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Left ventricular diastolic dysfunction in idiopathic pulmonary fibrosis: A tissue-Doppler echocardiographic study

Christodoulos E. Papadopoulos, MD[1], Georgia Pitsiou, MD[2], Theodoros D. Karamitsos, MD[1], Haralambos I. Karvounis, MD[1], Theodoros Kontakiotis, MD[2], Georgios Giannakoulas, MD[1], Georgios K. Efthimiadis, MD[1], Paraskevi Argiropoulou, MD[2] , Georgios E. Parharidis, MD[1] Demosthenes Bouros, MD, FCCP[3]

[1] 1st Cardiology Department, AHEPA University Hospital, Thessaloniki, Greece

[2] Respiratory Failure Unit, Aristotle University of Thessaloniki, Greece

[3] Department of Pneumonology, Medical School University of Thrace, Alexandroupolis 68100, Greece

Short title: LV function in Idiopathic Pneumonic Fibrosis

Corresponding author

Prof. Demosthenes Bouros, MD, FCCP

Department of Pneumonology, Medical School, Democritus University of Thrace, Alexandroupolis 68100, Greece

E-mail: bouros@med.duth.gr

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ABSTRACT

Background: We hypothesised that apart from right ventricular (RV) dysfunction, patients with idiopathic pulmonary fibrosis (IPF) also exhibit left ventricular (LV) impairment, which may affect disease progression and prognosis.

Objectives: To evaluate LV performance in a cohort of IPF patients using conventional and tissue Doppler echocardiography.

Methods: We studied 22 IPF patients (mean age 65±9 years) exhibiting mild to moderate pulmonary artery hypertension and 22 healthy individuals (mean age 61±6 years). We used conventional and tissue Doppler echocardiography for the evaluation of RV and LV systolic and diastolic function.

Results: Apart from the expected impairment in RV function, all patients showed a characteristic reversal of LV diastolic filling to late diastole compared to controls (E/A 0.7±0.2 vs. 1.5±0.1 respectively, $p<0.001$). Patients with IPF also exhibited lower peak myocardial velocities in early diastole (Em 5.7±1.1 vs. 10.3±1.6 respectively, $p<0.001$), higher in late diastole (Am 8.9±1.3 vs.5.5±0.8 respectively, $p<0.001$), lower Em/Am (0.6±0.1 vs.1.9±0.5 respectively, $p<0.001$) and higher E/Em ratio (10.8±3 vs. 6±0.6 respectively, $p<0.001$), all indicative of LV diastolic dysfunction. Moreover, LV propagation velocity was significantly lower in IPF patients (46±13 vs. 83±21 respectively, $p<0.001$).

Conclusions: Physicians should be aware that patients with IPF exhibit early impairment of LV diastolic function.

Introduction

Idiopathic pulmonary fibrosis (IPF) is a progressive fibrosing inflammatory lung disease leading progressively to pulmonary hypertension (PH) with increased morbidity and mortality and a mean length of survival after diagnosis ranging from 3 to 5 years **[1-3]**.

Right ventricular (RV) dysfunction has been well described in IPF patients and in several conditions affecting pulmonary circulation, such as primary pulmonary hypertension, chronic obstructive pulmonary disease, chronic thromboembolic pulmonary hypertension, systemic sclerosis, systemic lupus erythematosus and cystic fibrosis [**4-10**]. Moreover, left ventricular (LV) diastolic dysfunction has been reported in some of these conditions [**5-7,11,12**] mainly as a consequence of RV pressure overload. Nevertheless, the prevalence of LV dysfunction in patients with IPF and mild to moderate PH is not known. Importantly, LV dysfunction, if present, could be an additional factor which may further impair exercise performance and affect prognosis early in the course of the disease.

