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ORIGINAL ARTICLE

The relationship between functional status, natriuretic peptide levels and echocardiographic parameters in patients with precapillary pulmonary hypertension

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Summary

Introduction/Aim While echocardiography plays an important role in the follow-up of patients with precapillary pulmonary hypertension (PH), several studies have identified World Health Oganization's functional class (WHO FC), 6-minute walk distance (6MWD) and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) as the strongest prognostic markers. We investigated the relationship between echocardiographic indices, functional status and NT-proBNP in patients with precapillary PH.

Material and Methods A total of 23 patients were included in this retrospective study. Data were collected from routine risk assessments, including WHO FC, 6MWD, NT-proBNP, standard, strain and three-dimensional echocardiography. The echocardiographic data were analysed in terms of the patients' functional status as determined by WHO FC, 6MWD and NT-proBNP values.

Results Patients in WHO FC III or IV had a shorter 6MWD [180 (interquartile range 85-240 m)] than patients in WHO FC I or II [409 (interquartile range 364-494 m), p=0.02)], while the difference in NT-proBNP was not statistically significant [FC I or II: 1297 (interquartile range 283-3196) versus FC III or IV: 343 (interquartile range 274-598) pg/ml, p=0.146]. There were inverse correlations between 6MWD and left and right ventricular longitudinal strain and a direct correlation between 6MWD and pulmonary acceleration time (r=0.73; p=0.001). NT-proBNP measurements were directly correlated with right heart dimensions and right ventricular strain and inversely correlated with pulmonary acceleration time (r=-0.70; p=0.004).

Conclusion Standard and advanced echocardiographic indices of right ventricular structure, function and hemodynamics correlate with functional status and natriuretic peptide levels in a heterogeneous cohort of patients with precapillary PH and may be useful ancillary parameters in clinical practice.

Keywords: pulmonary hypertension, echocardiography, functional status, natriuretic peptides

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INTRODUCTION

Pulmonary hypertension (PH) is characterized by chronic elevation of pulmonary artery pressure (PAP), defined as a mean PAP of ≥20 mmHg measured invasively by right heart catheterization (RHC) (1). It most frequently results from cardiac, respiratory, and connective tissue diseases, and the current classification has divided PH into five distinct groups based on the underlying mechanism (1). Group 1 (pulmonary arterial hypertension, PAH) and Group 4 (chronic thromboembolic pulmonary hypertension, CTEPH) belong to the spectrum of precapillary PH, which is hemodynamically defined as a mean resting PAP of ≥20 mmHg, pulmonary capillary wedge pressure (PCWP) ≤15 mmHg, and pulmonary vascular resistance (PVR) >2 Wood units (1). Although the understanding of the pathophysiologic mechanisms and therapeutic options of precapillary PH has improved considerably during past two decades, morbidity and mortality rates are still high (2).

While echocardiography and other cardiac imaging modalities play an important role in the follow-up of patients with precapillary PH, several studies have identified World Health Organization's functional class (WHO FC), 6-minute walk distance (6MWD), and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) as the strongest prognostic markers in this population of patients (3,4).

Accordingly, recent guidelines recommend using only these three variables for a simplified four-strata risk assessment during regular follow-up, with additional variables considered as needed (1). It should be noted that in the absence of one variable (WHO-FC, 6MWD or NT-proBNP), risk prediction is still accurate, but when two of these variables are not available, this risk assessment tool is no longer reliable (4,5).

On the other hand, three conventional echocardiographic parameters (right atrial systolic area, the presence of pericardial effusion, and the ratio of tricuspid annular plane systolic excursion (TAPSE) to systolic PAP) are included in a comprehensive risk assessment (three-strata model), but only at the time of diagnosis. Meanwhile, new echocardiographic techniques (e.g., strain-rate imaging and three-dimensional echocardiography) have not only emerged but have also become commercially available (6,7). It has not been fully explored if the parameters derived from advanced echocardiographic techniques are related to functional status and natriuretic peptides. Therefore, in this observational study, we investigated the relationship between conventional and advanced echocardiographic parameters, functional status, and the level of NT -proBNP in patients with precapillary PH.

METHODS

This retrospective study included 23 patients (21 patients with PAH and 2 patients with CTEPH) diagnosed with precapillary PH or treated with PAH-specific therapies between January 2018 and December 2022 at the Department of Cardiology, Clinical Hospital Centre Zemun, Belgrade, Serbia. All patients were diagnosed and followed up according to the algorithms proposed in the guidelines, including RHC to confirm the presence of hemodynamic criteria (1,8). Risk stratification was routinely performed at the time of diagnosis and reassessed every 6-12 months thereafter, with frequency depending from individual patient characteristics. Data on WHO FC, the 6-minute walk test (6MWT), NT-proBNP, and comprehensive echocardiography were obtained from the hospital electronic medical records and the local PH database. If all key parameters were available, data from the last examination were recorded; otherwise, data from the most complete examination were used for the study. The study was approved by the Institutional Ethics Committee (licence number 21/2022-1).

