Noninvasive Predictors of Functional Capacity in Patients with Pulmonary Hypertension due to Congenital Heart Disease: A Pilot Echocardiography Single-Center Study

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Abstract

Background: Pulmonary hypertension (PH) with congenital heart disease (CHD) affects the functional capacity (FC), quality of life, and survival. However, the importance of different echocardiographic parameters and their correlation with FC is unclear. Methods and Results: A custom-made sheet for 34 consecutive patients with PH due to CHD was made to include patient's demographic data, underlying cardiac disorder, and FC by 6-min walk test (6MWT). The patients were subdivided into Group 1 with 6MWT < 330 m and Group 2 with 6MWT > 330 m. A cutoff value of 330 m was selected because it reflected the survival and outcome of patients in many studies before. Left ventricle global radial strain, baseline saturation, and saturation after 6MWT showed a significant strong positive correlation with 6MWT (r = 0.755, 0.714, and 0.721, P = 0.001, 0.000, and 0.000, respectively). Multiple regression analysis using a multivariate model showed that the mean pulmonary artery pressure (MPAP) and baseline saturation are the most independent predictors of the FC (P = 0.028 and 0.049, respectively), with a cutoff point for MPAP > 30 mmHg (area under the curve [AUC]: 0.85) with a sensitivity and specificity of 69.23% and 95.24%, respectively, and cutoff point for saturation < 94% (AUC: 0.852) with a sensitivity and specificity of 92.31% and 76.19%, respectively. Conclusion: The MPAP and the baseline oxygen saturation were the most independent predictors of impaired FC. They can be used for risk stratification and as surrogate predictors of outcome in this group of patients.

Keywords: 6-min walk test, congenital heart disease, functional capacity, pulmonary hypertension

INTRODUCTION

Pulmonary hypertension (PH) is caused by a heterogeneous condition including congenital heart disease (CHD), but it is defined as a mean pulmonary arterial pressure of 25 mmHg or greater at rest as measured by right-side heart catheterization.[1] Most of the previous studies and clinical trials focused on patients with idiopathic-primary-PH, patients with chronic thromboembolic PH (CTEPH) and patients with PH associated with connective tissue disease, especially scleroderma. The data of patients with PH due to CHD were scarce. Furthermore, the importance of different echocardiographic parameters and their correlation with exercise capacity in those patients was unclear, so we sought to study the echocardiographic predictors of exercise capacity in patients with PH due to CHD.

METHODS

This study was approved by our institutional and local review board. Informed consent was obtained from all patients enrolled in this study. This study was a prospective study which included 34 consecutive patients with PH secondary to CHDs referred for elective echocardiography in our congenital and structural heart disease unit. A custom-made sheet was made to include patient demographic data including age at the time of the study, gender, body weight, left ventricle global radial strain, baseline saturation, and saturation after 6MWT showed a significant strong positive correlation with 6MWT (r = 0.755, 0.714, and 0.721, P = 0.001, 0.000, and 0.000, respectively). Multiple regression analysis using a multivariate model showed that the mean pulmonary artery pressure (MPAP) and baseline saturation are the most independent predictors of the FC (P = 0.028 and 0.049, respectively), with a cutoff point for MPAP > 30 mmHg (area under the curve [AUC]: 0.85) with a sensitivity and specificity of 69.23% and 95.24%, respectively, and cutoff point for saturation < 94% (AUC: 0.852) with a sensitivity and specificity of 92.31% and 76.19%, respectively. Conclusion: The MPAP and the baseline oxygen saturation were the most independent predictors of impaired FC. They can be used for risk stratification and as surrogate predictors of outcome in this group of patients.

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body surface area (BSA), and underlying cardiac disorder. Thorough clinical assessment was done with emphasis on NYHA functional class, baseline oxygen saturation, and signs of heart failure.

We excluded patients with PH secondary to other causes other than CHD; patients who were not able to perform the 6-min walk test (6MWT) due to significant physical or mental causes; patients who were not co-operative; patients with sustained arrhythmia, pacemaker rhythm, and high-grade AV block; patients with single ventricle; and patients with poor echocardiographic window.

