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Quality of Life Outcomes in Patients with Pulmonary Hypertension Receiving Prostacyclin Therapy: Impact of Anxiety, Depression, Sociodemographic Characteristics, and Treatment-Related Factors

Prostasiklin Tedavisi Alan Pulmoner Hipertansiyon Hastalarında Yaşam Kalitesi Sonuçları: Anksiyete, Depresyon, Sosyodemografik Özellikler ve Tedaviye İlişkin Faktörlerin Etkisi

ABSTRACT

Objective: Despite advances in prostacyclin therapy, pulmonary hypertension (PH) continues to impair patients' quality of life (QoL). This study aimed to identify the clinical and psychological factors associated with QoL in patients receiving prostacyclin therapy.

Method: This cross-sectional study was conducted between July 2023 and September 2024 and included 58 patients with PH receiving prostacyclin therapy. Data were collected using a structured questionnaire assessing sociodemographic and disease-related characteristics. Symptom severity, anxiety, depression, and QoL were evaluated using the Pulmonary Arterial Hypertension Symptom Scale (PAHSS), the Hospital Anxiety and Depression Scale (HADS), and the EmPHasis-10 Questionnaire.

Results: The mean age of the patients was 48.89 ± 16.17 years, and 69% were female. Overall, 69% had at least one chronic comorbidity, 19% required continuous oxygen therapy, and the mean disease duration was 7.45 ± 6.84 years. The average duration of prostacyclin therapy was 28.03 ± 34.21 months. Mean scores were 71.52 ± 36.40 for PAHSS, 8.70 ± 5.23 for HADS-Anxiety, 7.82 ± 5.32 for HADS-Depression, and 30.05 ± 14.92 for EmPHasis-10. EmPHasis-10 scores showed moderate correlations with PAHSS, HADS-Anxiety, HADS-Depression, and 6-minute walk test (6MWT) scores. In multivariate analysis, age, PAHSS score, anxiety, depression, and vomiting explained 80% of the variance in EmPHasis-10 scores.

Conclusion: QoL was substantially impaired in patients with PH receiving prostacyclin therapy and was influenced by age, symptom severity, anxiety, depression, and vomiting.

Keywords: Depressive symptoms, prostacyclin therapy, pulmonary hypertension, quality of life, symptom burden

ÖZET

Amaç: Prostasiklin tedavisindeki ilerlemelere rağmen, pulmoner hipertansiyon (PH) hastaların yaşam kalitesini (QoL) olumsuz etkilemeye devam etmektedir. Bu çalışma, QoL ile ilişkili klinik ve psikolojik faktörleri belirlemeyi amaçlamaktadır.

Yöntem: Çalışma, Temmuz 2023 ile Eylül 2024 tarihleri arasında kesitsel olarak yürütüldü ve prostasiklin tedavisi alan 58 PH hastası çalışmaya dahil edildi. Veriler, sosyodemografik ve hastalığa ilişkin özellikleri değerlendiren yapılandırılmış bir anket kullanılarak toplandı. Semptom şiddeti, anksiyete, depresyon ve yaşam kalitesi; Pulmoner Arteriyel Hipertansiyon Semptom Ölçeği (PAHSS), Hastane Anksiyete ve Depresyon Ölçeği (HADS) ve EmPHasis-10 Anketi kullanılarak değerlendirildi.

Bulgular: Hastaların ortalama yaşı 48,89 ± 16,17 idi ve %69'u kadındı. Toplamda, hastaların %69'unda en az bir kronik komorbidite mevcuttu, %19'u sürekli oksijen tedavisine ihtiyaç duyuyordu ve ortalama hastalık süresi 7,45 ± 6,84 yıldı. Prostasiklin tedavisinin ortalama süresi 28,03 ± 34,21 aydı. Ortalama puanlar PAHSS için 71,52 ± 36,40, HADS-Anksiyete için 8,70 ± 5,23, HADS-Depresyon için 7,82 ± 5,32 ve EmPHasis-10 için 30,05 ± 14,92 idi. EmPHasis-10 skorları; PAHSS, HADS-Anksiyete, HADS-Depresyon ve 6 dakikalık yürüme testi (6DYT) skorları ile orta düzeyde ilişkiliydi. Çok değişkenli analizde yaş, PAHSS, anksiyete, depresyon ve kusma, EmPHasis-10 skorlarındaki varyansın %80'ini açıklıyordu.

ORIGINAL ARTICLE
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Sonuç: Prostasiklin tedavisi gören pulmoner hipertansiyon hastalarının yaşam kalitesinin düşük olduğu ve bunun yaş, semptom şiddeti, anksiyete, depresyon ve kusma gibi faktörlerden etkilendiği saptanmıştır.