New noninvasive echocardiographic techniques that are relatively load-independent, such as Tissue Doppler Imaging (TDI) and Colour M-Mode, have made echocardiography the clinical standard for the assessment of LV diastolic function [**13,14**]. Regional myocardial velocities and time intervals in systole and diastole can be accurately and reproducibly measured by TDI, allowing the detection of subclinical abnormalities [**15**]. Furthermore, mitral annulus TDI derived velocities have proven their ability to estimate LV filling pressures and to provide prognostic information in various cardiovascular diseases **[16,17]**.

On these grounds, the main aim of the present study was to determine LV and RV systolic and diastolic function in IPF patients.

Material and Methods

Twenty-two patients (15 male, mean age 66 years; range, 53 to 75 years) with IPF were studied. The diagnosis of IPF was based on the American Thoracic Society/ European Respiratory Society major and minor criteria [**18**]. For HRCT criteria, appearances compatible with fibrotic idiopathic interstitial pneumonia were required, as previously described [**19,20]**. The patients were clinically stable and ambulatory at the time of echocardiographic study and were recruited from the Outpatient Respiratory Failure Clinic over a period of 18 months. Throughout the study they continued to receive the same medical treatment.

Patients with a history of known significant coronary artery disease, cardiomyopathy, valvular heart disease, arterial hypertension, and symptoms/signs of RV failure were excluded from further evaluation. Furthermore, subjects with atrial fibrillation and other rhythm abnormalities were excluded from the study.

The control group consisted of 22 age- and sex-matched control subjects without any history of pulmonary and/or cardiac disease. An important technical inclusion criterion of the study was the presence of an adequate tricuspid valve regurgitation Doppler signal in order to assess pulmonary artery systolic pressure in all subjects enrolled in the study.

The institutional research ethics committee approved our study. All participants gave written informed consent.

Pulmonary Function Studies

All patients had a spirometry (Transferrscreen II, Jaeger; Germany) within 1 week of the echocardiographic study according to current guidelines [**21**]. Arterial blood was taken with the patient sitting, breathing room air;

pH, pCO_2 and PO_2 were measured with a commercially available blood gas analyzer (ABL, Radiometer Copenhagen). The functional capacity of subjects was quantitatively measured by performing the 6-min walk test, according to current guidelines [**22**].

Echocardiographic study

All patients and controls underwent a complete echocardiographic study, including 2D, colour flow, spectral Doppler as well as TDI using a GE Vingmed Vivid 7 system (GE Vingmed Ultrasound AS, Horten, Norway). All images were saved digitally in raw-data format to magneto optical discs for offline analysis. Brachial systolic and diastolic blood pressure measurements in a sitting position with a standard mercury sphygmomanometer were undertaken before each echo evaluation.

Standard two-dimensional (2D) and colour flow Doppler images were obtained using the parasternal long and short axis and apical views. M-mode traces were recorded at a speed of50mm/s. Three consecutive cycles were averaged for every parameter. Left ventricular diameter and wall thickness were measured from two-dimensional targeted M-mode echocardiography according to the principals-recommendations of the American Society of Echocardiography [**23]**. Resting LV ejection fraction was obtained using modified Simpson's biplane method. The RV end-diastolic diameter and RV free wall thickness were measured from the 2D parasternal long axis view. Right ventricular end-systolic and end-diastolic areas were measured from the apical 4-chamber view to calculate RV fractional area change. Pulmonary artery systolic pressure (PASP) was estimated by calculating the maximal velocity of the tricuspid regurgitant jet and by further using the Bernoulli equation and then adding to this value an estimated right atrial pressure

based on both the size of the inferior vena cava and the change in diameter of this vessel during respiration **[24].**

Pulsed Doppler echocardiography in order to assess standard diastolic filling velocities of both LV and RV was performed using the apical four chamber view. Thus, the peak early filling velocity (E wave), peak late filling velocity (A wave), their ratio (E/A) and E wave deceleration time (DT) were recorded. Additionally, colour M-Mode was used to obtain LV propagation velocity (Vp) which serves as another index of LV diastolic function assessment [**13]**. All measurements were averaged from three end-expiratory cycles at a sweep speed of 100mm/s.

