Journal of Advances in Medical and Pharmaceutical Sciences
2(3): 107-116, 2015, Article no.JAMPS.2015.014

SCIENCEDOMAIN *international*
www.sciencedomain.org

SCIENCEDOMAIN

Evaluation of Right Ventricular Diastolic Function in Patients with Chronic Obstructive Pulmonary Disease Using Pulsed Doppler Tissue Imaging

Aylin Ozsancak Ugurlu[1*], Asli I Atar[2], Ilyas Atar[3], Oyku Gulmez[4], Serife Savas Bozbas[5], Haldun Muderrisoglu[3] and Fusun Oner Eyuboglu[5]

[1]Pulmonary Medicine Department, Baskent University Hospital, Istanbul, Turkey.
[2]Cardiology Department, Turgut Ozal University Hospital, Ankara, Turkey.
[3]Cardiology Department, Baskent University Hospital, Ankara, Turkey.
[4]Cardiology Department, Baskent University Hospital, Istanbul, Turkey.
[5]Pulmonary Medicine Department, Baskent University Hospital, Ankara, Turkey.

Authors' contributions

This work was carried out in collaboration among all authors. Authors AOU, AIA and IA designed the study and wrote the protocol. Authors AOU, AIA, IA, OG and SSB collected all data. Author IA performed the statistical analysis. Author AOU wrote the first draft of the manuscript. Authors AIA, IA and OG did the literature search, wrote the later drafts. Authors HM and FOU edited parts of the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMPS/2015/14459
Editor(s):
(1) Esam Z. Dajani, Loyola University Chicago, USA.
Reviewers:
(1) Anonymous, Italy.
(2) Anonymous, France.
(3) Miguel Souto, Department of Radiology, University Hospital Complex of Santiago (CHUS), Santiago de Compostela, Spain.
(4) Salah A. M. Said, Department of Cardiology, Hospital Group Twente, Netherlands.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=887&id=36&aid=7561

Original Research Article

Received 30th September 2014
Accepted 6th December 2014
Published 31st December 2014

ABSTRACT

Objective: To evaluate the global and segmental diastolic function of the right ventricle using pulsed tissue Doppler imaging (TDI) in patients with clinically stable chronic obstructive pulmonary disease (COPD) without pulmonary hypertension (PHT).
Methods: Twenty stable patients with COPD (mean age 61.4±8.6, 16 males) with normal pulmonary artery pressure (PAP) (Group I) and 20 age-matched normal subjects (mean age

**Corresponding author: E-mail: aozsancak@hotmail.com;*

57.8±4.0, 11 males, Group II) were enrolled. All the participants underwent conventional echocardiography and TDI. TDI of the right ventricle was performed from four different segments. The early myocardial diastolic peak velocity (Em), late myocardial diastolic peak velocity (Am), systolic peak velocity (Sm), early diastolic velocity deceleration time (eDTm), duration of the S wave, isovolumetric relaxation time (IVRTm), and isovolumetric contraction time (IVCTm) were measured.

Results: The conventional echocardiographic measurements of the two groups were similar, but specific TDI parameters differed between the groups. The Em of the anterior wall was lower, and the duration of the anterior S wave and IVRTm in the apical 4-chamber (A4C) view for all the right ventricular (RV) segments were longer. The eDTm measured from the apex was shorter in the COPD patients (parasternal Em, *p*=0.003; duration of anterior wall S wave, *p*=0.02; A4C apical IVRTm, *p*=0.02; A4C middle IVRTm, p=0.001; A4C basal IVRTm, *p*=0.01; A4C apical eDTm, *p*=0.05).

Conclusion: TDI was more sensitive than conventional echocardiography in the evaluation of diastolic function in the patients with COPD. In COPD patients with an unlikely diagnosis of PHT, the diastolic functions of the right ventricle seemed to show some deterioration, but this difference failed to reach a significant level. Measurements of the basal segment of the RV free wall can be used to determine global RV diastolic function.

Keywords: Chronic obstructive pulmonary disease; diastole; echocardiography; pulmonary heart disease; ventricular dysfunction; right ventricle.

ABBREVIATIONS

A: Late diastolic peak velocity; A4C: Apical 4-chamber; Am: Myocardial late diastolic peak velocity; COPD: Chronic obstructive pulmonary disease; DT: Early diastolic wave deceleration time; eDTm: Myocardial early diastolic velocity deceleration time; E: Early diastolic peak velocity; Em: Myocardial early diastolic peak velocity; FEV_1: Forced expiratory volume in first second; FVC: Forced vital capacity; IVRT: Isovolumetric relaxation time; IVRTm: Myocardial isovolumetric relaxation time; IVCT: Isovolumetric contraction time; IVCTm: Myocardial isovolumetric contraction time; NS: Not significant; PAP: Pulmonary artery pressure; pO_2: Partial arterial oxygen pressure; pCO_2: Partial carbondioxide pressure; PHT: Pulmonary hypertension; RV: Right ventricular; Sm: Myocardial systolic peak velocity; TDI: Tissue Doppler imaging.

