostal view.[13]

Statistical analysis

Paired values were compared using a paired t-test. Correlations were examined using Spearman's correlation coefficient for non-parametric data. Bland-Altman analysis was used for the estimation of agreement between two methods (Doppler and tissue Doppler imaging).[14] The MPI as measured by Doppler was correlated with the qualitative estimation of the right ventricle, and major echocardiographic parameters such as tricuspid regurgitant jet velocity, eccentricity index and fractional shortening of the left ventricle, the evidence of pericardial effusion and right atrial volume. Both MPI and the tricuspid regurgitant jet velocity were correlated with the values recorded by a second observer who was unaware of the findings of the first. All data are expressed as mean ± standard deviation (SD). A p-value <0.05 was considered statistically significant. The interobserver reproducibility between two cardiologists' measurements was estimated by taking the differences between pairs of values and calculating the mean value of these. Medcalc software was used for the analyses.

Table 4. Classification of pericardial effusion.

1	No evidence
2	Trivial
3	Mild

Results

Of the 93 patients with pulmonary hypertension (50 women, 53.7%, and 43 men, 46.3%), 46 (49.5%) had primary pulmonary hypertension, 20 (21.5%) had a systemic to pulmonary circulation shunt related to pulmonary hypertension, 11 patients (11.8%) had chronic thromboembolic disease, 7 (7.5%) had systemic disease, 5 (5.4%) had portal hypertension and 4 (4.3%) had a pulmonary cause of the disease (Table 1).

Mean values (Table 5)

Mean right ventricular systolic pressure was 88.53 ± 21.98 mmHg (range 35 mmHg [borderline pulmonary hypertension] to 174 mmHg [severe pulmonary hypertension]). Mean tricuspid regurgitant velocity was 4.36 ± 0.6 m/s (minimum 2.6 m/s, maximum 6.3 m/s). The eccentricity index was 1.47 ± 0.33 in diastole and 2.06 ± 0.7 in systole. The mean diameter of the inferior

Table 5. Echocardiographic data of 93 patients.

Parameters	Minimum	Maximum	Mean	SD
Age (yrs)	24	84	49.88	15.74
RVSP (mmHg)	35	174	88.53	21.98
TR (m/s)	2.6	6.3	4.36	0.6
MPI	0.23	1.7	0.67	0.27
EID	1	2.95	1.47	0.33
EIS	1	5.8	2.06	0.7
IVC (cm)	1	3.4	2.1	0.51
AT (ms)	30	130	72.04	18.07
RA (ml)	21	350	134.02	69.81
AoV (m/s)	0.7	2	1.16	0.22
LVOTV (m/s)	0.6	1.4	0.84	0.16
FS (%)	9	60	35.69	7.51

RVSP – right ventricular systolic pressure; TR – tricuspid regurgitation; MPI – myocardial performance index; EID – eccentricity index of left ventricle in diastole; EIS – eccentricity index of left ventricle in systole; IVC – diameter of inferior *vena cava*; RA – right atrial volume; AoV – aortic valve velocity; LVOTV – velocity of left ventricular outflow tract; FS – left ventricular fractional shortening.

vena cava was 2.1 ± 0.51 cm. Right ventricular acceleration time was 72 ± 18 ms (minimum 30 ms, maximum 130 ms). Right atrial volume was 134 ± 69.81 ml. Left ventricular fractional shortening was 35.69 ± 7.51.

Analysis

The MPI measured with Doppler had a significant association with some of the established echocardiographic parameters. Tricuspid regurgitation velocity was not correlated with MPI (r=0.075, p=0.322) (Figure 4). However, there was a strong positive correlation (r=0.714, p=0.001) between MPI and the visual estimation of right ventricular impairment performed by two different cardiologists, with the severity of impairment associated with higher levels of the index (Figure 5).

MPI was also positively correlated with the degree of pulmonary regurgitation (r=0.155, p=0.048). It was positively correlated with the eccentricity index, both in diastole (r=0.189, p=0.012) and in systole (r=0.299, p=0.001) (Figure 6). Moreover, the higher the MPI, the lower the left ventricular fractional shortening (r=-0.284, p=0.001), while there was a positive correlation between MPI and the evidence of pericardial effusion (r=0.199, p=0.008). Finally, there was no statistically significant association between MPI and right ventricular acceleration time (r=0.007, p=0.93), or between MPI and right atrial volume (r=0.142, p=0.051) (Figure 7).