Pulsed-wave TDI was used to assess mitral and tricuspid annulus velocities. Filters were set to exclude high-frequency signals, and the Nyquist limit was adjusted to a velocity range of 15 to 20 cm/s. Gains were minimized to allow for a clear tissue signal with minimum background noise. All TDI recordings were obtained during normal respiration. A 5-mm sample volume was placed at the apical four-chamber view on the lateral corner of the mitral and tricuspid annulus. The peak myocardial velocities during systole (Sm), early diastole (Em), late diastole (Am) and their ratio (Em/Am) were recorded at a sweep speed of 100 mm/sec. We did not evaluate velocities at the septal corner of the mitral annulus, due to a possible interaction of the disturbed RV function. Furthermore, the ratio of early transmitral filling velocity (E wave) to early diastolic mitral annulus velocity (LV E/Em index) was calculated.

Statistical analysis

Data are expressed as mean ± SD and frequencies are expressed as percentages. All continuous variables were normally distributed. Differences between groups were assessed by Student's unpaired *t* test. Categorical variables were compared using χ^2 test or Fisher's exact test, as appropriate.

Pearson's correlation coefficients were calculated for pairs of continuous variables. A probability value of $p < 0.05$ was considered significant and two-tailed p values were used for all statistics. The SPSS statistical software (version 13.0, Inc., Chicago, Illinois) was used.

Results

Study population characteristics (Table 1)

Of the total 32 IPF patients evaluated and characterized, 22 were finally included in the study. Five patients were excluded due to inadequate echocardiographic tricuspid regurgitation Doppler signal, 2 due to arterial hypertension, 1 due to severe mitral valve regurgitation, 1 due to a history of coronary artery disease and 1 due to atrial fibrillation. Mean time from initial diagnosis of the disease was 9 months.

Patients with IPF did not differ significantly in terms of body mass index, smoking habits, baseline heart rate and blood pressure when compared to controls. Table 1 presents lung function parameters, resting gas exchange and 6-min walk test data of patients with IPF. Amongst IPF patients at the time of initial evaluation, 5 were on acetylcysteine therapy, 6 on azathioprine, 9 on prednisone and 5 on intermittent O_2 therapy.

RV function assessment (Table 2)

We documented that IPF patients exhibited impaired both systolic and diastolic RV function compared to controls. They showed worse RV area change, greater RV chamber dilatation and more RV free wall hypertrophy, all findings indicative of a RV remodeling process secondary to increased afterload. This increased afterload was established by the higher PASP values in the group of patients compared to controls. None of our patients had a distorted (D-shaped septum). Additionally, we found a characteristic reversal

of E/A ratio in IPF patients reflecting a progressive greater contribution of late diastole to RV ventricular filling.

LV function assessment (Table 3)

A significant difference between the two groups was observed, regarding E/A ratio, DT of the E wave, and Vp, reflecting early diastolic filling impairment in this specific population. The two groups did not differ significantly in terms of LV dimensions and systolic function.

Mitral annulus TDI analysis confirmed the presence of LV diastolic dysfunction in IPF patients with lower LV Em velocities and Em/Am ratios compared to controls. Moreover, patients with IPF presented higher E/Em ratios compared with controls. On the contrary, peak mitral annulus systolic velocity was similar between the 2 groups.

Correlations

Bivariate correlation analysis revealed significant relations between indices of LV diastolic function and PASP (Table 4). Of note are the negative correlations of LV E/A ratio ($r= -0.61$, $p<0.001$), Em/Am ratio ($r=-0.64$, $p<0.001$) and Vp ($r= -0.6$, $p<0.001$) with PASP (Figure 1).

Discussion

In the present study we demonstrated that patients with clinically stable IPF exhibit not only RV diastolic and systolic dysfunction, but also impaired LV diastolic filling. On the contrary, LV systolic function seems to be preserved. We believe that our findings have important implications in the management and possibly the prognosis of patients with IPF.