**Exercise capacity assessment**
Assessment of the patient’s exercise capacity was done using 6MWT considering it as an objective surrogate for the patient’s functional capacity (FC) and NYHA class. The test was performed in a long, straight, and flat corridor. Before starting the test, instructions to the patients were given to ensure that they would be comfortable and able to walk for 6 min. The test was performed without a warm-up period. We explained the instructions to each patient orally and in detail. Then, a demonstration of the first lap in front of the patient was done by the doctor. Blood oxygen saturation before test (rest SAT) and desaturation at the maximum effort were obtained by a pulse oximeter. The test was terminated at the end of the 6 min whenever the patient refuses to continue or the doctor decides to stop for the patient’s safety. At the end of the 6 min, the patient was allowed to rest on a nearby chair and offered water. A cutoff value of 330 m was selected because it reflected the survival and outcome of patients in many studies before.[2]

**Echocardiographic study**
This was done with machine-integrated ECG recording, with the patients lying in the left lateral decubitus, using a General Electric VinGmed Ultrasound Vivid 5 or Vivid 9 system with the suitable probe frequency for the patient.

The examination was done for all patients in standard apical (two-, three-, and four-chamber views), parasternal (long- and short-axis views), and subcostal (four-chamber and inferior vena cava [IVC] long-axis views), and the measurements were done in conjunction with the recommendations endorsed by the American Society of Echocardiography and the European Association of Cardiovascular Imaging performance and acquisition guidelines.[3]

All measurements were indexed to the patient’s BSA which was calculated using the Mosteller equation: BSA = \( \sqrt{\text{weight (kg)} \times \text{height (cm)}} \times 3600 \).[4]

**Left ventricle assessment**

*Two-dimensional and M-mode linear measurements*
After acquiring a proper parasternal short-axis view, linear measurements of the left ventricle (LV) internal dimensions were obtained using two-dimensional (2D)-guided M-mode with the M-mode cursor positioned perpendicular to the interventricular septum (IVS) and LV posterior wall below the level of mitral valve leaflet’s tips; ejection fraction (EF) by M-mode was estimated using the computed volume calculation derived from these linear measurements according to Teichholz method and fractional shortening (FS).[3]

**Volumetric measurements**
After manual tracing of the LV endocardial borders at the end-diastole and the end-systole while excluding the papillary muscles, the LV end-diastolic volume (EDV) and end-systolic volume (ESVs) in the apical two and four chambers were calculated. The LVEF was calculated using the biplane Simpson’s method: EF = (EDV − ESV)/EDV in percentage.[3]

**Myocardial performance index**
Tissue Doppler (TD)-derived MPI was calculated by measuring the isovolumetric contraction time (IVCT) (defined as the time from the end of A’ to the onset of S’), isovolumetric relaxation time (IVRT) (from the end of S’ to the beginning of E’), and ejection time (ET) (as estimated from the onset till the end of S’) and computing the following formula: TD-derived MPI = ([IVRT + IVCT]/ET).[9]

**Diastolic function assessment**
The mitral inflow pattern and TD imaging (TDI) were used as a simple way to assess the LV diastolic function.[6]

**Two-dimensional speckle-tracking echocardiography**
A three-beat loop of 2D digital clip for each of the apical and short-axis views was acquired while ensuring proper and optimal visualization of both myocardial borders (endocardium and epicardium) at a frame rate between 40 and 80 Hz for proper offline analysis. The parasternal short-axis view of the LV at different levels (basal, mid, and apical) was acquired for calculation of the LV deformation in the circumferential and radial directions and in the apical views for calculation of the LV deformation in the longitudinal direction. A semi-automated analysis of the LV strain was done by tracing the generated speckles with manual optimization of the automatically traced endocardial borders by the machine when needed, while the epicardial borders were automatically traced by the software.[7]

Automatic division of each LV wall into three segments was done in the apical views (apical, mid, and basal), into six segments in each of the parasternal short-axis views levels (mid and basal levels), and into only four segments in the parasternal short-axis apical level. We excluded segments with poor image quality from the analysis.[8] The global longitudinal strain (GLS) of the LV was defined as the mean value of all LV segments in the three apical views. The global circumferential strain (GCS) and global radial strain (GRS) of the LV [Figure 1] were calculated also as the mean value of all the LV segments calculated from the parasternal short axis at the different LV levels.[3]