WHO functional class

On the basis of the presence or absence of excessive dyspnea or fatigue, chest pain, or near syncope at rest or with varying degrees of exertion, patients were divided into four functional classes. Patients in FC I had no limitation of physical activity, patients in classes FC II and III had mild and marked limitation of physical activity, respectively, whereas patients in class FC IV were unable to perform physical activity without symptoms (1).

Due to a relatively small sample size, instead of comparing patients from all functional groups separately, the comparisons were made between two major groups, assembling patients with no or mild symptoms (WHO FC I and II) and patients with pronounced symptoms (WHO FC III and IV).

6-minute walk test

The 6MWT was performed in accordance with international guidelines (9). Patients were instructed to walk along a straight 30-metre corridor for 6 minutes and were allowed to rest if necessary and continue or discontinue the test depending on their condition. The total distance at the end of the test was recorded. The start line was marked on the ground, while the turnaround points were marked with a cone. During the test, patients were directly observed by physicians (K.G., I.V., B.G.) and encouraged using standardized sentences.

NT-proBNP

NT-proBNP was measured on the day of echocardiographic examination with the Elecsys NT-proBNP assay (Roche

Diagnostic, Mannheim, Germany). The assay was performed in the laboratory of Clinical Hospital Centre Zemun, Belgrade, Serbia. Normal values were below 125 pg/ml.

Standard Doppler echocardiography

Echocardiographic examinations were performed using a commercially available Vivid E9 scanner (GE Healthcare, Horten, Norway). In accordance with hospital protocol, image loops from three consecutive cardiac cycles were digitally stored for further off-line analysis on a dedicated workstation (EchoPac, version 204, GE Healthcare). All measurements (standard and advanced) were performed by a single experienced echocardiographer (I.S.) who was blinded to all other data and complied with guideline recommendations (10,11). Left ventricular (LV) diameter was measured at the end of diastole in the parasternal long-axis view using the two-dimensional (2D) technique. LV ejection fraction (LVEF) was assessed using the modified Simpson rule (biplane disk summation method). Left atrial (LA) volume was determined by manually tracing LA contours in the apical 4- and 2-chamber views at the end of systole, excluding the area under the mitral annulus and the inlet of the pulmonary veins. The obtained value was indexed with the patient's body surface area to calculate the LA volume index (LAVI). The ratio of peak mitral velocity of early filling to early diastolic mitral annular velocity (E/e') was calculated using the average of septal and lateral e' velocities (11). The basal dimension of the right ventricle (RV) was measured at the end of diastole, while right atrial (RA) area was traced at the end of systole, excluding the area under the tricuspid annulus; both measurements were made from an RV-focused A4C view **(Figure 1)**. RA volume index (RAVi) was assessed from the same window using the area-length method. RV systolic function was assessed by measuring TAPSE and systolic velocity of the tricuspid annulus (s') using the M-mode and tissue Doppler methods, respectively. Fractional area change of the RV (FAC) was assessed by tracing the endocardial border of the RV at end-diastole and end-systole and dividing the difference of the areas at end-diastole and end-systole by the area at end-diastole. RA pressure (RAP) was estimated from the subcostal view by assessing the diameter of the inferior vena cava (IVC) and its respiratory variations. Tricuspid gradient (TRG) was estimated from the maximum velocity of tricuspid regurgitation ($4Vmax^2$). Right ventricular systolic pressure (RVSP, also systolic PAP) was estimated by adding the estimated RA pressure to TRG. The ratio of TAPSE/systolic PAP was calculated as a non-invasive marker of RV-PA coupling (1). Acceleration time (AccT) of systolic pulmonary artery flow was measured from the forward velocity profile obtained with pulsed Doppler in the RV outflow tract near the pulmonary valve **(Figure 1)**. PA diameter was measured in the parasternal short-axis view at the level of maximum diameter above the pulmonary root at the end of diastole.