To the best of our knowledge, there are no reports in the literature regarding any association between IPF and LV diastolic function. Our findings from either standard Doppler (E/A ratio) or less load-dependent techniques [**13,15]**, like colour M-Mode (Vp) and TDI (Em, E/Em, Em/Am), suggest that

LV diastolic function and especially early relaxation is impaired in these patients. Similar disturbances in LV diastolic filling were also reported in previous studies that evaluated LV diastolic performance in diseases that mainly affect RV function [**5-7,11,12**]. On the contrary, LV systolic function as measured by both standard 2D and TDI echocardiography was preserved in our IPF patients, another finding that is in keeping with previous reports that evaluated LV systolic function in clinical entities that affect RV performance [**4-12**].

It is well known that diastolic dysfunction, particularly in the early phase of diastole, is the most common type of LV dysfunction seen in patients with chronic PH [**25]**. This impairment in early relaxation could be explained by different mechanisms. One of these is the distortion of the interventricular septum towards the left ventricle as the right ventricle adapts to pressure or volume overload and increases in size and mass [**26]**. This is less likely in our study population because PH was only mild to moderate. Secondly, since the right and left ventricle operate as a syncytium, diastolic function of one ventricle may influence diastolic function of the other, and this phenomenon is well recognized as ventricular interdependence [**26,27]**. Our finding of significant association between PASP and LV diastolic function indices underlines the presence of ventricular interdependence in patients with IPF. Finally, a compensatory neurohormonal activation seems to exist while RV function declines and this may influence loading conditions in both ventricles. In more detail, it has been shown in experimental settings, that peptides with positive inotropic effect, such as angiotensin II, endothelin-1, atrial natriuretic peptide and noradrenaline are produced. These substances may affect the remodelling process of both ventricles, by changing their loading conditions,

by inducing collagen synthesis and by inhibiting collagen degradation [**28,29]**.

Patients in the early stages of IPF may demonstrate normal or only slightly elevated PASP [**1-3**], but with the progression of the disease, pulmonary pressure increases dramatically within some months [**2**]. Therefore, it is important to determine in the early stages of the disease whether these patients suffer from LV diastolic dysfunction and to further investigate, if there is any association with the severity of PH and consequently with IPF disease progression. Our finding of significant associations between LV diastolic function indices and PASP further supports this hypothesis. If this is the case, echocardiographic parameters of LV diastolic dysfunction could be routinely used for the risk stratification and for therapy monitoring and guidance in such cohort. Moreover, young patients who have successfully undergone lung transplantation with long-term survival from improved allograft preservation, may eventually present symptomatic left heart failure from progressive LV diastolic dysfunction. Thus, the study of LV function in IPF patients after transplantation is warranted.

Limitations

The main limitation of our study is that the evaluation of PH was performed by using Doppler echocardiography and not by right heart catheterization, which is the gold standard method. Moreover, mitral annulus TDI recordings could be influenced by the overall heart motion and the contraction of adjacent myocardial segments, rendering this modality less sensitive than strain rate imaging [**30**].

In conclusion, patients with IPF exhibit predominantly type I LV diastolic dysfunction (impaired early relaxation) apart from the expected impairment in RV systolic and diastolic function. Whether LV diastolic

abnormalities have prognostic implication in the clinical course of patients with IPF, remains to be investigated. We believe that serial echocardiographic measurements particularly using TDI are warranted in this population to follow the progression of cardiac dysfunction.