**Right ventricle assessment**
We evaluated the following right ventricle (RV) systolic function’s parameters:
The RV fractional area change (FAC) was calculated from the apical four chambers or the modified apical RV view with
inclusion of the whole RV and proper tracing of the RV cavity including the trabeculae.\textsuperscript{[3]}

TD-derived tricuspid valve (TV) annular systolic excursion velocity (S’) and tricuspid annular plane systolic excursion (TAPSE) were calculated by applying the pulsed-wave TDI (PW-TDI) on the RV free wall basal and annular segment while maintaining adequate parallel alignment of the Doppler signal to avoid velocity underestimation and applying the 2D-guided M-mode cursor along the lateral annulus of the TV.\textsuperscript{[3]}

The TDI-derived RVMPI was calculated by applying the PW-TDI to the TV lateral annulus as follows:\textsuperscript{[5]}

\[ \text{TDI-derived RVMPI} = \frac{\text{IVRT} + \text{IVCT}}{\text{ET}}. \]

Speckle-tracking echocardiography of right ventricle free wall

The 2D speckle tracking derived GLS of the RV was measured by calculating the mean value of the three lateral RV free wall segments’ longitudinal strain in the apical four-chamber view or the focused RV view\textsuperscript{[9]} [Figure 2].

Right ventricle diastolic function

It was assessed using the PW-TDI to obtain E’ wave of the lateral TV annulus. The abnormal cutoff value was considered when E’ \(< 7.8 \text{ cm/s}.\textsuperscript{[3]}

Right ventricle linear dimensions

The 2D-derived RV linear dimensions were measured in the apical four-chamber or the RV focused view after obtaining proper images to avoid foreshortening. The distal RV outflow tract diameter was measured in the parasternal short-axis view at the level of the aortic root at end-diastole immediately proximal to the level of the pulmonary valve.

The RV wall thickness was measured in the subcostal view at end-diastole, below the level of the TV annulus after exclusion of the trabeculae, papillary muscles, and epicardium.\textsuperscript{[3]}

Assessment of the right ventricle and pulmonary circulation hemodynamics and pressures

The RV systolic pressure (RVSP) was calculated by applying the continuous wave Doppler to the tricuspid regurgitation jet using the modified Bernoulli equation; the right atrium (RA) pressure was estimated from the inferior vena cava dimensions at end-expiration and collapsibility just proximal to the junction of the hepatic veins with the IVC 0.5–3.0 cm away from the RA in the subcostal long-axis view.\textsuperscript{[10]}

The pulmonary artery diastolic pressure (PADP) was calculated using the peak velocity of the pulmonary regurgitation jet at end-diastole: \( \text{PADP} = 4 \times \text{end-diastolic pulmonary regurgitant velocity}^2 + \text{RA pressure} \).

The echo-derived mean PA pressure (MPAP) was calculated as follows: Mean PA pressure = \( \frac{1}{3} \times \text{systolic pulmonary artery pressure} + \frac{2}{3} \times \text{PADP} \).\textsuperscript{[10]}

Right atrial dimensions

RA dimensions were measured in the apical four-chamber view at end-systole.\textsuperscript{[10]}

After collection, revision, and coding of the data, they were analyzed using the Statistical Package for the Social Sciences (IBM SPSS) version 23. Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp. Representation of quantitative data was done using the mean, and the standard deviation, while representation of the qualitative data was done as numbers and percentages. We used Chi-square test for comparison of the qualitative data between the study groups and we used Independent t-test for comparison of the quantitative data. Spearman correlation coefficients tests were used for assessment of the correlation between two quantitative parameters in the same group. Multivariate linear regression analysis was performed to assess the independent predictors of 6MWT. We set the confidence interval value in this study to 95%, and we set the accepted margin of error to 5%. \( P < 0.05 \) was considered statistically significant.

Results

The study population included 14 patients with ventricular septal defect (41.2%), 10 patients with atrial septal defect (29.4%), 4 patients with common atrioventricular canal (11.8%), 1 patient with patent ductus arteriosus (2.9%), and 5 patients...
with complex CHD (14.7%). The study population was subdivided into two subgroups according to the results of the 6MWT: Group 1 with 6MWT < 330 m and Group 2 with 6MWT > 330 m. The demographic and clinical data of the study groups are listed in Table 1.