Advanced echocardiography

LV longitudinal strain was assessed by 2D speckle-tracking echocardiography from apical 4-, 2- and long-axis

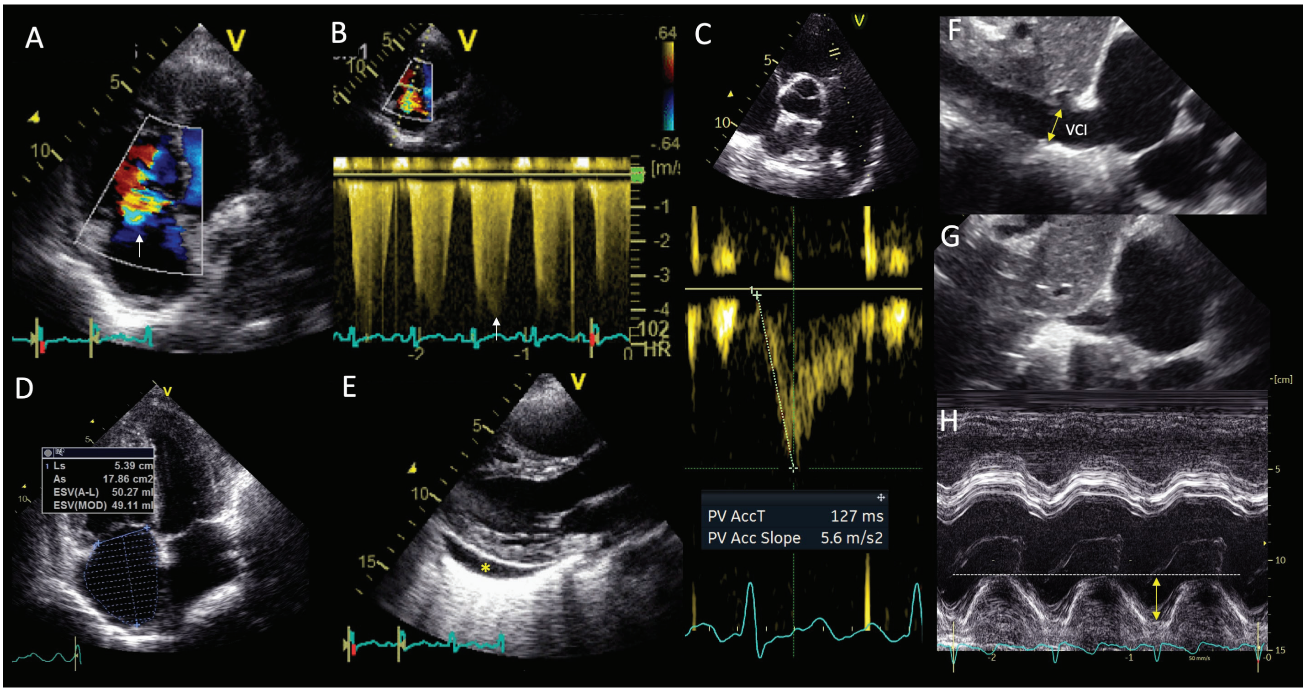

Figure 1. Representative examples of standard Doppler echocardiography for assessment of right ventricular structure, function, and hemodynamics in pulmonary hypertension. A. Tricuspid regurgitation (arrow); B. Continuous wave Doppler profile of tricuspid regurgitation; C. Measurement of pulmonary artery acceleration time (pulse wave Doppler); D. Measurement of right atrial area; E. Pericardial effusion (*) behind the posterior wall of the left ventricle; F. Measurement of inferior vena cava (VCI) diameter during normal respiration (arrow) and with inspiration (G); H. Tricuspid annular plane systolic excursion measurement (arrow).