REFERENCES

1. Noble PW, Homer RJ: Idiopathic pulmonary fibrosis: new insights into pathogenesis. *Clin Chest Med* 2004; 25: 749-758.
2. King TE Jr, Tooze JA, Schwarz MI, Brown KR, Cherniac RM: Predicting survival in idiopathic pulmonary fibrosis: scoring system and survival model. *Am J Respir Crit Care Med* 2001; 164: 1171-1181.
3. Bouros D, Antoniou KM: Current and future therapeutic approaches in idiopathic pulmonary fibrosis. *Eur Respir J* 2005 ; 26: 693-702
4. Lettieri CJ, Nathan SD, Barnett SD, Ahmad S, Shorr AF: Prevelance and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. *Chest* 2006; 129: 746-752
5. Bossone E, Duong-Wagner TH, Paciocco G, Oral H, Ricciardi M, Bach DS, Rubenfire M, Armstrong WF: Echocardiographic features of primary pulmonary hypertension*. J Am Soc Echocardiogr* 1999; 12: 655-662
6. Yilmaz R, Gencer M, Ceylan E, Demirbag R: Impact of chronic obstructive pulmonary disease with pulmonary hypertension on both left ventricular systolic and diastolic performance. *J Am Soc Echocardiogr* 2005; 18: 873-881
7. Menzel T, Wagner S, Kramm T, Mohr-Kahaly S, Mayer E, Braeuninger S, Meyer J: Pathophysiology of impaired right and left ventricular function in chronic embolic pulmonary hypertension: changes after pulmonary thromboendarterectomy. *Chest* 2000; 118: 897-903
8. Lindqvist P, Caidahl K, Neuman-Andersen G, Ozolins C, Rantapaa-Dahlqvist S, Waldenstrom A, Kazzam E: Disturbed right ventricular diastolic function in patients with systemic sclerosis: a Doppler tissue imaging study. *Chest* 2005; 128: 755-763

9. Gin PL, Wang WC, Yang SH, Hsiao SH, Tseng JC: Right heart function in Systemic Lupus Erythematosus: Insights from myocardial Doppler Tissue Imaging. *J Am Soc Echocardiogr* 2006; 19: 441-449
10. Ionescu AA, Ionescu AA, Payne N, Obieta-Fresnedo I, Fraser AG, Shale DJ: Subclinical right ventricular dysfunction in cystic fibrosis. A study using Tissue Doppler Echocardiography. *Am J Respir Crit Care Med* 2001; 163: 1212-1218
11. D'Andrea A, Stisi S, Bellissimo S, Vigorito F, Scotto di Uccio F, Tozzi N, Moscato F, Pezzullo E, Calabro R, Scherillo M: Early impairment of myocardial function in systemic sclerosis: Non-invasive assessment by Doppler myocardial and strain rate imaging. *Eur J Echocardiography* 2005; 6: 407-418
12. Mahmud E, Raisinghani A, Hassankhani A, Sadeghi HM, Strachan GM, Auger W, De Maria AN, Blanchard DG: Correlation of left ventricular diastolic filling characteristics with right ventricular overload and pulmonary artery pressure in chronic thromboembolic pulmonary hypertension. *J Am Coll Cardiol* 2002;40:318-324
13. Garcia MJ, Thomas JD, Klein AL: New Doppler echocardiographic applications for the study of diastolic function. *J Am Coll Cardiol* 1998; 32: 865-875
14. Nagueh SF, Middleton KJ, Kopelen HA, Zoghbi WA, Quinones MA: Doppler tissue imaging: a non-invasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. *J Am Coll Cardiol* 1997; 30: 1527-1533
15. Sutherland GR, Lange A, Palka P, Grubb N, Fleming A, McDicken WN: Does Doppler myocardial imaging give new insights or simply old information revisited. *Heart* 1996; 76: 197-199
16. Hillis GS, Moller JE, Pellikka PA, Gersh BJ, Wright RS, Ommen SR, Reeder GS, Oh JK: Noninvasive estimation of left ventricular filling pressure by e/e' is a

powerful predictor of survival after acute myocardial infarction. *J Am Coll Cardiol* 2004; 43: 360-367