Correlations between the echocardiographic, clinical data and 6-min walk test results
The calculated LVMPI, GLS, GCS, RV wall thickness, and IVC diameter showed a significant weak negative correlation with 6MWT \( (r = -0.42, -0.44, -0.28, -0.38, \text{and} -0.35, P = 0.013, 0.000, 0.058, 0.026, \text{and} 0.04, \text{respectively}) \). The E/E’ ratio, RVSP, the MPAP, and RVGLS showed a significant moderate negative correlation with the 6MWT \( (r = -0.63, -0.494, -0.511, \text{and} -0.559, P = 0.000, 0.003, 0.002, \text{and} 0.001, \text{respectively}) \).

The TD-derived LV septal wall and lateral wall E’, TAPSE, and RVFAC showed a significant moderate positive correlation with 6MWT \( (r = 0.489, 0.561, 0.402, \text{and} 0.492, P = 0.003, 0.000, 0.019, \text{and} 0.003, \text{respectively}) \). The LVGRS [Figure 3], baseline saturation, and saturation after 6MWT showed a significant strong positive correlation with 6MWT \( (r = 0.755, 0.714, \text{and} 0.721, P = 0.001, 0.000, 0.000, \text{and} 0.000, \text{respectively}) \).

The desaturation value defined as the difference between the baseline saturation and the saturation after the 6MWT showed a strong negative correlation with the 6MWT \( (r = -0.673, P = 0.000) \). The E/A ratio showed a significant weak positive correlation with 6MWT \( (r = 0.435, P = 0.011) \).

Univariate analysis using an independent t-test to compare the echocardiographic and clinical variables between the two groups was done [Table 2].

The RVSP, MPAP, E’ septal LV wall, E’ lateral LV wall, E/A ratio of MV inflow, E/E’ ratio of LV, LVMPI, LVGRS, RVFAC, RVGLS, RVMPI, and the oxygen saturation showed a significant difference between the two subgroups.

All significant variables in the univariate analysis were entered into the multivariate model. The multivariate regression analysis results showed that the MPAP [Figure 4] and baseline oxygen saturation were the most independent predictors of the FC in patients with pulmonary arterial hypertension (PAH)-CHD \( (P = 0.028 \text{ and} 0.049, \text{respectively}) \) [Table 3].

**Receiver operating characteristic curve analysis**
Receiver operating characteristic curve analysis was done to produce the cutoff points to predict patients with impaired FC (6MWT <330). The cutoff point for MPAP was >30 mmHg (area under the curve [AUC]: 0.85) with a sensitivity and specificity of 69.23% and 95.24%, respectively. The cutoff point for baseline saturation was < 94% (AUC: 0.852) with a sensitivity and specificity of 92.31% and 76.19%, respectively [Figure 4].

**Discussion**
Patients with PH-CHD have unfavorable prognosis and are usually underrepresented in the clinical trials with no available definite data regarding their risk assessment.

Since echocardiography is considered the basic investigation for diagnosis and follow-up patients with CHD, we thought to investigate the echocardiographic predictors of FC in patients with PH-CHD to noninvasively risk stratify them, identify patients with poor prognosis, and define patients who would benefit from extensive interventional programs such as rehabilitation programs and combined medical therapy.

We did not focus only on echocardiographic assessment of RV function like most of the previous studies, we also assessed...
the LV functions because it is anatomically and functionally connected to the RV, it shares with the RV IVS, and because it is equally surrounded by the pericardium.

We demonstrated that RVSP and MPAP values showed a moderate negative correlation with 6MWT. Similarly, the study performed by Gungor et al. demonstrated the same correlation between the RVSP value and 6MWT results.\[11\]

In our study, patients with impaired FC had significantly higher NYHA class. Kemal et al. performed a study on 92 patients with Group 1 and Group 4 PH, and they found that the 6MWD correlated well with NYHA class.\[12\] Furthermore, Demir and Küçükoğlu demonstrated that the distance covered in 6MWT significantly decreased in proportion to the severity of NYHA class,\[13\] and the same finding was demonstrated by the study of Miyamoto et al. in patients with primary PH.\[14\]

We did not find a significant difference between the LVEF, LVEDD, and ESD calculated in the two 6MWT groups. The same finding was found by Sunbul et al. in the study performed on 53 patients with CTEPH who were also subdivided into two groups according to the 6MW distance.\[15\] This indicates that these LV systolic parameters do not correlate with the patient’s FC.