1. INTRODUCTION

Right ventricular (RV) function can be altered in several diseases involving the lungs and heart. In patients with chronic obstructive pulmonary disease (COPD), alveolar hypoxia may lead to a rise in pulmonary artery pressure (PAP), subsequently resulting in the development of right ventricular hypertrophy, dilatation, dysfunction, and finally failure [1-3]. Diastolic abnormalities are one of the earliest manifestations of cardiac dysfunction in patients with COPD and can be a result of impaired myocardial relaxation.

Transthoracic echocardiography has become the primary tool in the assessment of RV function because right heart catheterization, magnetic resonance imaging, and radionuclide ventriculography are not feasible for daily practice and are not acceptable for screening RV functions mainly due to higher costs and difficult accessibility. Conventional Doppler has been used to estimate PAP [4,5]. Doppler echocardiography allows PAP to be estimated by measuring the tricuspid regurgitation velocity, pulmonary regurgitation velocity, and RV outflow tract flow acceleration time. In clinical practice, the most common way of estimating the systolic PAP (sPAP) is to incorporate the peak tricuspid regurgitation (TR) velocity into a modified Bernoulli equation to derive the transtricuspid gradient and then add the mean right atrial pressure [4,5]. However, this measurement depends on a good tricuspid regurgitation signal, which is not present in all patients.

Evaluation of RV function with echocardiography has limitations due to the complex geometry of the right ventricle [6,7]. Pulsed tissue Doppler imaging (TDI) is a rapid and noninvasive method for the evaluation of myocardial functions that measures regional velocities and time intervals [8]. Several studies have investigated the use of TDI to assess RV function in various diseases

involving the lungs [9-22]. However, few studies have employed TDI to evaluate RV segmental diastolic function in COPD patients without pulmonary hypertension (PHT) [10,13,16, 20,21,22].

The aim of our study was to compare global and segmental RV diastolic function using pulsed TDI in patients with stable COPD without PHT based on echocardiography findings with those of healthy control subjects. We also aimed to detect differences in the TDI measurements of different segments of the RV wall to determine the most affected part of the right ventricle in patients with COPD.

2. MATERIALS AND METHODS

We enrolled 20 patients with stable COPD, as defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Consensus Report (mean age 61.4±8.6, 16 males), with normal PAP (Group I) [23]. The control group (Group II) consisted of 20 consecutive age-matched healthy subjects (mean age 57.8±4.0, 11 males) with no pulmonary disease according to pulmonary function tests and saturation measurements. The study protocol was approved by the local ethics committee. All the patients provided written informed consent prior to participation in the study.

Patients with an acute COPD attack, systemic arterial hypertension, atrial fibrillation, significant valvular disease, coronary artery disease, left ventricular heart failure, and poor echocardiographic image quality were excluded. Additionally, patients were excluded if they had PHT according to echocardiographic parameters, such as the pulmonary artery ejection flow analysis (acceleration time and RV ejection time); pulmonary regurgitant flow-derived parameters (mean PAP and diastolic PAP), and indirect two-dimensional (2D) and M mode signs of PHT.

The COPD classification was based on the patient's history, a physical examination, and pulmonary function testing. Medications, such as inhaled β_2 agonists, anticholinergics, steroids, theophylline, and oxygen, were continued. The control subjects were normal volunteers with no systemic diseases who were not taking any medications.

Spirometric measurements of all patients were done (Sensor Medics V-max 229 Spectra, Bilthoven, The Netherlands) according to the standards of the American Thoracic Society [24]. The forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC), and FEV_1/FVC values were recorded. Saturation values were recorded for all the patients. Arterial blood was taken for measurements of pH, partial arterial oxygen pressure (pO2), and partial carbon dioxide pressure (pCO2) from patients whose oxygen saturation was <92%.

Echocardiographic examinations were performed using a commercially available ultrasound machine (Acuson Sequoia C 256, Acuson Siemens, Mountain View, CA, USA) equipped with a 3.5 MHz transducer. Parasternal and apical views were obtained according to the recommendations of the American Society of Echocardiography [4,5]. Recordings were made with a simultaneous superimposed ECG. Separate measurements were obtained for each subject with 2D and TDI. The left ventricular ejection fraction was derived from Simpson's modified single plane method using the apical 4-chamber (A4C) view.

The sPAP was assessed by measuring the gradient between the right ventricle and the right atrium by incorporating the peak velocity (V_{max}) of the TR by using a modified Bernoulli equation and then adding the mean right atrial pressure ($Spap=4V_{TR}^2$+right atrial max pressure). The right atrial pressure was estimated according to the respiratory variation in the inferior vena cava diameter at its entrance into the right atrium. The size of the inferior vena cava (IVC) was measured during quiet respiration and forced inspiration in the subcostal view. The right atrial pressure was estimated as follows: 5 mmHg if the IVC size was <1.5 cm and collapsed with inspiration, 10 mmHg if the IVC size was 1.5–2.5 cm and the diameter decreased by >50% with inspiration, 15 mmHg if the IVC size was over 2.5 cm and the diameter decreased by 50% with inspiration, and 20 mmHg if the IVC was dilated and the diameter did not change with inspiration [25]. Recent guideline by American College of Cardiology recommends use of mean PAP of ≥25 mmHg as a cut-off value for PHT in patients with chronic lung diseases [26]; however Turkish cardiologists generally follow European guidelines. Therefore European Society of Cardiology (ESC) criteria for detecting the presence of PHT, based on the TR peak velocity and Doppler-calculated sPAP at rest (assuming a normal right atrial pressure of 5 mmHg), and additional echocardiographic variables