17. Wang M, Yip GW, Wang AY, Zhang Y, Ho PY, Tse MK, Lam PK, Sanderson JE: Peak early diastolic mitral annulus velocity by tissue Doppler imaging adds independent and incremental prognostic value. *J Am Coll Cardiol* 2003; 41: 820-826
18. American Thoracic Society/European Respiratory Society international multidisciplinary consensus classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med* 2002; 165: 277-304
19. Wells AU, Rubens MB, du Bois RM, Hansell DM: Serial CT in fibrosing alveolitis: prognostic significance of the initial pattern. *Am J Roentgenol* 1993; 161: 1159-1165.
20. Wells AU, Hansell DM, Rubens B, Cullinan P, Black CM, du Bois RM: The predictive value of appearances on thin section computed tomography in fibrosing alveolitis. *Am Rev Respir Dis* 1993; 148: 1076-1082.
21. American Thoracic Society: Standarization of spirometry, 1994 update. *Am J Respir Crit Care Med* 1995; 152: 1107-1136
22. American Thoracic Society statement: Guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002; 166: 111-117
23. Schille NB: Two-dimensional echocardiographic determination of left ventricular volume, systolic function and mass. Summary and discussion of the 1989 recommendations of the American Society of Echocardiography. *Circulation* 1991; 83(3 Suppl): 1280-1287
24. Schiller NB: Pulmonary artery pressure estimation by Doppler and two-dimensional echocardiography. *Cardiol Clin* 1990; 8: 277-287

25. Louie EK, Lin SS, Reynertson SI, Brundage BH, Levitsky S, Rich S: Pressure and volume loading of the right ventricle have opposite effects on left ventricular ejection fraction. *Circulation* 1995; 92: 819-824
26. Morris-Thurgood J, Frenneaux M: Diastolic ventricular interaction and ventricular diastolic filling. *Heart Fail Rev* 2000; 5: 307-323
27. Lazar JM, Flores AR, Grandis DJ, Orie JE, Schulman DS: Effects of chronic right ventricular pressure overload on left ventricular diastolic function. *Am J Cardiol* 1993; 72: 1179-1182
28. Lamberts RR, Vaessen RJ, Westerhof N, Stienen GJM: Right ventricular hypertrophy causes impairment of left ventricular diastolic function in the rat. *Basic Res Cardiol* 2007; 102: 19-27
29. Brunner F: Cardiac endothelin in right-heart hypertrophy due to monocrotaline-induced pulmonary hypertension in rat. *Cardiovasc Res* 1999; 44: 197-206
30. Sutherland GR, Di Salvo G, Claus P, D'hooge J, Bijnens B: Strain and strain rate imaging: a new clinical approach to quantifying regional myocardial function. *J Am Soc Echocardiogr* 2004; 17: 788-802

Table 1. Characteristics of the study population.

	IPF patients (n=22)	Controls (n=22)
Male gender, n (%)	15 (68.2)	13 (59.1)
Age, y	65 ± 9	66± 6
BMI	27 ± 3	28 ± 4
Ex-smokers, %	23	32
Nonsmokers, %	77	50
Heart Rate, bpm	77 ± 8	70 ± 4
Systolic BP, mmHg	129 ± 7	131 ± 8
Diastolic BP, mmHg	82 ± 4	84 ± 5
Lung Function Parameters		
TLC, % predicted	55 ± 15	NA
FVC, % predicted	61 ± 15	NA
FEV_1, % predicted	69 ± 14	NA
RV, % predicted	52 ± 16	NA
DLco, % predicted	49 ± 22	NA
Resting gas exchange		
PaO_2, mmHg	62 ± 6	NA
$PaCO_2$, mmHg	38 ± 3	NA
6-min walk test		
Distance, m	450 ± 147	NA
O_2 desaturation, %	6.7 ± 2.6	NA

Values are given as the mean ± SD unless otherwise indicated.