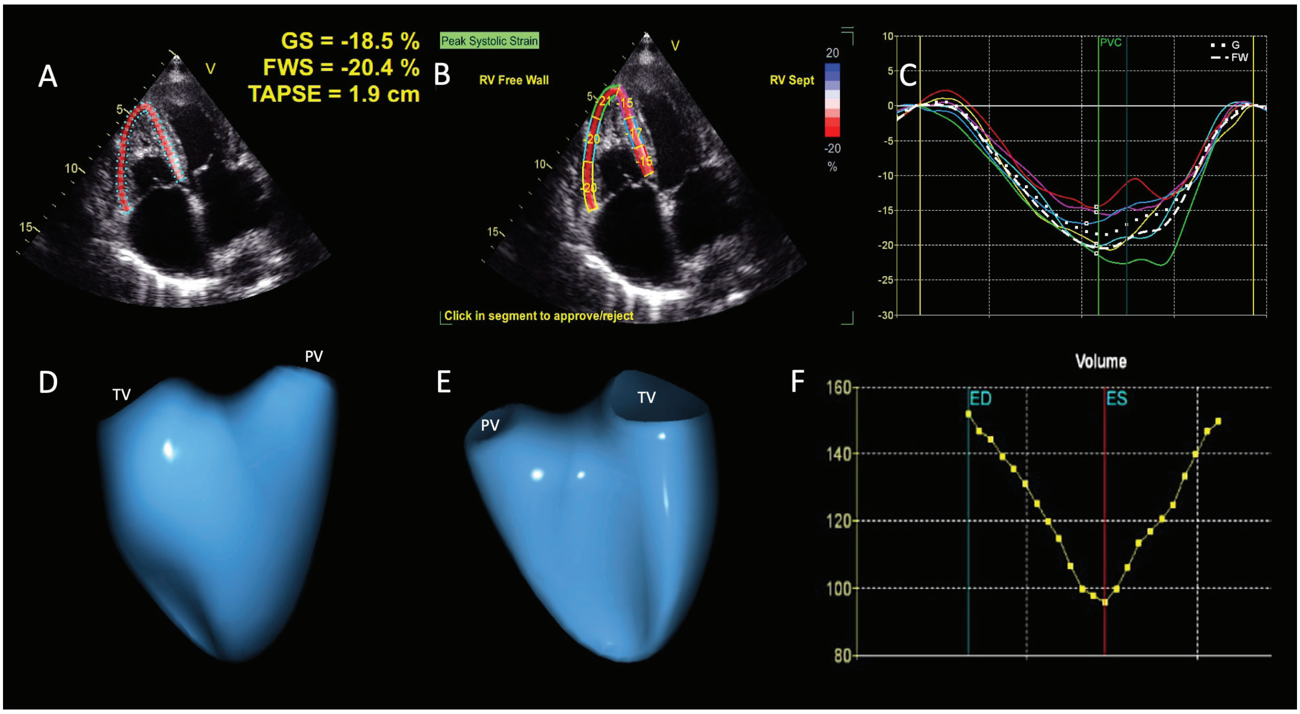

Figure 2. Advanced echocardiographic assessment of the right ventricle. A. Speckle-tracking echocardiography of the right ventricle (RV) from the focused apical view. B. Longitudinal strain values of six free wall and septal segments are shown as numbers within each segment. C. Longitudinal strain curves of all RV segments (the color of the curve corresponds to the color of the segment shown in panel B). A representative case of right ventricular (RV) quantification using three-dimensional echocardiography (3DE) is shown in panels D and F. After manual placement of six landmark points at two-dimensional views (not shown here), a model of the RV is automatically generated. F. RV volume calculation with 3DE - the curve represents the volume changes during the cardiac cycle. GS - global strain, FWS - free wall strain, PV - pulmonary valve, TAPSE - tricuspid annular plane systolic excursion, TV - tricuspid valve.

views with a temporal resolution of >50 frames per second (fps), using dedicated software (EchoPAC, version 204) and a semi-automated tool (AFI LV). Global longitudinal strain (GLS) was calculated by the software as the average of 18 LV segments (6 segments per view).

Longitudinal RV strain was determined by 2D speckle tracking echocardiography from RV-focused A4C acquisition, with a temporal resolution of >50 fps (6,12). Care was taken to ensure that the region of interest included both the RV free wall and the septum, with width adjusted to cover the thickness of the RV free wall. After checking the quality of the tracking, the longitudinal strain of the RV free wall (FWS) was calculated using the software (EchoPAC, version 204, AFI RV tool) as the average of the strain values of the three segments of the RV free wall, while the global longitudinal strain of the RV was calculated as the average of the six segmental strain values of the RV free wall and the interventricular septum **(Figure 2)**.

For three-dimensional (3D) echocardiography, 6-beat full-volume 3D data sets of the RV (volume rate > 30 volumes/s) were obtained during breath-hold from the focused A4C view of the RV, taking care to encompass the entire RV. Post-processing of the 3D images was done using commercially available software (EchoPAC, 4D AutoRVQ Tool) to calculate RV volumes and ejection fraction **(Figure 2)**.

Statistical analysis

Normally distributed continuous data are expressed as mean ± standard deviation, while categorical data are summarized by frequencies and percentages. Normally distributed data were compared between groups using unpaired t-tests for continuous variables and Fisher's exact test for categorical variables. Normality assumptions were tested using Shapiro-Wilk and Kolmogorov-Smirnov tests. If the results of either test indicated that the normality assumption was not met, median and interquartile ranges (IQR) and Mann-Whitney U test were used. Correlations between clinical, laboratory and echocardiographic parameters were described using the Spearman correlation coefficient.

RESULTS

The baseline characteristics of the patients and the breakdown of PH etiologies are shown in **Table 1**. The majority of patients were female, with arterial hypertension and hypothyroidism being the most common comorbidities. At the time of the study, 87% of patients were symptomatic (WHO FC II-IV), and all but one were receiving at least one PAH-targeted therapy. Two patients received monotherapy, 18 received combination therapy and 2 patients received triple PAH-specific therapy. Long-term oxygen therapy was used by 44% of patients. The