Anahtar Kelimeler: Depresif semptomlar, prostasiklin tedavisi, pulmoner hipertansiyon, yaşam kalitesi, semptom yükü

Pulmonary hypertension (PH) is a progressive and complex chronic disease characterized by a mean pulmonary artery pressure > 20 mmHg at rest and may result from a variety of cardiac, pulmonary, or rheumatologic conditions.[1] PH is classified into five groups: pulmonary arterial hypertension (PAH, Group 1), PH due to left heart disease (Group 2), PH associated with lung disease or hypoxia (Group 3), PH due to pulmonary artery obstruction (Group 4), and PH with unclear or multifactorial mechanisms (Group 5).[2-4] PH is also categorized according to World Health Organization (WHO) functional class, which reflects the degree of limitation in physical activity.[5]

Patients with PH commonly experience symptoms such as dyspnea, fatigue, abdominal distension, and peripheral edema, all of which negatively affect quality of life.[6] As the disease progresses, particularly in patients with PAH, complications such as palpitations, chest discomfort, syncope, and severe dyspnea may develop.[7] Additional symptoms related to the structural and hemodynamic abnormalities of PH include hemoptysis, hoarseness, and wheezing.[4,8,9]

Treatment strategies guided by WHO functional class II–IV recommendations aim to reduce symptoms, improve functional capacity, and slow disease progression. Therapies targeting the prostacyclin pathway are used primarily in PAH to improve hemodynamic parameters, exercise tolerance, and overall symptom burden, making them essential components of PAH management.[10-13]

To maximize the benefits of prostacyclin therapy in PAH, treatment-related adverse effects must be carefully monitored and managed. Common side effects include headache and gastrointestinal symptoms, particularly nausea and vomiting, which may trigger vagal responses and negatively affect treatment tolerability and adherence.[13] Importantly, these adverse effects, together with the overall symptom burden, may impair not only physical health but also the psychological and social well-being of patients with PAH.[14]

Pulmonary hypertension is a complex cardiovascular disorder associated with diagnostic and therapeutic challenges, substantial medical and psychological burden, reduced quality of life, and a high prevalence of symptoms such as anxiety, depression, fatigue, and pain.[8,15,16] Collectively, these factors may adversely affect psychological health and contribute to the development of anxiety and depressive disorders, particularly among patients with PAH.[17]

A patient-centered, multidisciplinary approach is recommended for PH, and the European Society of Cardiology (ESC) and the European Respiratory Society (ERS) guidelines emphasize the importance of coordinated treatment and psychological support.[5] Individualized care strategies have also been highlighted as essential for patients with PAH.[18] Healthcare professionals therefore play a central role in PH management through comprehensive multidisciplinary care.[19] Their responsibilities include monitoring cardiopulmonary function, optimizing treatment, assessing treatment response and adherence, educating patients, and promoting physical activity and healthy lifestyle behaviors.[20] Multidisciplinary, nurse-led, guideline-based care has been shown to improve long-term survival and clinical outcomes in patients with PH, including those with chronic thromboembolic pulmonary hypertension (CTEPH).[19,20] Although these components are essential in PH management, the effects of symptom burden and prostacyclin-related adverse effects on patients' quality of life are unclear. Therefore, this study aimed to identify factors associated with quality of life in patients receiving prostacyclin therapy.

ABBREVIATIONS

BPA	Balloon pulmonary angioplasty
ERA	Endothelin receptor antagonist
ERS	European Respiratory Society
ESC	European Society of Cardiology
HADS	Hospital Anxiety Depression Scale
PAH	Pulmonary arterial hypertension
PAHSS	Pulmonary Arterial Hypertension Symptom Scale
PDE-5İ	Phosphodiesterase type 5 inhibitor
PEA	Pulmonary endarterectomy
PH	Pulmonary hypertension
QoL	Quality of life
SD	Standard deviations
WHO	World Health Organization

This study contributes to the literature by evaluating quality of life (QoL) in a prostacyclin-treated cohort receiving various treatment modalities, including oral, inhaled, intravenous, and subcutaneous therapies. In addition, validated Turkish versions of PAH-specific instruments were used to assess symptom burden and psychological status. This cross-sectional study aimed to identify factors affecting the QoL of patients with PH receiving prostacyclin therapy.

Materials and Methods

Patients and Study Protocol

The study population consisted of patients followed at the PH center of a training and research hospital in Istanbul. Data were collected between July 2023 and September 2024.

Sample size calculation was not performed, and all patients receiving prostacyclin therapy during the study period were included. In 2022, a total of 478 patients with PH were followed at the center, of whom 63 were receiving prostacyclin therapy. During the data collection period, five patients died. All patients meeting the inclusion criteria were enrolled, resulting in a final sample of 58 patients. Data were collected through face-to-face interviews conducted during routine follow-up visits, each lasting approximately 20–25 minutes.