In the present study, the E/A ratio and E/e’ ratio showed a significant negative correlation with the 6MWT, while e’ prime showed a significant positive correlation with 6MWT. Similarly, Gurudevan et al. clearly demonstrated that the diastolic function improved after thrombus endarterectomy in patients with CTEPH.\[16\] They attributed that the LV diastolic abnormalities reflected an underfilled LV rather than a true diastolic dysfunction, and this was mainly caused by the shift of the IVS or the compression of the LV by the markedly dilated RV. Similarly, Menzel et al. demonstrated normalization of diastolic function after pulmonary thrombus endarterectomy.\[17\]

Our results showed a significant difference between the LV MPI between our groups with higher value in the group with shorter 6MWT distance. LV MPI showed a significant negative correlation with 6MWT. This concurs with the findings found by Puri et al. on 53 patients with PAH.\[18\]

We also found that LV GLS had a highly significant moderate negative correlation with 6MWT, while LV GRS had a highly significant strong positive correlation with 6MWT. The LV GRS values demonstrated a significant difference between the two groups with a higher mean value in the group of FC more than 330 m. de Amorim Corrêa et al. performed a study on a total of 37 patients with PAH, and they found that the 6MWT distance in patients with PAH was less than the distance in their control group and LV GLS and GRS values were lower in patients than in controls.\[19\]

Although we did not find any significant difference in the LV GCS between our study groups, and we did not find a linear correlation between the LV GCS and 6MWT distance. we have noticed that eighty five percent of our study population had a LV GCS value less negative than the lower accepted value of −20.9%. Eighty-five percent of our study population showed LV GCS less negative than the lower accepted value of −20.9%. The same finding was found in the study performed by Ichikawa et al. on 44 patients with PH.\[20,21\] The reduction in the LV GCS strain in patients with PAH may indicate an incipient LV dysfunction. This can be explained by the effect of ventricular interdependence Ichikawa et al.\[21,22\]

| Table 1: The demographic and clinical data of the two subgroups |
|---|---|---|---|---|
| **Group 1 (6MWT <330 m), n=21** | **Group 2 (6MWT ≥330 m), n=13** | Test value | **P** |
| **Age (years)** | Mean±SD | 27.19±14.26 | 18.04±13.06 | 1.877** | 0.070 |
| **Range** | 4–48 | 4.5–42 | | |
| **Gender (%)** | | | | |
| Female | 9 (42.9) | 10 (76.9) | 3.780* | 0.052 |
| Male | 12 (57.1) | 3 (23.1) | | |
| **Weight (kg)** | Mean±SD | 57.14±20.55 | 51.69±26.58 | 0.672** | 0.507 |
| **Range** | 15–82 | 19–85 | | |
| **Height (cm)** | Mean±SD | 149.33±26.96 | 138.46±30.72 | 1.084** | 0.287 |
| **Range** | 90–178 | 90–170 | | |
| **BSA (m²)** | Mean±SD | 1.48±0.38 | 1.3±0.48 | 1.156** | 0.256 |
| **Range** | 0.6–1.8 | 0.7–1.7 | | |
| **NYHA class (%)** | | | | |
| II | 8 (38.1) | 13 (100.0) | 13.029* | 0.000 |
| III | 13 (61.9) | 0 (0.0) | | |