suggestive of PHT were used to determine the Spap [27,28]. In summary, PHT was unlikely if the sPAP was ≤36 mmHg, with no additional echocardiographic variables suggestive of PHT. A diagnosis of PHT was possible if the sPAP was 37–50 mmHg or if the sPAP was ≤36 mmHg, with additional echocardiographic variables suggestive of PHT. A diagnosis of PHT was likely if the sPAP was >50 mmHg.

For the TDI recordings, a 5-mm sample volume was placed at four different segments; including the basal, mid, and apical segments of the RV free wall from the A4C view and basal anterior wall from the parasternal long axis view. The early myocardial diastolic peak velocity (Em), late myocardial diastolic peak velocity (Am), systolic peak velocity (Sm), early diastolic velocity deceleration time (eDTm), duration of the S wave, isovolumetric relaxation time (IVRTm), and isovolumetric contraction time (IVCTm) were measured. IVRTm was measured from the end of Sm to the onset of Em. The IVCTm was measured from the end of Am to the onset of Sm (Fig. 1). The RV myocardial performance index (MPI) and E/Em ratio were also calculated. The MPI index was calculated as the sum of the IVRTm and IVCTm divided by the duration of Sm. Tissue Doppler images were recorded at a sweep speed of 100 m/sn, and all the measurements were calculated as the mean of three consecutive cardiac cycles. The results of the Doppler and 2D echocardiography and TDI were recorded on VHS videotape. All the echocardiographic examinations were performed and analyzed by the same investigator who was unaware of the subjects' clinical status.

3. STATISTICAL ANALYSIS

SPSS v.9.0 software (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL, USA) was used for statistical analyses. Continuous variables are expressed as the means ± standard deviation. The distribution of the continuous variables was checked with the Kolmogorov–Smirnov normality test. Continuous variables with normal distributions were compared using the unpaired Student's *t* test. Continuous variables with abnormal distributions were compared using the Mann–Whitney *U* test. For categorical variables, the chi-square test was used. A *p* value of less than 0.05 was considered statistically significant.

4. RESULTS

Forty subjects, 27 men, with a mean age of 59.6±13.3 years were included in the study. The demographic characteristics of the patients are shown in Table 1. The rates of smoking were similar in both groups. In the COPD patients, cough (75%), sputum (70%), and shortness of breath (55%) were the most frequent symptoms. Less frequent symptoms in this group of patients were wheezing (20%), chest tightness (25%), and edema (20%). All the patients were in sinus rhythm. The mean heart rate was 82.2±15.2 bpm in Group I and 79.8±13.6 bpm in Group II (p>0.05).

Table 1. Demographic and pulmonary function test findings of study population

	Group I	Group II
Age, year	61.4±8.6	57.8±4.0
Gender (n)	16 M, 4 F	11 M, 9 F
Weight (kg)	73.95±12.1	72.1±8.2
Height (cm)	169.0±10.3	163.2±8.4
Smoking, n (%)	17 (85.0)	16 (80.0)
Systolic blood pressure, mmHg	122±10	120±13
Diastolic blood pressure, mmHg	77±8	77±9
FEV_1 (% of predicted value)[1]	56.4±21.6	91.7±12.8
FVC (% of predicted value)[2]	67.1±20.3	88.3±8.4
FEV_1/FVC (%)[1]	57.9±10.0	76.1±5.3
Oxygen Saturation (%)[2]	91.7±2.2	94.36±2.1

F: Female, FEV_1: Forced expiratory volume in first second, FVC: Forced vital capacity, M: Male.

[1]p<0.001, [2]p<0.0005; for the rest of the variables the p value was non-significant

The mean FEV_1, mean FVC, and FEV_1/ FVC values were significantly lower in Group I than in Group II (Table 1). When classified according to the criteria of the GOLD Consensus Report, 4 (20%) patients had mild, 8 (40%) had moderate, 5 (25%) had severe, and 3 (15%) had very severe COPD. The saturation values were also significantly lower in the COPD group. Arterial blood gas was analyzed for 15 patients in Group I whose oxygen saturation was less than 92%. Their mean pO_2 was 62.6±9.5 mmHg, and their pCO_2 was 43.2±6.9 mmHg. The oxygen saturation of all the other patients was higher than 92%.