According to the 2022 ESC/ERS guidelines, prostacyclin therapy is initiated following multidisciplinary evaluation by the PH team. In patients with Group 1 PH, oral or inhaled prostanoid agonists are added when low-risk status according to ESC risk stratification cannot be achieved despite combination therapy with an endothelin receptor antagonist (ERA) and a phosphodiesterase type 5 inhibitor (PDE-5i). Patients classified as intermediate-high or high risk receive parenteral prostanoid therapy. In Group 4 PH patients with residual or recurrent PH following pulmonary endarterectomy (PEA) and/or balloon pulmonary angioplasty (BPA), parenteral prostanoid therapy is initiated. For patients in whom definitive classification between Group 1 and Group 3 PH is not possible, inhaled prostanoid therapy with a lower systemic adverse-effect profile may be administered when hemodynamic impairment is severe.

Patients aged ≥ 18 years who were receiving prostacyclin therapy (oral, subcutaneous, inhaled, or intravenous) according to these indications were included in the study. Patients who had been receiving treatment for less than three months were excluded.

The adequacy of the sample size for multivariate linear regression was evaluated according to the number of predictor variables included in the model. With a total of 58 participants and five independent variables, the study met the criterion of at least 10 observations per predictor, indicating acceptable model stability. In addition, the model demonstrated high explanatory power (R^2 = 0.805), corresponding to a very large effect size.

To further support sample size adequacy, a post hoc power analysis was conducted using G*Power version 3.1.9.7. The statistical power of the linear regression model including five independent variables was calculated as 0.961 (f^2 = 0.40, α = 0.05, n = 58). These findings indicate that the study has sufficient statistical power to detect the observed effect size.

Data Collection Tools

Sociodemographic and Disease-Related Characteristics Form

This form was developed by the researchers based on a review of the relevant literature.[16,17,21] It consists of 17 items assessing patients' sociodemographic characteristics and disease-related clinical features.

Pulmonary Arterial Hypertension Symptom Scale (PAHSS)

Developed to identify core health problems reported by individuals with PAH, this scale provides a structured method for summarizing symptom patterns. Studies have demonstrated that both the original and Turkish versions provide reliable assessment of symptom severity.[22,23] Responses to 17 items are summed to generate a total score reflecting symptom severity. In the present study, the scale also demonstrated good reliability.

Hospital Anxiety and Depression Scale (HADS)

The HADS is a brief instrument used to assess anxiety and depressive symptoms in adults.[24] The Turkish version has been validated and shown to have good reliability. The questionnaire contains 14 items equally divided into anxiety and depression subscales. Each subscale is scored from 0 to 21, with cutoff values of 7/8 for anxiety and 10/11 for depression. Scores above these thresholds indicate clinically significant symptoms. In the Turkish validation study, Cronbach's alpha coefficients were 0.85 for anxiety and 0.77 for depression. In our study, Cronbach's alpha coefficients were 0.88 for both subscales, indicating strong internal consistency.[25]

EmPHasis-10

The EmPHasis-10 questionnaire was developed to assess QoL in patients with PH.[26] The Turkish version has been validated and shown to be reliable. The questionnaire consists of 10 items rated on a 6-point Likert scale. Scores range from 0 to 50, with higher scores indicating poorer QoL. In the Turkish validation study, the Cronbach's alpha coefficient was 0.98, whereas in the present study it was 0.95, indicating excellent interval consistency.[27]

Ethics Committee Approval

Ethical approval was obtained from the Acıbadem Mehmet Ali Aydınlar University Medical Research Evaluation Ethics Committee (Approval Number: 2023/10, Date: 16.06.2023). Institutional permission was also obtained. All participants provided written and verbal informed consent after receiving information about the study. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). Demographic and descriptive variables are presented as numbers (n) and percentages (%). Skewness and kurtosis values for HADS, PAHSS, and EmPHasis-10 scores ranged between -1.5 and + 1.5, indicating approximate normal distribution.[28] Accordingly, parametric tests were used, and variables are presented as mean ± standard deviation (SD). Differences between groups were analyzed using Student's t-test and one-way analysis of variance. Correlations between variables were analyzed using Pearson correlation analysis. A backward linear regression analysis was conducted to identify factors affecting QoL. Statistical significance was set at $P < 0.05$, with all analyses evaluated at a 95% confidence interval.