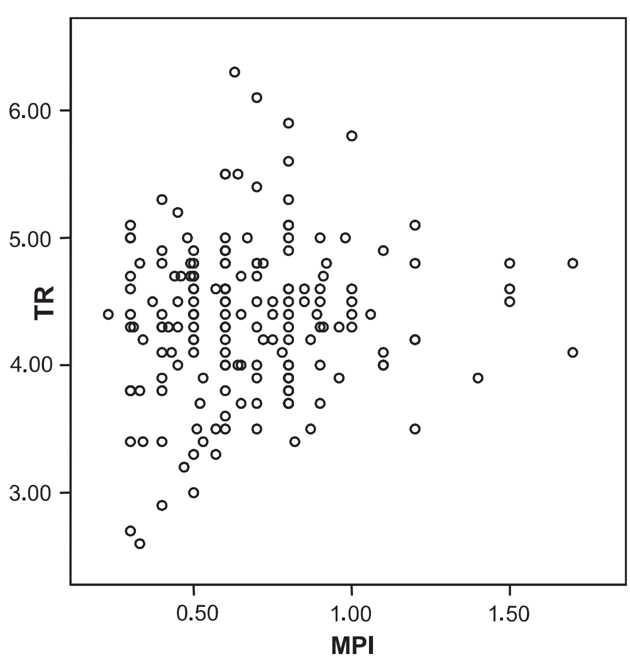

Figure 4. Absence of correlation between tricuspid regurgitation (TR) and myocardial performance index (MPI) (r=0.075, p=0.322).

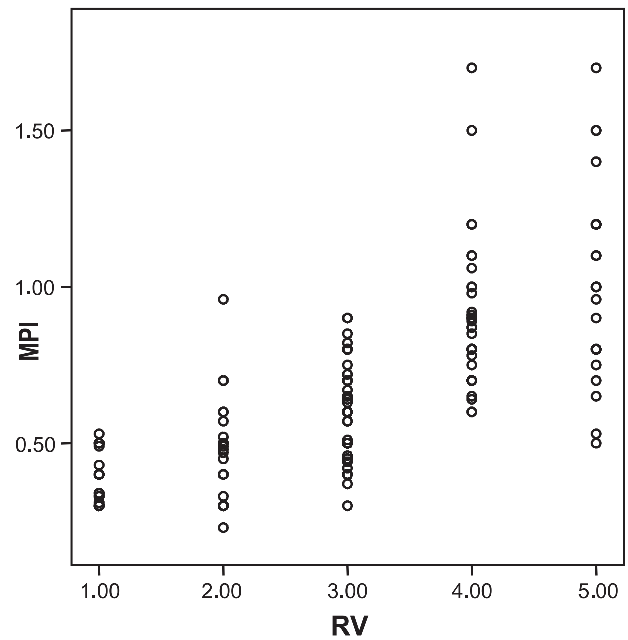

Figure 5. Strong positive correlation between myocardial performance index (MPI) and visual estimation of right ventricular impairment (RV) (r=0.714, p=0.001).

Agreement between Doppler and tissue Doppler imaging – Bland-Altman analysis

The measurement of MPI with both techniques demonstrated a high degree of agreement between Doppler and tissue Doppler imaging (r=0.83, p<0.001; mean value -0.10, SD 0.2, Figure 8). The study of tricuspid regurgitation velocity and MPI had good reproducibility, as there was strong interobserver agreement in the measurement of MPI (r=0.948, p=0.0001) (Figure 9) and tricuspid regurgitation velocity (r=0.983, p=0.0001).