Table 1. Characteristics of study population

Age, years	57±17
Female sex, n (%)	17 (74)
Arterial hypertension, n (%)	13 (57)
Hypothyroidism, n (%)	6 (26)
Atrial fibrillation, n (%)	4 (17)
Diabetes mellitus, n (%)	2 (9)
Coronary artery disease, n (%)	2 (9)
WHO functional class	
I, n (%)	3 (13)
II, n (%)	9 (39)
III, n (%)	7 (30)
IV, n (%)	4 (17)
6MWD, m	316±176
NT-proBNP, pg/mL	370 [274-1935]
PH etiology	
Idiopathic, n (%)	7 (30)
Connective tissue disease, n (%)	4 (17)
Congenital heart disease, n (%)	10 (44)
Chronic thromboembolic PH, n (%)	2 (9)
PH specific therapies	
Sildenafil, n (%)	21 (91)
Riociguat, n (%)	1 (4)
Bosentan, n (%)	7 (30)
Ambrisentan, n (%)	2 (9)
Macitentan, n (%)	8 (35)
Selexipag, n (%)	2 (9)

6MWD – 6-minute walk distance; NT-proBNP – N-terminal pro-B-type natriuretic peptide; PH – pulmonary hypertension; WHO – World Health Organization.

6MWT could not be performed in four patients due to their general condition or inability to walk without support. NT-proBNP measurements were not performed in five patients due to unavailability of lab kits or technical issues with the blood samples.

Standard and advanced echocardiographic data on LV and RV morphology and function are summarised in **Table 2**. Standard echocardiographic and speckle-tracking longitudinal strain-derived parameters were available in all patients. RV ejection fraction could not be reliably determined with 3D echocardiography in 35% of patients because of the presence of atrial fibrillation, insufficient patient cooperation during image acquisition, or inability to encompass the entire RV while maintaining adequate volume rates. There were no patients with reduced LVEF (<50%) or with more than mild mitral or aortic valve disease. Pericardial effusion was observed in 30% of patients and was mild in all cases (<10 mm at the end of diastole). In our study population, there was a moderate direct correlation between LV GLS and RV 6-segment strain (r=0.47, p=0.037), while no significant correlation was observed between LV GLS and RV FWS (r=0.17, p=0.464). There were significant differences in RV FWS, sPAP, pulmonary AccT and TAPSE/sPAP ratio between asymptomatic or mildly symptomatic patients (WHO FC I and II) and those with marked symptoms (WHO FC III and IV) (**Table 2**). On the other hand, the RA areas were similar (p=0.496), and there was no significant difference in the prevalence of pericardial effusion

Table 2. Standard and advanced echocardiographic parameters in all patients and with regard to the patient functional status

	All patients (n=23)	WHO FC I or II (n=12)	WHO FC III or IV (n=11)	p-value
LVEDD, mm	44±9	45±5	42±12	0.448
LVEF, %	58±7	57±7	59±6	0.618
LV GLS, %	-17±3	-16.8±2.9	-17.9±2.3	0.391
LAVI, ml/m^2	32±10	34±9	30±10	0.269
Mitral E/e' ratio	10.5±3.2	10.6±3.5	10.4±2.9	0.899
Pericardial effusion, n (%)	7 (30)	3 (25)	4 (36)	0.667
RV basal diameter, mm	45±9	46±10	45±8	0.917
RA area, cm^2	23±9	22±8	25±10	0.496
RAVI, ml/m^2	44±19	44±22	45±18	0.880
TAPSE, mm	19±5	20±5	18±4	0.215
RV FAC, %	34±9	37±8	31±10	0.104
sPAP, mmHg	73±30	58±28	89±25	0.013
TAPSE/sPAP, mm/mmHg	0.31±0.16	0.40±0.17	0.21±0.06	0.002
S', cm/s	11±3	12±3	10±2	0.075
RV FWS, %	-16.5±5.5	-18.9±5.1	-13.9±4.9	0.029
RV 6-segment strain, %	-14.4±4.4	-15.9±4.6	-12.9±3.6	0.108
PA diameter, mm	34±8	34±5	33±10	0.853
PA AccT, ms	88±27	103±29	76±18	0.025

AccT – acceleration time, FAC – fractional area change, FWS – free wall strain, LV GLS – global longitudinal strain of the left ventricle, LAVI – left atrial volume index, LVEDD – left ventricular end-diastolic diameter, LVEF – left ventricular ejection fraction, PA – pulmonary artery, RA – right atrial, RAVI – right atrial volume index, RV – right ventricular, S' – tricuspid annular systolic velocity, sPAP – systolic pulmonary artery pressure, TAPSE – tricuspid annular plane systolic excursion, WHO – World Health Organization.