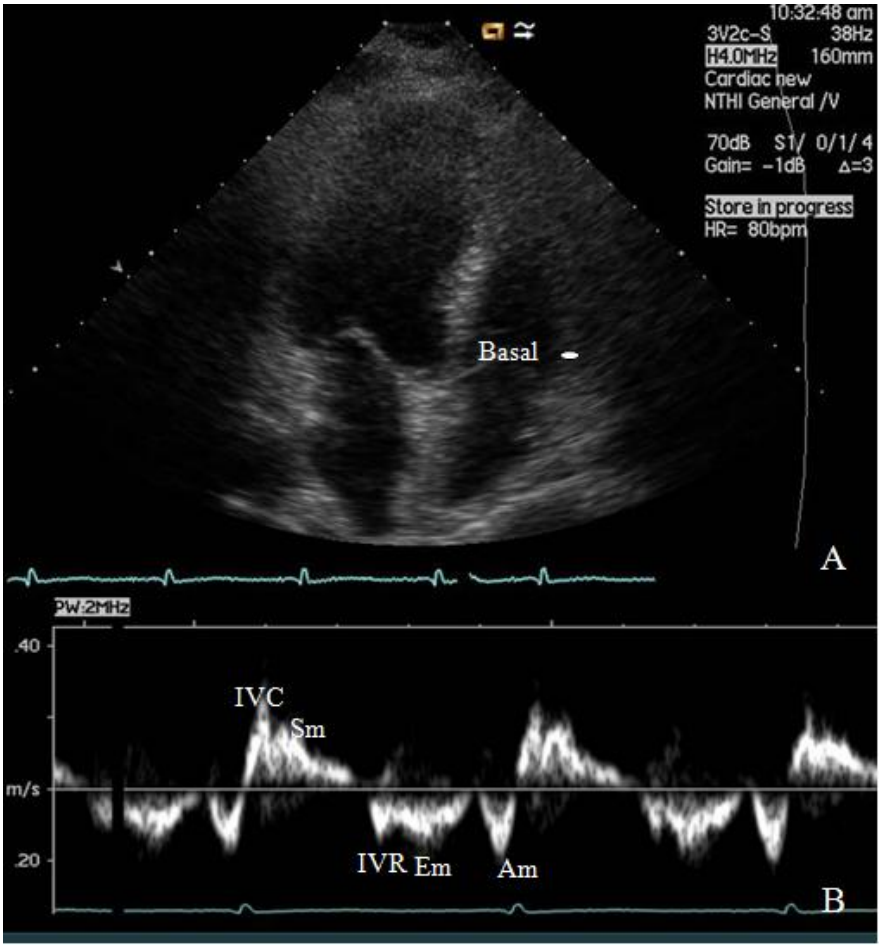

Fig. 1. A- Apical 4-chamber view, B- Tissue Doppler of basal right ventricle

Am: Myocardial late diastolic peak velocity, Em: Myocardial early diastolic peak velocity, IVC: Myocardial isovolumetric contraction, IVR: Myocardial isovolumetric relaxation, Sm: Myocardial systolic peak velocity

The segmental and global systolic function of the left ventricle was normal in both groups. There was no significant between-group difference in the results of the 2D and Doppler echocardiographic examination (p>0.05) (Tables 2,3). As all the inferior vena cava diameters were <1.5 cm in both groups, the right atrial pressure was accepted as 5 mmHg. Tricuspid regurgitation was detected in 14 of the patients with COPD and none of the patients in Group II had more than mild TR. The mean sPAP was 29.0±5.3 mmHg (Table 3).

The 2D Doppler measurements of the tricuspid valve revealed a similar E/A ratio in both groups (p=0.293). The TDI parameters obtained from the anterior wall of the right ventricle in the parasternal long axis view and from the tricuspid basal, mid, and apical segments of the RV free wall in the A4C view are presented in Table 4–7.

The IVRTm was longer in all the segments of the A4C view in Group I than in Group II. In addition, the eDTm was shorter in Group I at the A4C apical level. There was no significant difference in the other parameters from the A4C view. In the RV parasternal long axis view, the patients in Group I had lower tricuspid Em (13.8±4.6 cm/sec; p=0.003) and a shorter S wave duration (215.1±57.3 msec; p=0.02) than those in Group II. All other parameters were similar between the two groups. No differences were detected when the TDI Sm values of all the segments were compared. Comparison of the E/Em ratios of the two groups revealed that the E/Em ratio of the anterior RV wall was significantly higher in the COPD group, whereas there were no differences in any of the other segments (Table 8). There were also no differences in the global function of the right ventricle according to the MPI (Table 8).

Table 2. Left ventricular echocardiographic parameters of COPD patients and control group[1]

	Group I	Group II
Left atrium diameters, (cm)	3.2±0.3	3.3±0.4
Left ventricle diameters, end systole (cm)	2.6±0.6	2.7±0.4
Left ventricle diameters, end diastole (cm)	4.2±0.6	4.3±0.5
Posterior wall thickness (cm), end diastole	1.2±0.2	1.2±0.2
Interventricular septum thickness (cm), end diastole	1.2±0.2	1.2±0.2
Fractional shortening (%)	37.7±5.7	37.3±5.9
Ejection fraction (%)	55.6±5.5	57.3±3.3
Mitral E wave velocity (cm/sec)	61.8±12.1	64.9±10.2
Mitral A wave velocity (cm/sec)	78.6±18.2	77.8±16.0