Follow up

The follow up of patients, including the initiation of drug therapy, showed that transthoracic echocardiography was a very good predictor of the efficacy of the treatment. Thus, interestingly, there was a reduction in tricuspid regurgitation velocity in 46 patients (49.5%) by a mean of 0.8 ± 0.17 m/s. MPI decreased in 55 patients (59.1%) with a mean reduction of 0.4 ± 0.17, in concordance with a decrease in right ventricular impairment in 40 patients (43%), as visually estimated. The remaining

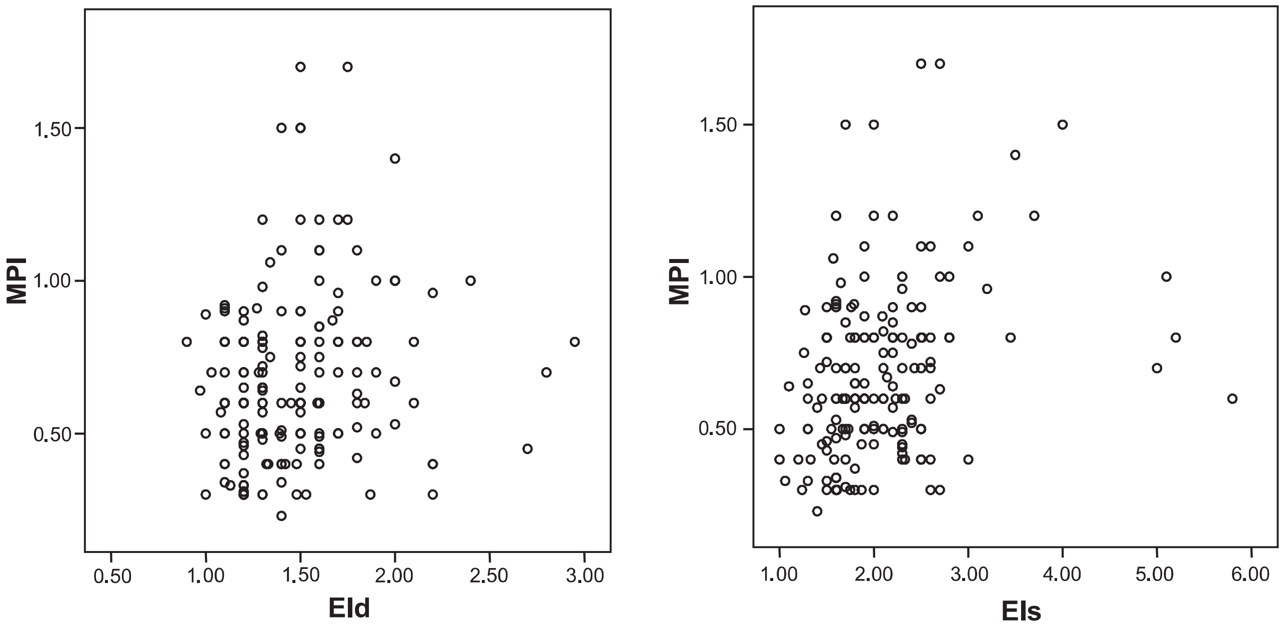

Figure 6. Positive correlation between myocardial performance index (MPI) and eccentricity index (EI), in both diastole (r=0.189, p=0.012), and systole (r=0.299, p=0.001).

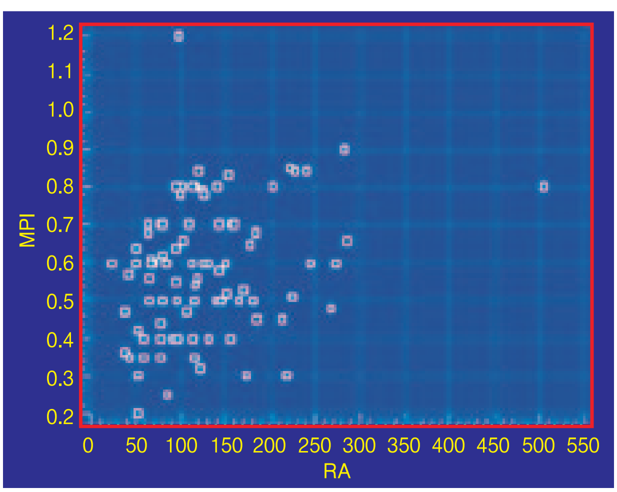

Figure 7. Relationship between myocardial performance index (MPI) and right atrial volume (RA) (r=0.142, p=0.051).