Table 3. Correlations between 6MWD, NT-proBNP values and echocardiographic parameters

	6MWD, m		NT-proBNP, pg/ml	
LV EDD, mm	r=0.13	p=0.606	r=0.13	p=0.606
LVEF, %	r=0.13	p=0.606	r=-0.11	p=0.653
LV GLS, %	r=-0.53	p=0.030	r=0.33	p=0.180
LAVI, ml/m²	r=0.31	p=0.213	r=-0.15	p=0.566
Mitral E/e' ratio	r=-0.15	p=0.587	r=0.09	p=0.741
RV basal diameter, mm	r=-0.02	p=0.994	r=0.53	p=0.024
RA area, cm²	r=-0.13	p=0.598	r=0.64	p=0.005
TAPSE, mm	r=0.35	p=0.147	r=-0.38	p=0.125
RV FAC, %	r=0.14	p=0.571	r=0.01	p=0.981
sPAP, mmHg	r=-0.22	p=0.368	r=0.29	p=0.245
TAPSE/sPAP, mm/mmHg	r=0.41	p=0.081	r=-0.41	p=0.089
S', cm/s	r=0.12	p=0.659	r=-0.07	p=0.811
RV FWS, %	r=-0.59	p=0.008	r=0.65	p=0.004
RV 6-segment strain, %	r=-0.55	p=0.015	r=0.72	p=0.001
RVEF, %	r=0.31	p=0.301	r=-0.18	p=0.577
PA AccT, ms	r=0.73	p=0.001	r= -0.70	p=0.004
PA diameter, mm	r=0.31	p=0.261	r=-0.21	p=0.464

6MWD – 6-minute walk distance, AccT – acceleration time, FAC – fractional area change, FWS – free wall strain, GLS – global longitudinal strain, LAVI – left atrial volume index, LV – left ventricular, LVEDD – left ventricular end-diastolic diameter, LVEF – left ventricular ejection fraction, NT-proBNP - N-terminal prohormone of brain natriuretic peptide, PA – pulmonary artery, RA – right atrial, RV – right ventricular, RVEF – right ventricular ejection fraction, S' – tricuspid annular systolic velocity, sPAP – systolic pulmonary artery pressure, TAPSE – tricuspid annular plane systolic excursion, WHO – World Health Organization.

between the two groups (p=0.667). Patients in WHO FC III or IV had a shorter 6MWD [180 (IQR 85-240 m)] than patients in WHO FC I or II [409 (IQR 364-494 m), p=0.02)], while the difference in NT-proBNP was not statistically significant [FC I or II: 1297 (IQR 283-3196) versus FC III or IV: 343 (IQR 274-598) pg/ml, p=0.146].

The correlations between 6MWD, NT-proBNP values and echocardiographic parameters are shown in **Table 3**. There were moderately strong inverse correlations between 6MWD and LV GLS, RV FWS and 6-segment longitudinal strain and a strong direct correlation between 6MWD and pulmonary AccT **(Figure 3A)**. Other echocardiographic parameters were not significantly correlated with 6MWD. NT-proBNP measurements correlated moderately with basal RV diameter, RA area and RV FWS; there was a strong direct correlation with RV 6-segment strain and a strong inverse correlation with pulmonary AccT **(Figure 3B)**.

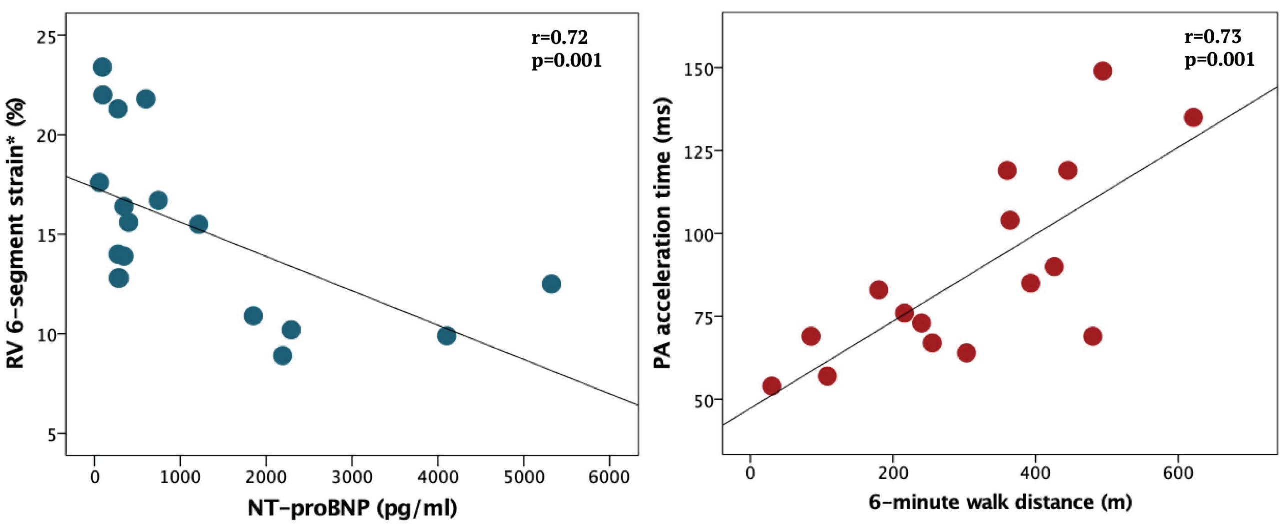

Figure 3. Scatter plots showing correlations between clinical and echocardiographic parameters. A. Correlation between right ventricular (RV) 6-segment strain and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels (* absolute values of RV strain are shown). B. Correlation between pulmonary artery (PA) acceleration time and 6-minute walk distance.