Results

Table 1 presents the sociodemographic and disease-related characteristics of the participants (n = 58). The mean age was 48.89 ± 16.17 years, and 69% of the participants were female. Most participants were married (72.4%), and 46.6% had completed high school education or higher. The majority were unemployed (69%), and 84.5% reported that their income was equal to their expenses. Regarding clinical characteristics, the mean duration since diagnosis was 7.45 ± 6.84 years, and the mean duration of prostacyclin therapy was 28.03 ± 34.21 months. Mean oxygen saturation was 93.19 ± 6.69%, mean pro–B-type natriuretic peptide (pro-BNP) level was 800.26 ± 1124.80 pg/mL, mean ejection fraction was 58.59 ± 7.14%, and the mean

Table 1. Sociodemographic and disease-related characteristics of the participants (n = 58)

Characteristics	Mean ± SD / n	Range / %
Age (years)	48.89 ± 16.17	20–84
Duration of diagnosis (years)	7.45 ± 6.84	1–31
Duration of prostacyclin therapy (months)	28.03 ± 34.21	6–204
Saturation (%)	93.19 ± 6.69	70–99
Pro-BNP (pg/mL)	800.26 ± 1124.80	10–4370
Left ventricular ejection fraction (%)	58.59 ± 7.14	35–65
6-minute walk test (m)	310.37 ± 166.64	0–515
	n	**%**
Sex		
Female	40	69
Male	18	31
Marital status		
Married	42	72.4
Single	16	27.6
Educational status		
Illiterate	8	13.8
Primary education	23	39.6
High school and above	27	46.6
Economic status		
Income less than expenditure	9	15.5
Income equal to expenditure	49	84.5
Employment status		
Employed	18	31
Unemployed	40	69
Comorbid chronic disease		
Yes	36	62.1
No	22	37.9
Therapy type		
Selexipag (oral)	40	69
Epoprestenol (IV)	2	3.4
Iloprost (inhaled)	14	24.2
Treprostinil (subcutaneous)	2	3.4
Continuous oxygen therapy		
Yes	11	19
No	47	81
PH group		
Group 1	44	75.9
Group 3	7	12.1
Group 4	7	12.1
WHO functional classification		
Stage II	20	34.5
Stage III	28	48.3
Stage IV	10	17.2

WHO, World Health Organization; PH, Pulmonary hypertension; Pro-BNP, Pro-B-type natriuretic peptide; 6MWT, 6-minute walk test; EF, Ejection fraction.

Table 2. Distribution of mean scores for the PAHSS, HADS, and EmPHasis-10 (n = 58

Scales	Mean ± SD	Range
Pulmonary Arterial Hypertension Symptom Scale (PAHSS)	71.52 ± 36.40	3–145
Shortness of breath with exertion	7.64 ± 2.68	0–10
Fatigue	7.00 ± 2.59	0–10
Rapid heartbeat / palpitations	5.81 ± 3.49	0–10
Shortness of breath while lying down	5.55 ± 3.37	0–10
Sleep disturbance	5.21 ± 3.81	0–10
Awakening with shortness of breath	4.88 ± 3.76	0–10
Shortness of breath at rest	4.76 ± 3.53	0–10
Chest pain / discomfort	4.29 ± 3.41	0–10
Loss of appetite	4.07 ± 3.35	0–10
Abdominal bloating	3.93 ± 3.41	0–10
Nausea	3.86 ± 3.53	0–10
Dizziness / lightheadedness	3.66 ± 2.81	0–10
Foot / ankle swelling	3.59 ± 3.23	0–10
Cough	2.53 ± 2.96	0–10
Cold, numb, painful hands or feet (Raynaud's phenomenon)	1.98 ± 3.40	0–10
Hoarseness	1.62 ± 2.62	0–10
Fainting / syncope	1.16 ± 2.15	0–9
EmPHasis-10	30.05 ± 14.92	2–50
HADS-anxiety	8.70 ± 5.23	0–21
HADS-depression	7.82 ± 5.32	0–21
	n	**%**
HADS-anxiety (presence of anxiety)		
≥ 8 points (yes)	34	58.6
<8 points (no)	24	41.4
HADS-depression (presence of depression)		
≥ 11 points (yes)	17	29.3
< 11 points (no)	41	70.7

HADS, Hospital Anxiety & Depression Scale.

6-minute walk test (6MWT) distance was 310.37 ± 166.64 meters. Comorbid chronic diseases were present in 62.1% of participants. Most patients were receiving oral selexipag therapy (69%), and 19% required continuous oxygen therapy. Group 1 PH accounted for 75.9% of the study population, and nearly half of the participants were classified as WHO functional class III (48.3%).

Table 2 presents the mean PAHSS, HADS-Anxiety (HADS-A), HADS-Depression (HADS-D), and EmPHasis-10 scores of the participants. Mean scores were 71.52 ± 36.40 for PAHSS, 8.70 ± 5.23 for HADS-Anxiety, 7.82 ± 5.32 for HADS-Depression, and 30.05 ± 14.92 for EmPHasis-10. According to the PAHSS, the most severe symptoms were shortness of breath on exertion, fatigue, palpitations, and shortness of breath while lying down. Based on HADS cutoff values, 58.6% of participants had anxiety symptoms, and 29.3% had depression.