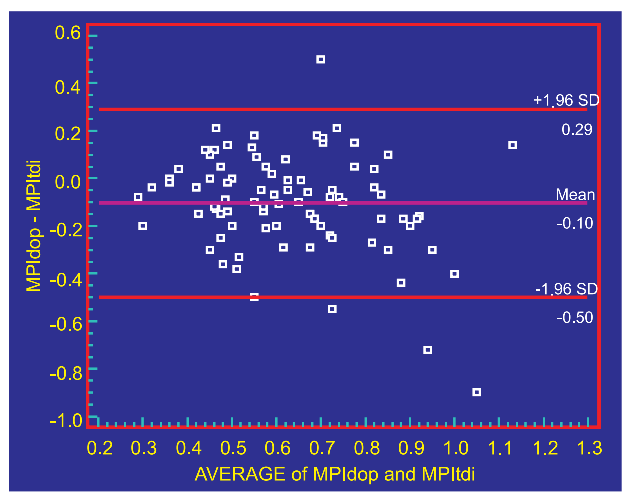

Figure 8. Agreement between myocardial performance index (MPI) as measured with conventional Doppler (dop) and tissue Doppler imaging (tdi) (r=0.83, p<0.001; mean -0.1, SD 0.2) (Bland-Altman analysis).

15 patients of this group (16.1%) had stable right ventricular dysfunction despite the reduction of MPI, while 12 patients showed no change in either right ventricular functional status or MPI. Thus, in 27 patients in all (29.4%) there was no significant change in right ventricular impairment compared to the previous study.

During follow up, inferior *vena cava* diameter decreased in 46 patients (49.5%) by a mean value of 0.2 ± 0.05 cm. Right ventricular acceleration time increased in 22 patients (23.6%) and right atrial volume increased in 55 patients (59%). One year after the onset of the disease, type I left ventricular diastolic dysfunction was noticed in 55 patients (59%), by the assessment of mitral inflow (E and A waves) and myocardial tissue velocities of septal and lateral left ventricular walls. Finally, left ventricular fractional shortening was improved in 73 patients (78.5%) with a mean increase of 5.6 ± 1.34.

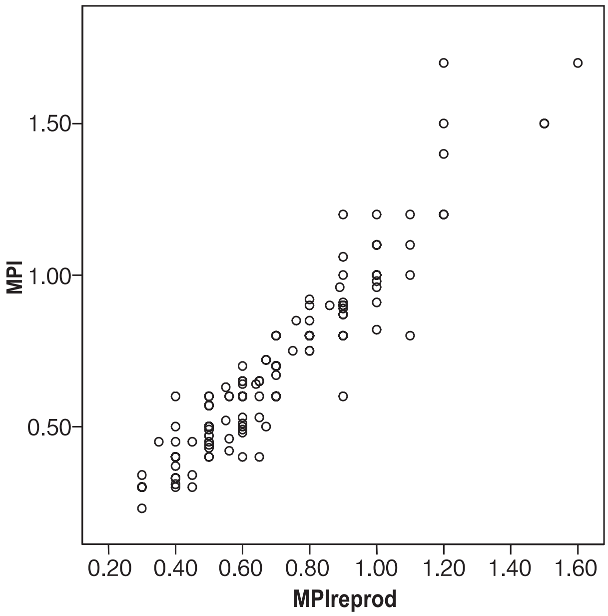

Figure 9. Strong positive correlation between two observers in the measurement of myocardial performance index (MPI) ($r=0.948$, $p=0.0001$).

Discussion

Pulmonary hypertension is more common in young women, with a ratio of 3:2 compared to men. When the right ventricle is exposed chronically to increased afterload, it hypertrophies and assumes a more important role in maintaining flow through the pulmonary circulation. Right ventricular afterload can increase as a result of obstruction or destruction of the pulmonary circulation, hypoxic pulmonary vasoconstriction, cardiac disease, or idiopathic causes. Chronic pulmonary disease, chest wall diseases, obstructive sleep apnoea, and interstitial fibrosis all cause pulmonary hypertension. Cardiac disease can result in pulmonary hypertension, either through increased left atrial pressures (mitral stenosis) or through chronic left to right shunting. Systemic diseases, such as rheumatoid arthritis, systemic lupus, or sarcoidosis, can influence the pulmonary vasculature and cause pulmonary hypertension.