A: Late diastolic peak velocity, DT: Early diastolic wave deceleration time, E: Early diastolic peak velocity, IVRT: Isovolumetric relaxation time, NS: Not significant, [1]p value was non-significant for all of the variables

Table 3. Right ventricular echocardiographic parameters of COPD patients and control group[1]

	Group I	Group II
Right ventricle diameters(cm)	3.2±0.6	3.0±0.4
Right atrium diameters(cm)	3.4±0.5	3.3±0.3
Pulmonary flow velocity (cm/sec)	90.2±24.5	90.3±20.5
Tricuspid E wave velocity (cm/sec)	57.5±13.8	55.8±5.0
Tricuspid A wave velocity (cm/sec)	57.5±15.5	51.1±8.1
Tricuspid DT (msec)	236.9±51.8	219.2±44.8
IVRT (msec)	103.0±20.0	103.0±12.5

A: Late diastolic peak velocity, DT: Early diastolic wave deceleration time, E: Early diastolic peak velocity, NS: Not significant, [1]p value was non-significant for all of the variables

5. DISCUSSION

The evaluation of RV function is clinically useful in patients with COPD because the presence of RV failure has prognostic implications [29]. However, very few studies in the literature have evaluated segmental diastolic functions of the right ventricle, and none of these studies have been conducted in patients with COPD [30,31]. In this first study on segmental diastolic functions of the right ventricle in COPD patients, we found that although Doppler echocardiographic measurements were normal, TDI parameters, especially IVRTm, may be a new useful tool to detect RV diastolic dysfunction in clinically stable COPD patients without PHT. Segmental analysis of the right ventricle with TDI did not seem to provide any additional information on diastolic functions, and the measurements of the lateral basal segment were representative of the whole ventricle.

Table 4. Apical 4-chamber basal segment TDI findings

	Group I	Group II
Sm (cm/sec)	23.6 ± 9.2	22.3 ±4.9
Em (cm/sec)	19.4 ± 6.9	20.4±3.5
Am (cm/sec)	26.5 ± 6.9	28.1±8.4
Duration of S wave (msec)	229.9±41.1	239.8±46.0
IVRTm (msec)[1]	131.1±31.9	104.5±22.9
IVCTm (msec)	79.3 ±26.7	70.6 ±16.6
eDTm (msec)	130.3±39.6	149.0±37.7

Am: Myocardial late diastolic peak velocity, eDTm: Myocardial early diastolic velocity deceleration time, Em: Myocardial early diastolic peak velocity, IVCTm: Myocardial isovolumetric contraction time, IVRTm: Myocardial isovolumetric relaxation time, NS: Not significant, Sm: Myocardial systolic peak velocity, [1]p<0.01; for the rest of the variables the p value was non-significant

Table 5. Apical 4-chamber mid-segment TDI findings

	Group I	Group II
Sm (cm/sec)	20.4 ± 5.8	18.3 ± 4.2
Em (cm/sec)	17.0 ± 5.6	17.9 ± 5.2
Am (cm/sec)	24.6 ± 7.7	23.2 ± 7.7
Duration of S wave (msec)	206.1±43.8	315.7 ± 30.8
IVRTm (msec)[1]	148.9±52.4	97.8 ± 15.8
IVCTm (msec)	79.8 ±35.4	67.8 ± 13.0
eDTm (msec)	110.9±34.2	139.9 ± 49.6

Abbreviations as in Table 4, [1]p=0.001; for the rest of the variables the p value was non-significant

Table 6. Apical 4-chamber apical segment TDI findings

	Group I	Group II
Sm (cm/sec)	15.8±5.3	14.9±4.9
Em (cm/sec)	13.6±5.7	11.8±3.8
Am (cm/sec)	17.9±7.8	16.1±6.0
Duration of S wave (msec)	173.8±83.6	211.2±51.6
IVRTm (msec)[1]	172.1±60.5	132.8±26.2
IVCTm (msec)	85.6±59.0	73.3±8.1
eDTm (msec)[2]	86.0±24.8	106.6±28.0

Abbreviations as in Table 4, [1]p=0.02, [2]p=0.05; for the rest of the variables the p value was non-significant

Table 7. Parasternal long axis right ventricle anterior wall TDI findings

	Group I	Group II
Sm (cm/sn)	15.9±3.1	15.0±3.5
Em (cm/sn)[1]	13.8 ±4.6	18.7±3.4
Am (cm/sn)	17.1±5.6	22.1±14.1
Duration of S wave (msn)[2]	215.1±57.3	259.4±34.5
IVRTm (msn)	137.1±58.2	110.1±30.5
IVCTm (msn)	86.3±33.9	70.6±18.3
eDTm (msn)	101.0±37.5	100.8±21.2

Abbreviations as in Table 4, [1]p=0.003, [2]p=0.02; for the rest of the variables the p value was non-significant