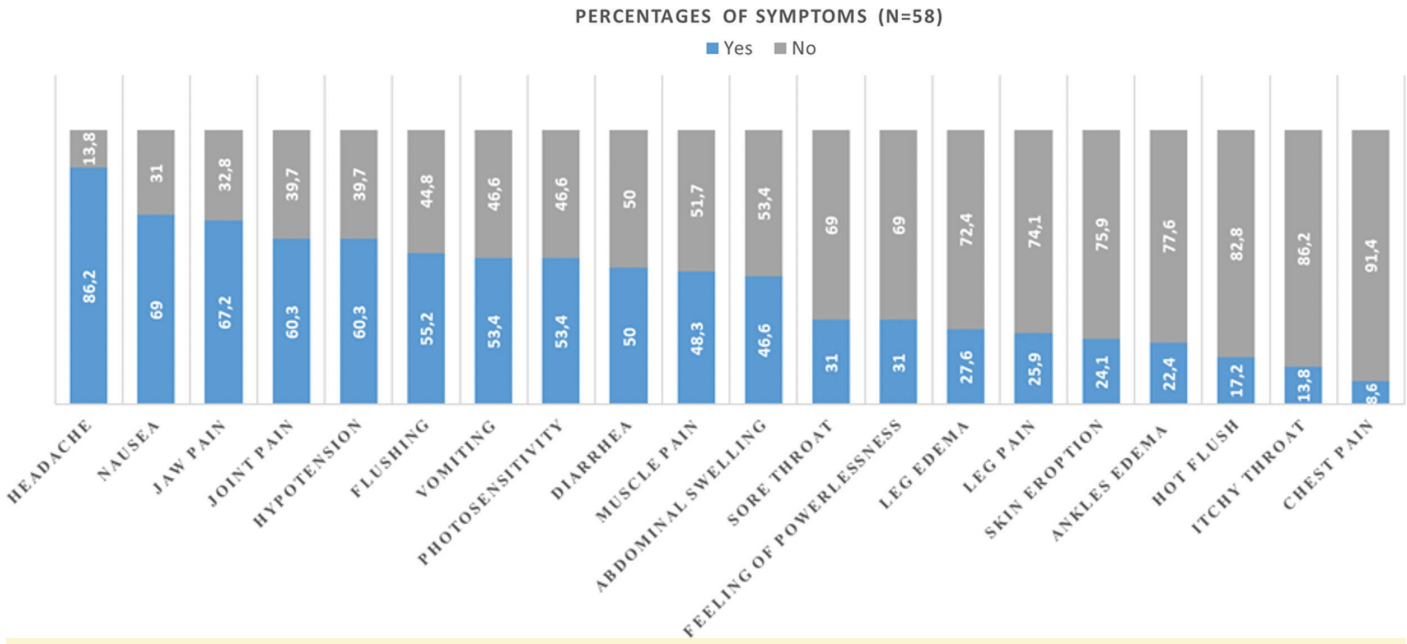

Figure 1. Distribution of symptoms experienced by patients receiving prostacyclin therapy.

Figure 1 illustrates the distribution of symptoms experienced by participants in relation to prostacyclin therapy. Symptoms reported by more than 50% of patients related to prostacyclin therapy included headache, nausea, jaw pain, hypotension, flushing, vomiting, and photosensitivity.

Table 3 presents PAHSS, EmPHasis-10, and HADS scores according to participants' sociodemographic and clinical characteristics. Single participants had significantly lower HADS-D (P = 0.03) and EmPHasis-10 (P = 0.006) scores than married participants. Illiterate participants had higher PAHSS (P = 0.006) and EmPHasis-10 (P = 0.001) scores than participants with a high school education or higher. Employment status was significantly associated with all scale scores, with employed participants reporting lower scores (PAHSS, P = 0.04; HADS-A, P = 0.01; HADS-D, P < 0.001; EmPHasis-10, P = 0.002). Participants without comorbid chronic diseases had lower PAHSS (P < 0.001), HADS-A (P = 0.02), HADS-D (P = 0.003), and EmPHasis-10 (P < 0.001) scores compared with those with comorbidities. Functional class significantly affected all scale scores (PAHSS, P = 0.002; HADS-A, P = 0.01; HADS-D, P = 0.01; EmPHasis-10, P < 0.001), with patients in functional classes III and IV demonstrating higher scores than those in class II. Continuous oxygen therapy was also associated with higher scores across all measures (PAHSS, P = 0.004; HADS-A, P < 0.001; HADS-D, P = 0.01; EmPHasis-10, P < 0.001), indicating greater symptom burden among patients receiving oxygen therapy.