Transthoracic echocardiography is the main non-invasive technique used for the diagnosis of pulmonary hypertension, because there is usually a period of 1-2 years during which changes in the pulmonary vasculature status are not obvious and elevation in pulmonary artery pressure cannot easily be detected. The examinations most preferred for evaluation of the status of the right ventricle are right heart catheterisation and transthoracic echocardiography. With the new technique of tissue Doppler imaging, MPI can be measured as easily and accurately as with conventional Doppler echocardiography, since the two methods have a significant agreement.

Nowadays, cardiac magnetic resonance imaging has emerged as a new method for assessing right ventricular volumes. However, echocardiography offers real-time imaging, in contrast to the reconstructive imaging of cardiac magnetic resonance, and it takes less time than other procedures, rendering it a convenient tool for the evaluation of patients with pulmonary hypertension.

As far as echocardiographic parameters are concerned, MPI is well correlated with tricuspid regurgitation.[15] The index reflects right ventricular impairment and the severity of impairment is proportional to the velocity of tricuspid regurgitation. Pulmonary regurgitation also affects MPI. In addition, the eccentricity index reflects the compression of the left ventricle due to right ventricular enlargement and impairment. This index appears to be a reproducible measurement with an established clinical value for the evaluation of the severity of right ventricular pressure overload due to the displacement of the interventricular septum. A prognostic factor for pulmonary hypertension, pericardial effusion, seems to have a positive correlation with MPI.[16] A low MPI, meaning good right ventricular function, has a lower possibility of being followed by pericardial effusion. It was also a very significantly associated with a decrease in pericardial effusion during drug therapy.

Measurement of the peak velocities of the E and A waves and the deceleration time of the E wave provides important information. In most cases, the E/A ratio is <1 because of the increased right ventricular hypertrophy and reduced compliance. In an advanced stage, with ensuing systolic ventricular failure or severe tricuspid regurgitation, diastolic dysfunction becomes progressively pseudo-normalised, with an inverted E/A ratio (>1).[17]

The negative correlation between MPI and left ventricular fractional shortening indicates how the severity of right ventricular impairment influences the functional status of the left ventricle. When MPI decreases, there is evidence of better fractional shortening. Because of the close anatomical association between the two ventricles, the volume of one ventricle can be expected to affect the performance of the other. Many studies have discussed the myocardial interaction between the ventricles, and this issue is of great importance in the pathophysiology of pulmonary hypertension.[18]

There was no correlation between MPI and the right ventricular acceleration time. It seems that the short duration of acceleration time and its potential variation with a relatively small movement of the cursor during the measurement result in poor reproducibility.

Another prognostic factor of the disease, right atrial volume, appears not to be correlated with MPI. Even when the performance of the right ventricle improved, the right atrial volume continued to increase. Thus, although the presence of a severely dilated right atrium seems to influence the functional status, in this study it was not shown to be a determinant factor for the patients' prognosis.

The fact that there was a good interobserver correlation in the measurements of both MPI and tricuspid regurgitation velocity shows that MPI is a valuable index in the investigation of pulmonary hypertension.

The echocardiographic measurements also demonstrated the efficacy of drug therapy as regards the functional class and the survival of these patients. Today, drugs such bosentan (a *per os* antagonist of A and B receptors of endothelin-1) and sildenafil (antagonist of phosphodiesterase-5) are commonly used and their contribution is significant.[19-24]

Limitations of the study

It would have been interesting to measure the effect of each drug on right ventricular remodelling. However, we tested the overall effect of drug therapy, because the aim was not to compare drugs but to show the feasibility of using echocardiographic parameters before and after treatment of pulmonary hypertension.

Conclusions

MPI is an index that can be trusted for the prognosis of pulmonary hypertension, since it has been shown to have a good correlation with symptoms, while it is relatively unaffected by heart rate and loading conditions. The advantages of its use are good reproducibility, quick calculation, no need for use of geometric models and application even in the presence of a difficult acoustic window. MPI is also a useful measurement for the follow up evaluation of patients under drug treatment for pulmonary hypertension.

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