The gold standard for a diagnosis of PHT is right heart catheterization. However, this procedure is expensive and potentially risky. Transthoracic echocardiography is the most commonly used diagnostic tool for estimation of PAP because it is an inexpensive, easy, reliable, and reproducible technique. For the last two decades, the most common way of estimating the sPAP has been to incorporate the TR velocity into a modified Bernoulli equation. However, sPAP can be determined by echocardiography in less than one-half of patients with COPD. The limitations are the absence of adequate TR velocity, suboptimal echocardiographic images because of hyperinflation of the lungs, and expansion of the thoracic cage [32]. Moreover, right heart catheterization, magnetic resonance imaging, and radionuclide ventriculography are not acceptable for screening RV function in daily practice. Instead, transthoracic echocardiography and TDI are used to evaluate RV function. TDI has been used to assess RV systolic and diastolic functions and LV function, and some studies have suggested that TDI might be more sensitive than standard echocardiography [18,33-36]. The advantage of using TDI to assess RV function is that the measurement is independent of geometric assumptions and endocardial border tracing. There are few studies with contradictory results in the literature assessing RV diastolic function with conventional Doppler in patients with COPD without PHT [16,20,37,38]. The present study revealed no significant difference in RV diastolic function with conventional echocardiography in patients with COPD without PHT compared to healthy controls. In the evaluation of diastolic function, a sample volume was placed only at the tricuspid annular level in earlier studies. We evaluated RV functions with TDI at four different segments and detected no difference in the segmental measurements compared to the measurement at only the tricuspid annular level. Thus, the measurements of the basal segment might be sufficient to evaluate RV diastolic function.

Table 8. E/Em ratios from different segments of right ventricle and myocardial performance index calculated from the basal lateral tricuspid wall TDI measurements

	Group I	Group II
Tricuspid E/paras Em[1]	4.6±1.9	3.2±0.8
Tricuspid E/apex Em	5.0±2.5	5.0±1.3
Tricuspid E/basal Em	3.6±2.0	2.7±0.5
Tricuspid E/mid Em	3.7±1.6	3.4±0.9
MPI bazal	0.47±0.15	0.54±0.15

E: Early diastolic peak velocity, Em: Myocardial early diastolic peak velocity, MPI: myocardial performance index, paras: parasternal, [1]p=0.02; for the rest of the variables the p value was non-significant

In the current study, a statistically significant difference was observed in all segmental IVRTm measurements in the A4C in the COPD patients compared to the controls. Although this parameter was longer in the COPD group than the controls in the parasternal long axis view, the difference was not statistically significant. Caso et al. [16] reported a significant positive correlation between the tricuspid annulus IVRTm and sPAP (r=0.76). They also reported that the IVRTm derived by TDI was the only parameter that distinguished patients with COPD with and without PHT and control group [16]. Moreover, other studies showed that, after excluding patients with elevated mean right atrial pressure (RAP), the correlation between IVRT and sPAP was improved [39,40]. In our study, the IVRTm was longer in the COPD patients without PHT compared to that of the controls. Given that the pulsed Doppler measurements in our study did not demonstrate any difference between the groups, the difference in the IVRTm, which is indicative of diastolic dysfunction, may be considered an early subclinical manifestation of myocardial diastolic derangement.

Melek et al reported lower Sm, Em, Em/Am and higher IVRTm values in COPD patients with PHT compared to patients without PHT [32]. There was a significant negative correlation between sPAP and Sm. We also observed that the RV Sm decreased from the tricuspid annulus toward the apex, whereas the IVRTm increased. This may be due to the geometry of the RV myocardium and is consistent with the literature [10,40]. The decrease in Em and the shortening of the duration of Sm detected in our study by TDI in the parasternal long axis view were likely

secondary to myocardial relaxation defects due to the COPD.

RV myocardial performance index (MPI) is a global functional value reflecting both systolic and diastolic functions. The RV MPI might be expected to be lower in COPD patients as the IVRTm decreases. The lack of difference between the RV MPI of the two groups might be explained by the small sample size.

There are potential limitations in this study. An invasive PAP measurement was not performed. Right heart catheterization might be able to clarify the relation between the IVRTm and sPAP. The incidence of TR in the patients with COPD is between 24 and 66%, which might limit estimations of PHT with Doppler echocardiography [41,42]. Despite technical difficulties, Doppler-measured TR is widely used in clinical settings for estimating PHT. The present study did not measure the pulmonary acceleration time, which shows a better correlation with the mean PAP in cardiac catheterization. The effect of loading conditions on TDI variables is already recognized as an inherent limitation of TDI and not particular to this study. TDI is preload dependent in cases of normal diastolic function [43]. Another important limitation is the small sample size and the lack of comparison of the data with gold standards, such as magnetic resonance imaging.