Table 4 presents the correlation analysis between participant characteristics and PAHSS, HADS, and EmPHasis-10 scores. EmPHasis-10 scores were significantly correlated with PAHSS (r = 0.72; P < 0.001), HADS-Anxiety (r = 0.61; P < 0.001), and HADS-Depression (r = 0.57; P < 0.001). PAHSS scores were positively correlated with both HADS-Anxiety (r = 0.39; P = 0.03) and HADS-Depression (r = 0.28; P = 0.03). Age was positively correlated with all scores (PAHSS: r = 0.32, P = 0.01; EmPHasis-10: r = 0.60, P < 0.001; HADS-Anxiety: r = 0.43, P = 0.001; HADS-Depression: r = 0.45, P < 0.001). Oxygen saturation was negatively correlated with PAHSS (r = -0.30; P = 0.02) and EmPHasis-10 (r = -0.28; P = 0.03). The 6MWT distance was negatively correlated with PAHSS (r = -0.50; P < 0.001), EmPHasis-10 (r = -0.60; P < 0.001), HADS-Anxiety (r = -0.61; P < 0.001), and HADS-Depression (r = -0.49; P < 0.001). No significant associations were found between pro-BNP or ejection fraction and EmPHasis-10 scores.

Table 5 presents the linear regression analysis of factors associated with EmPHasis-10 scores. The backward regression model identified age, PAHSS score, HADS-A score, HADS-D score, and prostacyclin-related vomiting as significant predictors. The model was statistically significant (F = 42.892; P < 0.001) and explained 80.5% of the variance in EmPHasis-10 scores (R^2 = 0.805). Older age, higher PAHSS scores, anxiety, depression, and prostacyclin-related vomiting were all independently associated with higher EmPHasis-10 scores.

Discussion

In this study, patients with PH receiving prostacyclin therapy had impaired QoL and moderate levels of PAH symptom severity. Anxiety and depression were present in 58.6% and 29.3% of patients, respectively. Factors associated with QoL included marital status, educational level, employment status, chronic comorbidities, PH functional class, and continuous oxygen therapy use. Higher levels of anxiety and depression, older age, greater symptom severity, lower oxygen saturation, and shorter 6MWT distance were associated with poorer QoL. Furthermore, age, symptom severity, anxiety, depression, and prostacyclin-related vomiting explained 80% of the variance in QoL scores, with QoL worsening as age and symptom severity increased and among patients experiencing anxiety, depression, or vomiting.

Table 3. Comparison of EmPHasis-10, PAHSS, and HADS scores according to sociodemographic and disease-related characteristics of the participants (n = 58)

Characteristics	PAHSS	HADS-anxiety	HADS-depression	EmPHasis-10
Sex				
Female (n = 40)	72.50 ± 37.29	8.82 ± 5.28	7.45 ± 5.21	28.55 ± 14.53
Male (n = 18)	69.33 ± 35.40	8.44 ± 5.24	8.66 ± 5.60	33.39 ± 15.63
Statistical analysis				
t	0.304	0.254	−0.803	−1.146
P	0.76	0.80	0.42	0.26
Marital status				
Married (n = 42)	75.38 ± 36.88	9.26 ± 5.56	8.73 ± 5.54	32.98 ± 15.24
Single (n = 16)	61.38 ± 34.15	7.25 ± 4.02	5.43 ± 3.88	22.38 ± 11.12
Statistical analysis				
t	1.318	1.317	2.179	2.910
P	0.19	0.19	**0.03**	**0.006**
Educational status				
Illiterate[a] (n = 8)	97.63 ± 19.73	9.50 ± 4.56	8.00 ± 6.48	44.50 ± 8.73
Primary education[b] (n = 23)	79.87 ± 35.44	10.26 ± 6.00	9.52 ± 6.30	32.48 ± 14.71
High school and above[c] (n = 27)	56.67 ± 35.16	7.14 ± 4.35	6.33 ± 3.50	23.70 ± 13.15
Statistical analysis				
F	5.723	2.420	2.339	8.123
P	**0.006 (a > c)**	0.98	0.10	**0.001 (a > c)**
Economic status				
Income less than expenditure (n = 9)	92.44 ± 31.86	10.88 ± 3.85	8.11 ± 6.71	37.22 ± 15.72
Income equal to expenditure (n = 49)	67.67 ± 36.15	8.30 ± 5.38	7.77 ± 5.10	28.73 ± 14.55
Statistical analysis				
t	1.920	1.372	0.172	1.589
P	0.06	0.17	0.86	0.11
Employment status				
Employed (n = 18)	57.33 ± 41.88	6.11 ± 4.43	4.22 ± 3.17	21.33 ± 14.34
Unemployed (n = 40)	77.90 ± 32.21	9.87 ± 5.18	9.45 ± 5.32	33.98 ± 13.59
Statistical analysis				
t	-2.045	-2.667	-4.645	-3.221
P	**0.04**	**0.01**	**<0.001**	**0.002**
Comorbid chronic disease				
Yes (n = 36)	86.44 ± 32.71	9.94 ± 5.41	9.25 ± 5.78	36.69 ± 13.21
No (n = 22)	47.09 ± 28.39	6.68 ± 4.29	5.50 ± 3.44	19.18 ± 10.65
Statistical analysis				
t	4.666	2.399	3.092	5.252
P	**<0.001**	**0.02**	**0.003**	**<0.001**
Functional classification				
Class II[a] (n = 20)	50.05 ± 31.58	6.25 ± 3.73	5.20 ± 3.17	18.15 ± 9.82
Class III[b] (n = 28)	80.31 ± 31.66	9.48 ± 5.26	8.65 ± 5.47	36.10 ± 13.35
Class IV[c] (n = 10)	90.89 ± 41.35	11.66 ± 6.14	11.00 ± 6.46	37.00 ± 13.83
Statistical analysis				
F	6.721	4.444	5.004	14.243
P	**0.002 (b > a; c > a)**	**0.01 (c > a)**	**0.01 (c > a)**	**<0.001 (b > a; c > a)**
Continuous oxygen therapy				
Yes (n = 11)	99.55 ± 28.89	14.54 ± 5.20	12.63 ± 6.28	44.09 ± 9.92
No (n = 47)	64.96 ± 35.05	7.34 ± 4.23	6.70 ± 4.37	26.77 ± 14.01
Statistical analysis				
t	3.034	4.860	2.965	3.868
P	**0.004**	**<0.001**	**0.01**	**<0.001**