BSA=Body surface area, SD=Standard deviation, NYHA=New York Heart Association, 6MWT=6-min walk test, * significant, ** non-significant
Table 2: Comparison between the echocardiographic data between the two groups

| Variables                              | Group type (mean±SD) | Paired t-test |
|----------------------------------------|----------------------|---------------|
|                                       | Group 1 (6MWT <330 m) | Group 2 (6MWT ≥330 m) | I   | P     |
| RV variables                           |                       |               |     |       |
| RV systolic pressure (mmHg)            | 87.8±22.79            | 60.0±19.38    | 3.642 | 0.001 |
| Mean pulmonary artery pressure (mmHg) | 47.1±12.92            | 33.2±10.76    | 3.243 | 0.003 |
| RV base diameter (cm)                  | 4.4±1.08              | 4.05±0.54     | 1.385 | 0.176 |
| Indexed RV base diameter (cm/m²)       | 2.97±0.81             | 3.26±1.09     | -0.889 | 0.381 |
| Indexed RV mid-diameter (cm/m²)        | 3.68±1.0              | 3.57±0.54     | 0.368 | 0.715 |
| RV longitudinal diameter (cm)          | 7.43±1.41             | 7.23±1.27     | 0.422 | 0.676 |
| Indexed RV longitudinal diameter (cm/m²)| 5.35±1.5             | 6.13±1.96     | -1.317 | 0.197 |
| RV outflow diameter (cm)               | 2.39±0.72             | 2.13±0.33     | 1.223 | 0.23  |
| Indexed RV outflow diameter (cm/m²)    | 1.75±0.67             | 1.88±0.72     | -0.512 | 0.612 |
| RA longitudinal dimension (cm)         | 4.77±1.09             | 4.55±1        | 0.593 | 0.558 |
| Indexed RA longitudinal dimension (cm/m²)| 3.46±1.2             | 3.9±1.37      | -0.975 | 0.337 |
| RA transverse dimension (cm)          | 4.37±1.33             | 3.74±0.91     | 1.499 | 0.144 |
| Indexed RA transverse dimension (cm/m²)| 3.18±1.24            | 3.2±1.22      | -0.055 | 0.957 |
| Inferior vena cava (cm)               | 1.45±0.34             | 1.25±0.25     | 1.882 | 0.069 |
| Indexed Inferior vena cava (cm/m²)    | 1.71±0.18             | 1.8±0.19      | 1.397 | 0.172 |
| Fractional area change (%)            | 37.07±5.54            | 40.92±4.77    | -2.074 | 0.046 |
| RV wall thickness (cm)                | 0.88±0.21             | 0.72±0.19     | 2.190 | 0.036 |
| RV global longitudinal strain (%)      | -19.33±3.55           | -22.53±5.23   | -2.127 | 0.041 |
| S of RV free wall (cm/sec)             | 10.62±1.83            | 11.38±1.71    | -1.215 | 0.233 |
| É of RV free wall (cm/sec)             | 11±2.28               | 12.08±1.98    | -1.405 | 0.170 |
| RV myocardial performance index        | 0.54±0.07             | 0.48±0.09     | 2.405 | 0.022 |
| LV variables                           |                       |               |     |       |
| EF by M-mode (%)                      | 63.23±6.54            | 66.85±4.65    | -1.732 | 0.093 |
| EF by Simpson’s method (%)             | 58.00±6.99            | 61.69±4.68    | -1.682 | 0.102 |
| LVEDD (cm)                             | 4.38±0.69             | 4.08±0.76     | 1.205 | 0.237 |
| Indexed LVEDD (cm/m²)                 | 3.06±0.81             | 3.23±0.94     | -0.571 | 0.572 |
| LVESD (cm)                             | 3.1±0.61              | 2.78±0.63     | 1.460 | 0.154 |
| Indexed LVESD (cm/m²)                 | 2.37±0.89             | 2.31±0.65     | 0.207 | 0.837 |
| E’ LV septal wall (cm/s)               | 10.52±2.86            | 12.31±1.6     | -2.053 | 0.048 |
| E’ LV lateral wall                     | 11.62±2.77            | 14.15±1.86    | -2.912 | 0.006 |
| E/A ratio                              | 0.95±0.28             | 1.24±0.26     | -3.033 | 0.005 |
| E’/e’                                  | 8.79±1.53             | 7.26±1.04     | 3.143 | 0.004 |
| LV myocardial performance index        | 0.51±0.08             | 0.42±0.06     | 3.440 | 0.002 |
| LV global longitudinal strain (%)      | -18.58±4.09           | -20.91±2.99   | 1.776 | 0.085 |
| LV global circumferential strain       | -14.08±7.2            | -15.75±11.1   | 0.536 | 0.596 |
| LV global radial strain                | 29.31±5.47            | 39.52±8.39    | -4.307 | 0.000 |
| Oxygen saturation                      |                       |               |     |       |
| Saturation (%) before                  | 89.86±6.39            | 95.85±2.61    | -3.203 | 0.003 |
| Saturation (%) after                   | 85.24±9.39            | 94.46±3.95    | -3.347 | 0.002 |
| Desaturation value                     | 4.62±3.46             | 1.38±1.66     | 3.143 | 0.004 |