6. CONCLUSION

RV diastolic dysfunction, which cannot be detected by conventional echocardiography techniques, including M mode, 2D, and spectral Doppler, can be determined with TDI from different segmental levels in patients with COPD, even in the absence of PHT. TDI-derived indexes of RV diastolic function obtained from different segmental levels of the RV free wall are usually easily measurable and can reflect global RV function. In the present study, the measurements of basal RV free wall adequately reflected those of the other segments. The IVRTm may be an early indicator of RV diastolic dysfunction in this group of patients. The findings of the present study suggest that TDI-derived IVRTm can be used as a follow-up diagnostic tool in COPD patients for the early diagnosis of RV diastolic dysfunction, even before the development of PHT. Therefore, with prompt treatment, right heart failure might be prevented. Further longitudinal studies evaluating RV diastolic function in patients with COPD are needed of to investigate whether RV diastolic dysfunction in stable COPD patients represents an early stage in the disease before the development of PHT or whether it is a consequence of modified loading conditions, as well as its relation to bronchodilator, long-term oxygen, or vasodilator treatment. Finally, we believe that this study should be repeated with a larger sample size to reach a definitive conclusion.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Hida W, Tun Y, Kikuchi Y, Okabe S, Shirato K. Pulmonary hypertension in patients with chronic obstructive pulmonary disease: Recent advances in pathophysiology and management. Respirology. 2002;7(1):3-13.
2. Weitzenblum E. Chronic cor pulmonale. Heart. 2003;89(2):225-30.
3. Naeije R, MacNee W. Pulmonary circulation. In: Calverley P, MacNee W, Pride P, Rennard S, eds. Chronic Obstructive Pulmonary Disease. London: Arnold Health Sciences. 2003;228-242.
4. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification: A report from the American Society of Echocardiography's Guidelines and Standards Committee and the chamber quantification writing group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005;18(12):1440–1463.
5. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekeran K, et al. Guidelines for echocardiographic assessment of the right heart in adults: A report from the American Society of Echocardiography. Endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr. 2010;23:685-713.
6. Nishimura E, Ikeda S, Naito T, Yamaguchi K, Yakabe K, Iwasaki T, et al. Evaluation of right-ventricular function by Doppler echocardiography in patients with chronic

respiratory failure. J Int Med Res. 1999;27(2):65-73.
7. Burgess MI, Bright-Thomas RJ, Ray SG. Echocardiographic evaluation of right ventricular function. Eur J Echocardiogr. 2002;3(4):252-62.
8. Lindqvist P, Calcutteea A, Henein M. Echocardiography in the assessment of right heart function. Eur J Echocardiogr. 2008;9(2):225-34.
9. Turhan S, Dincer I, Ozdol C, Rahimov U, Kilickap M, Altin T, et al. Value of tissue Doppler myocardial velocities of tricuspid lateral annulus for the diagnosis of right heart failure in patients with COPD. Echocardiography. 2007;24(2):126-33.
10. Vitarelli A, Conde Y, Cimino E, Stellato S, D'Orazio S, D'Angeli I, et al. Assessment of right ventricular function by strain rate imaging in chronic obstructive pulmonary disease. Eur Respir J. 2006;27(2):268-75.
11. Tavil Y, Kanbay A, Sen N, Ciftci TU, Abaci A, Yalcin MR, et al. Comparison of right ventricular functions by tissue Doppler imaging in patients with obstructive sleep apnea syndrome with or without hypertension. Int J Cardiovasc Imaging. 2007;23(4):469-77.
12. Gencer M, Ceylan E, Yilmaz R, Gur M. Impact of bronchiectasis on right and left ventricular functions. Respir Med. 2006;100(11):1933-43.
13. Melek M, Esen O, Esen AM, Barutcu I, Fidan F, Onrat E, Kaya D. Tissue Doppler evaluation of tricuspid annulus for estimation of pulmonary artery pressure in patients with COPD. Lung. 2006; 184(3):121-31.
14. Kjaergaard J, Schaadt BK, Lund JO, Hassager C. Quantitative measures of right ventricular dysfunction by echocardiography in the diagnosis of acute nonmassive pulmonary embolism. J Am Soc Echocardiogr. 2006;19(10):1264-71.
15. Akao M, Katsube Y, Kamisago M, Watanabe M, Abe M, Fukazawa R, Ogawa S, Itoh Y. Developmental changes in left and right ventricular function evaluated with color tissue Doppler imaging and strain echocardiography. J Nippon Med Sch. 2013;80(4):260-7.
16. Caso P, Galderisi M, Cicala S, Cioppa C, D'Andrea A, Lagioia G, et al. Association between myocardial right ventricular relaxation time and pulmonary arterial pressure in chronic obstructive lung disease: Analysis by pulsed Doppler tissue imaging. J Am Soc Echocardiogr. 2001;14(10):970-7.
17. Gromadziński L, Targoński R, Pruszczyk P. Assessment of right and left ventricular diastolic functions with tissue Doppler echocardiography in congestive heart failure patients with coexisting acute pulmonary embolism. Adv Clin Exp Med. 2014;23(3):371-6.
18. Kaushik V, Kang SH, Barasch E. Interrogation of the tricuspid annulus by Doppler tissue imaging in patients with chronic pulmonary hypertension: Implications for the assessment of right-ventricular systolic and diastolic function. Cardiology. 2001;95(2):101-4.
19. Elnoamany MF, Dawood AA. Right ventricular myocardial isovolumetric relaxation time as novel method for evaluation of pulmonary hypertension: Correlation with Endothelin-1 levels. J Am Soc Echocardiogr. 2007;20(5):462-469.
20. 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(8):873-81.
21. Sabit R, Bolton CM, Fraser AG, Edwards JM, Edwards PH, Ionescu AA, et al. Sub-clinical left and right ventricular dysfunction in patients with COPD. Respir Med. 2010;104(8):1171-1178.
22. Yemenici H, Yimaz A, Kilci H, Ceyahn K, Etikan İ, Doruk S, et al. Assessment of right ventricular diastolic function in chronic obstructive lung disease. Turkish Thoracic Journal. 2012;13:152-157.
23. NHLBI WHO. NHLBI/WHO Workshop Report: Global Initiative For Chronic Obstructive Lung Disease (GOLD) Updated. 2004;2004.
24. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. American Thoracic Society. Am J Respir Crit Care Med. 1995;152(5 Pt 2):77-121.
25. Wong SP, Otto CM. Echocardiographic findings in acute and chronic pulmonary disease. In: Otto CM, ed. The practice of clinical Echocardiography. Philadelphia: W.B. Saunders Company 2002;747.
26. Seeger W, Adir Y, Barbera JA, Champion H, Coghlan JG, Cottin V, et al. Pulmonary hypertension in chronic lung diseases. J Am Coll Cardiol. 2013;62:109-116.