BMI= Body Mass Index, TLC= total lung capacity, FVC= forced vital capacity, FEV_1= forced expiratory volume in 1 s, RV= residual volume, DLco= diffusing

capacity for carbon monoxide, PaO_2= arterial O_2 tension, $PaCO_2$= arterial CO_2 tension, NA= Non Applicable

Table 2. Right ventricular echocardiographic parameters in patients with IPF and normal controls

Echocardiographic parameters	**Controls (n=22)**	**IPF patients (n=22)**	**p value**
RV area change, %	57 ± 6	42 ± 5	<0.001
RVWT, cm	0.38 ± 0.15	0.56 ± 0.12	0.001
RVEDD, cm	2.3 ± 0.1	2.7 ± 0.3	<0.001
PASP, mmHg	24 ± 2	47 ± 12	<0.001
RV E/A	1.4 ± 0.1	0.7 ± 0.07	<0.001
RV DT, ms	216± 26	248± 42	0.004
IVRT, ms	49 ± 9	59 ± 15	<0.001
RV Sm, cm/s	10.4 ± 1	15 ± 3	<0.001
RV Em, cm/s	11 ± 2	9.6 ± 3	0.08
RV Am, cm/s	7.1 ± 1.9	17.6 ± 4.3	<0.001
RV Em/Am	1.5 ± 0.4	0.54 ± 0.1	<0.001

RV= Right Ventricular; RVWT= RV wall thickness; RVEDD= RV end diastolic diameter; PASP= peak pulmonary artery systolic pressure; E/A= transtricuspid E to A wave ratio; DT=deceleration time

Table 3. Left ventricular echocardiographic parameters in patients with IPF and normal controls

Echocardiographic parameter	**Controls (n=22)**	**IPF patients (n=22)**	**p value**
IVSD, cm	1.1 ± 0.2	1.0 ± 0.1	NS
LVEDD, cm	4.7 ± 0.5	4.8 ± 0.7	NS
EF, %	70 ± 6	70 ± 5	NS
E, m/s	0.8 ± 0.1	0.6 ± 0.1	<0.001
A, m/s	0.5 ± 0.1	0.8 ± 0.1	<0.001
E/A	1.5 ± 0.1	0.7 ± 0.2	<0.001
DT, ms	169 ± 15	217 ± 16	<0.001
Type of diastolic dysfunction,			
Normal, n(%)	22 (100)	-	
Impaired relaxation, n(%)	-	20 (91%)	
Pseudonormal, n(%)	-	2 (9%)	
Restrictive, n(%)	-	-	
Vp, cm/s	83 ± 21	46 ± 13	<0.001
Sm, cm/s	9.2 ± 1	8.7 ± 3	NS
Em, cm/s	10.3± 1.6	5.7± 1.1	<0.001
Am, cm/s	5.5 ± 0.8	8.9± 1.3	<0.001
Em/Am	1.9 ± 0.5	0.6 ± 0.1	<0.001
E/Em	6 ± 0.6	10.8 ± 3	<0.001

IVSD= interventricular septum thickness; LVEDD= LV end-diastolic diameter; EF= LV ejection fraction; LA= left atrial end-systolic diameter; E/A= transmitral E to A wave ratio; DT= E wave deceleration time; Vp= LV propagation velocity

LV=mitral annulus; Sm= peak systolic velocity; Em= peak early diastolic velocity; Em/Am= Peak early to peak late diastolic velocity ratio; E/Em= E wave to peak early diastolic velocity

Table 4: Bivariate correlations between left ventricular echocardiographic parameters and pulmonary artery systolic pressures

Echocardiographic parameter	**r**	**p**
E	-0.55	<0.001
A	0.5	0.001
E/A	-0.61	<0.001
DT	0.56	<0.001
Vp	-0.6	<0.001
Sm	0.26	0.08
Em	-0.55	<0.001
Am	0.59	<0.001
Em/Am	-0.64	<0.001
E/Em	0.04	0.04

FIGURE LEGEND

Figure 1. Scatterplots showing the correlation between pulmonary artery systolic pressure (PASP) and A) E/A ratio, B) Em/Am ratio and C) propagation velocity (Vp).