DISCUSSION

In this retrospective observational study, we found significant correlations between functional status, standard and advanced echocardiographic indices and natriuretic peptides in patients with precapillary PH. Functional class correlated with strain parameters reflecting RV systolic function and with noninvasive surrogates of pulmonary arterial pressure, pulmonary vascular resistance and RV-PA coupling. In addition, 6MWD correlated with longitudinal strain-derived echocardiographic parameters reflecting left and right ventricular function, whereas NT-proBNP correlated with parameters reflecting structure and function of right heart chambers. Only pulmonary acceleration time, as a surrogate measure of pulmonary vascular resistance, correlated with WHO FC, 6MWD, and NT-proBNP values.

Elevated NT-proBNP is commonly used in cardiology as a biomarker for heart failure and atrial fibrillation and indicates poor prognosis (13). The association between NT-proBNP and right heart function and morphology has been investigated in various patient populations with PH, where right heart chambers were usually assessed by cardiovascular magnetic resonance (CMR), whereas right heart hemodynamics were determined by RHC (14-16). For example, in a study of patients with PAH and CTEPH, NT-proBNP correlated negatively with RVEF, assessed by CMR (14). Furthermore, NT-proBNP correlated with RV volumes determined by CMR and pulmonary pressures assessed by echocardiography in patients with PAH, who had congenital heart disease (atrial septal defect) (15). In addition, NT-proBNP, RV dimensions, systolic PAP, and pulmonary AccT were higher in patients with functional limitations after pulmonary embolism and suspected CTEPH (16). Our data support the notion that NT-proBNP reflects RV structure and function in the precapillary PH and suggest that comprehensive echocardiographic data and NT-proBNP may be clinically useful when CMR and 6MWT are unavailable, impractical, or contraindicated.

Previous studies showed that RV strain imaging can also provide important clinical information (17,18). In chronic PH, RV strain, derived from 2D and 3D speckle tracking echocardiography, and 3D RVEF were lower in patients with pre- and post-capillary PH compared with controls. Advanced echocardiographic indices (e.g. 2D and 3D strain) reflected global and regional RV dysfunction better than conventional echo parameters and were independent predictors of mortality (17). Moreover, it was recently reported that in patients with idiopathic PAH, not only the numerical values of RV strain but also the patterns of the curves might be progostically important (18). In this patient population, speckle-tracking echocardiography allowed the identification of three phenotypically distinct RV strain-derived post-systolic patterns that were associated with prognosis (18).

In a recent study, RV strain abnormalities were associated with 6MWD, NT-proBNP, and mortality (19). In another report, global RV longitudinal strain predicted long-term prognosis in patients with PAH but showed only a weak correlation with B-natriuretic peptide concentration (20).

In a large study including 575 patients with confirmed or suspected PAH, RV longitudinal strain predicted clinical outcomes and decreased in parallel with functional class, 6MWD, increase in NT-proBNP levels and the presence of RV failure (21). While the association between reduced functional capacity, RV pressure overload, and marked reduction in RV systolic strain was expected, our data showed that 6WMD was also related to LV global longitudinal strain. This observation is prognostically important because it has been demonstrated that reduction in LV GLS was associated with early mortality despite preserved LVEF, underscoring the importance of ventricular interdependence in PAH (22).

3D echocardiography allows not only analysis of RV strain and measurement of RV ejection fraction but also a comprehensive analysis of RV shape. Increased eccentricity, apical rounding, and bulging at the base have been shown to characterize RV shape in PH, but interestingly, the shape changes were not associated with symptoms as assessed by WHO FC (23). Different loading conditions have also been shown to be associated with specific RV curvature changes associated with longitudinal and radial RV dysfunction (7).

In our study, the ratio of TAPSE/systolic PAP was lower in patients with more severe symptoms than in patients with milder symptoms. It has been suggested that this index of RV-arterial coupling can be improved by using RV strain instead of TAPSE (24). In a recent study, the RV strain/sPAP ratio predicted all-cause mortality and heart-lung transplantation and was superior to other established parameters in patients with precapillary PH (24).