27. Galie N, Hoeper MM, Humbert M, Torbicki A, Vachiery J, Barbera JA, et al. Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J. 2009;30(20):2493–2537.
28. Gaine SP, Rubin LJ. Primary pulmonary hypertension. Lancet. 1998; 352(9129):719-25.
29. Burgess M, Mogulkoc N, Bright-Thomas R, Bishop P, Egan J, Ray S. Comparison of echocardiographic markers of right ventricular function in determining prognosis in chronic pulmonary disease. J Am Soc Echocardiogr. 2002;15:633-39.
30. Ng KS, Gibson DG. Impairment of diastolic function by shortened filling period in severe left ventricular disease. Br Heart J. 1989;62(4):246-52.
31. Galderisi M, Caso P, Severino S, Petrocelli A, De Simone L, Izzo A, et al. Myocardial diastolic impairment caused by left ventricular hypertrophy involves basal septum more than other walls: Analysis by pulsed Doppler tissue imaging. J Hypertens. 1999;17(5):685-93.
32. Melek M, Esen O, Esen AM, Barutcu I, Fidan F, Onrat E, Kaya D. Tissue Doppler evaluation of tricuspid annulus for estimation of pulmonary artery pressure in patients with COPD. Lung. 2006;184:121-131.
33. Cicala S, Galderisi M, Caso P, Petrocelli A, D'Errico A, de Divitiis O, Calabro R. Right ventricular diastolic dysfunction in arterial systemic hypertension: Analysis by pulsed tissue Doppler. Eur J Echocardiogr. 2002;3(2):135-42.
34. Ozdemir K, Altunkeser BB, Icli A, Ozdil H, Gok H. New parameters in identification of right ventricular myocardial infarction and proximal right coronary artery lesion. Chest. 2003;124(1):219-26.
35. Galderisi M, Severino S, Cicala S, Caso P. The usefulness of pulsed tissue Doppler for the clinical assessment of right ventricular function. Ital Heart J. 2002;3(4):241-7.
36. Emilsson K, Loiske K. Isovolumetric relaxation time of the right ventricle assessed by tissue Doppler imaging. Scand Cardiovasc J. 2004;38(5):278-82.
37. Marangoni S, Scalvini S, Schena M, Vitacca M, Quadri A, Levi G. Right ventricular diastolic function in chronic obstructive lung disease. Eur Respir J. 1992;5(4):438-43.
38. Ozer N, Tokgozoglu L, Coplu L, Kes S. Echocardiographic evaluation of left and right ventricular diastolic function in patients with chronic obstructive pulmonary disease. J Am Soc Echocardiogr. 2001;14(6):557-61.
39. Cabrita IZ, Ruisanchez C, Grapsa J, Dawson D, North B, Pinto FJ, et al. Validation of the isovolumetric relaxation time for the estimation of pulmonary systolic arterial blood pressure in chronic pulmonary hypertension. Eur Heart J Cardiovasc Imaging. 2013;14(1):51-55.
40. Pai RG, Gill KS. Amplitudes, durations, and timings of apically directed left ventricular myocardial velocities: I. Their normal pattern and coupling to ventricular filling and ejection. J Am Soc Echocardiogr. 1998;11(2):105-11.
41. Naeije R, Torbicki A. More on the noninvasive diagnosis of pulmonary hypertension: Doppler echocardiography revisited. Eur Respir J. 1995;8(9):1445-9.
42. Oswald-Mammosser M, Oswald T, Nyankiye E, Dickele MC, Grange D, Weitzenblum E. Non-invasive diagnosis of pulmonary hypertension in chronic obstructive pulmonary disease. Comparison of ECG, radiological measurements, echocardiography and myocardial scintigraphy. Eur J Respir Dis. 1987;71(5):419-29.
43. Firstenberg MS, Greenberg NL, Main ML, Drinko JK, Odabashian JA, Thomas JD, Garcia MJ. Determinants of diastolic myocardial tissue Doppler velocities: Influences of relaxation and preload. J Appl Physiol. 2001;90(1):299-307.
44.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=887&id=36&aid=7561