Educational status: a = Illiterate, b = Primary education, c = High school and above. Functional classification: a = Class II, b = Class III, c = Class IV; t: Student's t-test; F: One-way analysis of variance (ANOVA); PAHSS, Pulmonary Arterial Hypertension Symptom Scale; HADS, Hospital Anxiety & Depression Scale.

Table 4. Correlations between participant characteristics and EmPHasis-10, PAHSS, and HADS scores (n = 58)

Scales and characteristics	PAHSS	EmPHasis-10	HADS-anxiety	HADS-depression
EmPHasis-10				
r	0.72	–	0.61	0.57
P	**< 0.001**	–	**< 0.001**	**< 0.001**
HADS-anxiety				
r	0.39	0.61	–	0.73
P	**0.03**	**< 0.001**	–	**< 0.001**
HADS-depression				
r	0.28	0.57	0.73	–
P	**0.03**	**< 0.001**	**< 0.001**	–
Age				
r	0.32	0.60	0.43	0.45
P	**0.01**	**< 0.001**	**0.001**	**< 0.001**
Saturation				
r	-0.30	-0.28	-0.08	-0.06
P	**0.02**	**0.03**	0.51	0.63
Pro-BNP				
r	0.20	0.20	-0.08	0.08
P	0.13	0.13	0.55	0.54
Ejection fraction				
r	-0.01	0.002	0.27	0.22
P	0.91	0.98	**0.04**	0.09
6-minute walk test				
r	-0.50	-0.60	-0.61	-0.49
P	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**

PAHSS, Pulmonary Arterial Hypertension Symptom Scale; HADS, Hospital Anxiety & Depression Scale.

Table 5. Effects of participant characteristics, anxiety, depression, and PAHSS scores on EmPHasis-10 scores (n = 58)

Independent variables	B	SEB	t	P	95% CI	
Age	0.205	0.067	3.063	**0.003**	[0.071–0.339]	
PAHSS	0.247	0.029	8.617	**< 0.001**	[0.189–0.304]	**F = 42.892**
HADS-anxiety (ref: non-anxious)	6.417	2.126	3.08	**0.004**	[2.151–10.683]	**P < 0.001**
HADS-depression (ref: non-depressive)	5.214	2.261	2.306	**0.025**	[0.677–9.750]	**R = 0.897**
Vomiting (ref: not vomiting)	7.559	1.935	3.905	**< 0.001**	[3.675–11.443]	**R^2 = 0.805**

Linear regression analysis using the backward model. PAHSS, Pulmonary Arterial Hypertension Symptom Scale; HADS, Hospital Anxiety & Depression Scale; CI: Confidence interval.

Pulmonary hypertension symptoms are primarily associated with right ventricular dysfunction, with shortness of breath being the most prominent symptom, even during mild exertion.[5] Limitations in physical activity, shortness of breath, and fatigue may impair patients' ability to perform daily activities and meet basic self-care needs, thereby contributing to reduced QoL. Low energy levels and sleep disturbances may further exacerbate these limitations, highlighting the importance of effective symptom-management interventions.[29-31]

Although PH treatments improve symptoms and slow disease progression, treatment-related adverse effects and the complexity of treatment regimens may lead to poor adherence or treatment discontinuation, negatively affecting both QoL and clinical outcomes.[32] Therapies targeting the prostacyclin pathway provide substantial clinical and survival benefits in PH; however, they are also associated with a challenging adverse-effect profile.[11] During prostacyclin therapy, patients are closely monitored by nurses and physicians for treatment-related adverse effects.