TAPSE=Tricuspid annular plan systolic excursion, LVEDD=Left ventricle end-diastolic dimension, LVESD=Left ventricle end-systolic dimension, LV=Left ventricle, RV=Right ventricle, SD=Standard deviation, 6MWT=6-min walk test

Table 3: The cutoff points for the predictors of functional capacity in the whole study population

| Cutoff point | AUC | Sensitivity | Specificity | +PV | −PV |
|--------------|-----|-------------|-------------|-----|-----|
| MPAP >30     | 0.85| 69.23       | 95.24       | 90.0| 83.3|

MPAP=Mean pulmonary artery pressure, AUC=Area under the curve, PV=Area under the curve

In our study, a significantly lower RVFAC was found in patients with shorter 6MWT distance; FAC showed a significant positive correlation with 6MWT, while TAPSE, S’, and IVC showed a weak significant positive correlation with 6MWT; the RVFAC was related to survival in the study done by Ghio et al. on 59 patients with primary PH.[23]

In the present study, we demonstrated that the RVGLS showed a significant moderate negative correlation with 6MWT. The same finding was found in their study performed by Park et al.[24] on 34 patients with PAH. They found that RVGLS showed a significant correlation with FC assessed by 6MWT.[25]
Furthermore, Sunbul et al. found that patients with poorer FC by 6MWT had a significantly lower RVFAC and RVGLS than those with longer 6MWT distances. This was explained by the fact that the RV does not tolerate chronic pressure overload due to its thinner wall and higher compliance, which in turn leads to a gradual change in RV structure and function leading We found a significant difference between the two groups regarding the RVMPI values. These findings were concordant with the results found by Sunbul et al., who showed that patients with a shorter 6MWT distance had a significantly higher value of the RVMPI. We did not find a significant difference between the two study groups regarding the RA dimensions. Moreover, this concurs with the results reported by Sunbul et al.[15]

In the current study, multivariate analysis showed that the most independent predictor for the FC was the MPAP with cutoff value >30 mmHg Table 4. Sasayama et al.[26] Serino G, et al. demonstrated in their study on patients with PH that a regimen of treatment with bosentan for long term or for short term (2 years) using a dose of 125 mg twice daily for 12 weeks had led to significant improvement in their cardiopulmonary hemodynamics values including MPAP, and this was translated into improvement in their symptoms and FC.[2] and this was translated into improvement in their symptoms and FC.[2] Furthermore, Park et al. [24] had demonstrated that with pulmonary vasodilator therapy and reduction in the MPAP values, improvement in the clinical symptoms and 6MWT distance occurs.[25] Furthermore, Sims et al. [26] conducted a multivariate analysis on 362 patients with PH secondary to severe COPD and showed that patients with higher MPAP have a shorter distance of 6MWT.[27]

In the present study, the second most independent predictor of FC was the oxygen saturation. In accordance with our findings, the study involved 576 patients with PH due to COPD Casanova et al. who demonstrated that oxygen saturation and desaturation measured by pulse oximetry significantly correlated with distance achieved during the 6MWT.[2]

**Limitations and recommendations**

Our study was conducted on relatively small number of patients and in one center. Long-term follow-up is needed to confirm the correlation between the MPAP and 6MWD and survival in patients with PH-CHD.

**Conclusion**

Many right and left ventricular echocardiographic systolic and diastolic parameters showed correlations with the exercise capacity in patients with PH-CHD, however, we have found that the MPAP and the baseline oxygen saturation were the most independent noninvasive objective predictors of impaired FC in patients with PH-CHD. They can be used as a surrogate for survival and in risk stratification to identify the highest risk group of these patients.

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**Conflicts of interest**

There are no conflicts of interest.

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