In the current study, pulmonary AccT was strongly correlated with patients' functional status and NT-proBNP level. In previous reports, pulmonary AccT was inversely correlated with pulmonary haemodynamics measured with RHC and was able to accurately predict PAP and PVR (25). Furthermore, in the paediatric population, the addition of pulmonary AccT improved the specificity of NT-proBNP for the diagnosis of PH (26). In adult patients, pulmonary AccT <90 ms was a strong non-invasive predictor of PVR >3 WU, which could distinguish patients with pre- and post-capillary PH (27).

Finally, owing to advances in diagnosis and therapy, the majority of patients with CHD reach adulthood (28). In our study, a heterogeneous cohort of patients with adult congenital heart disease (ACHD)-related PAH accounted for more than 40% of the study population. In these patients, RV function may be impaired even without PH because of pressure and/or volume overload (28). While patients with ACHD-related PAH are treated similarly to other patients with PAH, there are some differences in RV response to PH, including more pronounced RV hypertrophy but also a longer period of stable RV function in patients with Eisenmenger syndrome compared with patients with idiopathic PAH (29). Other predictors of survival in PAH, such as 6MWT, WHO functional class, and NT-proBNP levels, are also applicable in Eisenmenger patients (30).

LIMITATIONS

Our study is limited by its retrospective, observational design and small number of participants. RV systolic strain was highly feasible, similar to previous reports (20), while RV 3D assessment was feasible in 65% of patients. Feasibility in our study was slightly lower than in a recent report, where feasibility in the focused A4C view using different 3D settings was 72% (31).

The characteristics of our patient population (markedly enlarged right ventricles, patients' inability to hold their breath and prevalent atrial fibrillation) as well as our conservative approach to obtaining reliable 3D sets probably contributed to this discrepancy.

CONCLUSION

Standard and advanced echocardiographic indices of RV structure, function and hemodynamics correlate with functional status and natriuretic peptide levels in a heterogeneous cohort of patients with precapillary PH and may be useful ancillary parameters in clinical practice.

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None.

Conflict of interest

None to declare.

Ethical approval

The study was approved by the Ethics committee of ***blinded*** (the license number 21/2022-1).

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POVEZANOST FUNKCIONALNOG STATUSA, NIVOA NATRIURETSKIH PEPTIDA I EHOKARDIOGRAFSKIH PARAMETARA KOD BOLESNIKA SA PREKAPILARNOM PLUĆNOM HIPERTENZIJOM

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Sažetak

Uvod/Cilj Iako ehokardiografija ima važnu ulogu u praćenju bolesnika sa prekapilarnom plućnom hipertenzijom (PH), više studija je identifikovalo funkcionalnu klasu Svetske zdravstvene organizacije (FK SZO), šestominutnu distancu hodom (6MDH) i N-terminalni prohormon moždanog natriuretskog peptida (NT-proBNP) kao najjače prognostičke parametre. Cilj istraživanja je ispitivanje povezanosti konvencionalnih i naprednih ehokardiografskih parametara, funkcionalnog statusa i NT-proBNP-a kod bolesnika sa prekapilarnom PH.

Materijal i metode Ova retrospektivna studija je obuhvatila 23 bolesnika. Podaci su prikupljeni iz rutinskih ispitivanja procene rizika, uključujući FK SZO, 6MDH i NT-proBNP, kao i standardnu, strejn i trodimenzionalnu ehokardiografiju. Ehokardiografski podaci su upoređeni sa funkcionalnim statusom bolesnika utvrđenog FK SZO, 6MDH i vrednostima NT-proBNP-a.

Rezultati Bolesnici u FK SZO III ili IV imali su kraću 6MDH [180 (interkvartilni raspon 85-240 m)] od bolesnika u FK SZO I ili II [409 (interkvartilni raspon 364-494 m), p=0,02], dok razlika u NT-proBNP nije bila statistički značajna [FK I ili II: 1297 (interkvartilni raspon 283-3196) u odnosu na FK III ili IV: 343 (interkvartilni raspon 274-598) pg/ml, p=0,146]. Uočene su inverzne korelacije između 6MDH i longitudinalnog strejna leve i desne komore i direktna korelacija između 6MDH i vremena plućne akceleracije (r=0,73; p=0,001). Merenja NT-proBNP-a su bila u direktnoj korelaciji sa dimenzijama desnog srca i strejnom desne komore, i inverznoj korelaciji sa vremenom plućne akceleracije (r=-0,70; p=0,004).

Zaključak Standardni i napredni ehokardiografski pokazatelji strukture, funkcije i hemodinamike desne komore koreliraju sa funkcionalnim statusom i nivoima natriuretskih peptida u heterogenoj kohorti bolesnika sa prekapilarnom PH i mogu biti korisni pomoćni parametri u kliničkoj praksi.

Ključne reči: plućna hipertenzija, ehokardiografija, funkcionalni status, natriuretski peptidi

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