The most commonly reported adverse effects in the present study were headache, flushing, nausea, vomiting, and diarrhea, most of which were mild to moderate in severity. Depending on the type and severity of these adverse effects, both pharmacological and non-pharmacological interventions are recommended to

support symptom management. Patients may experience more pronounced adverse effects during the dose-titration phase of prostacyclin therapy; however, these effects can largely be managed through close monitoring by physicians and nurses.[33,34] Patients with low socioeconomic status may initiate treatment later and experience poorer health outcomes, possibly because the disease progresses to more advanced stages before treatment begins.[35,36] Additionally, the financial burden associated with PH treatment may indirectly contribute to higher mortality by limiting treatment access and adherence.[37,38] Previous studies have shown that low socioeconomic status negatively affects survival in patients with PAH.[39]

Chronic comorbidities frequently observed in patients with PH may significantly influence disease prognosis and treatment response. Cardiovascular and pulmonary comorbidities are associated with increased symptom burden and mortality, and the prognostic significance of comorbidity burden on clinical outcomes has been emphasized.[40,41] Regarding functional capacity, significant associations have been reported between 6MWT distance, oxygen saturation, and QoL. In a multicenter study conducted at centers treating the majority of PAH patients in the United Kingdom, EmPHasis-10 scores demonstrated a moderate correlation with 6MWT distance, consistent with the findings of the present study.[42] Furthermore, reduced 6MWT distance in patients with PH has been associated with poorer functional status and adverse clinical outcomes, both of which are strongly related to increased symptom burden and impaired health-related QoL.[6,43,44]

The challenges associated with both the disease and treatment processes have a substantial impact on the mental health of patients with PH.[16,17] A meta-analysis of 24 studies reported a pooled prevalence of 37.1% for anxiety and 28% for depression among patients with PH.[21] Numerous studies have demonstrated that anxiety and depression are common in PH and negatively affect health-related QoL.[10,21,45,46,47] Anxiety and depression levels were found to be higher in patients with comorbidities, those requiring continuous oxygen therapy, and those with advanced functional class. Increasing levels of anxiety and depression were also associated with greater symptom burden and poorer QoL.[45] A study evaluating EmPHasis-10 scores in[1,745] patients with PAH over a three-year period demonstrated that these scores are independently associated with QoL and provide important prognostic information regarding patients' future health status and risk profile. This strong association may reflect the close relationship between symptom burden and PH severity. Accordingly, the EmPHasis-10 questionnaire may serve not only as a measure of QoL in patients with PH but also as a valid clinical outcome and prognostic indicator in routine practice.[40,48]

Prostacyclin therapy is frequently associated with vomiting and other gastrointestinal adverse effects, which may negatively affect nutritional status and health-related QoL.[12,33] These symptoms were also among the most commonly reported adverse effects in the present study.

The cross-sectional design of the study, the lack of baseline (pre-prostacyclin) symptom and QoL data, and the relatively small sample size from a single center may limit causal interpretation and generalizability of the findings.

Limitations

This study did not include baseline data on symptom frequency, symptom severity, or quality of life prior to prostacyclin therapy; therefore, pre- and post-treatment comparisons could not be performed. Although treatment-related adverse effects were recorded, their frequency and severity were not systematically assessed, which may have limited a more comprehensive evaluation of their impact on QoL. In addition, the absence of detailed hemodynamic parameters, such as mean pulmonary artery pressure (mPAP) and pulmonary vascular resistance (PVR) obtained by right heart catheterization, limits the clinical applicability of the findings. The cross-sectional design prevented determination of causal relationships among symptom burden, psychological status, and QoL, and the findings may not be generalizable to the broader PH population because of the sample-specific nature of the study. Furthermore, differences in QoL according to the route of prostacyclin administration (oral, inhaled, or parenteral), as well as associations with hemodynamic and echocardiographic parameters, were not evaluated. These limitations should be considered when interpreting the findings and applying them to broader clinical practice.

Conclusion

Patients with pulmonary hypertension receiving prostacyclin therapy experience impaired QoL, which is influenced by factors such as age, symptom severity, anxiety, depression, and vomiting. Vomiting, a common adverse effect of prostacyclin therapy, may substantially impair daily functioning and overall QoL. Routine assessment and effective management of treatment-related adverse effects, particularly gastrointestinal symptoms, may improve treatment adherence and enhance patient QoL.

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