Functional class and health-related quality of life in patients with pulmonary arterial hypertension associated with congenital heart disease: Findings from a real-world study in the US

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INTRODUCTION

- Pulmonary arterial hypertension (PAH) is a progressive, incurable complication of some forms of congenital heart disease (CHD), imposing a high patient burden and impact on daily life, particularly as the disease progresses.
- Prevalence of PAH has been estimated to be between 5 and 10% in CHD patients.[1]
- Results of PAH clinical trials, such as the SERAPHIN[2] trial of macitentan, are helping increase the understanding of the positive impact of drug treatment on patients' health related quality of life (HRQoL).
- However, there is a lack of patient reported data on the impact of PAH-CHD across different stages of the disease, as categorised by New York Heart Association Functional Class (NYHA FC), a measure of PAH disease severity ranging from FC I, no limitation of usual activity to FC IV, unable to perform any physical activity.

Aim

- **This study aimed to understand the relationship between functional class (FC) and HRQoL in PAH-CHD patients across the United States (US) in a real-world setting.**

METHODS

- Data were drawn from the Adelphi PAH-CHD Disease-Specific Programme™ (DSP)[3], a point-in-time survey of pulmonologists and cardiologists and their consulting PAH-CHD patients in the US, conducted between November 2021 and May 2022. Physicians returned data on 1-2 consecutively consulting patients.
- A subset of the same patients voluntarily completed the 5-level version of the EuroQol 5-dimension (EQ-5D-5L) instrument which captured two measures of HRQoL: EQ-5D-visual analogue scale (EQ-5D-VAS, range 0-100 with higher scores indicating a better health state) and EQ-5D utility score (range 0-1 with higher scores indicating a greater quality of life).[4,5] These patients also completed the emPHasis-10 [6], a disease specific measure of HRQoL (range 0-50, higher scores indicating poorer HRQoL).
- Analyses were generated by the overall population and by physician-reported FC status. Patients were split into FC class I and class II/III (due to lower base sizes). T-tests were utilized to compare HRQoL scoring across FC. A bivariate linear regression was used to explore the relationship between hospitalisations and HRQoL scores. Data are shown as mean and standard deviation or n number and % of base.
- Pearl IRB exemption determination was granted on 11/16/2021 (Protocol #21-ADRW-125).

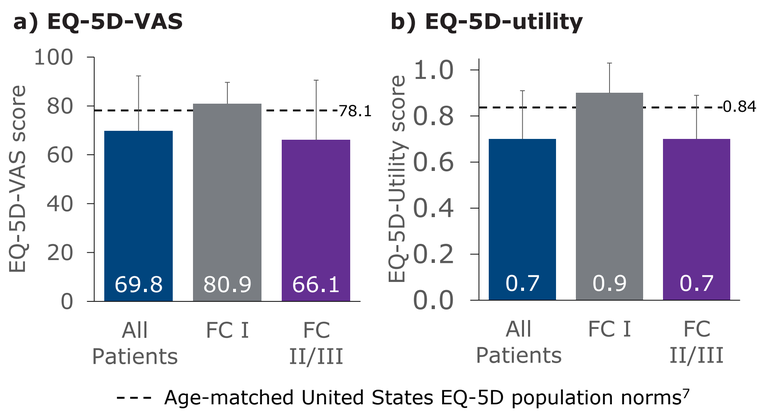
RESULTS

Table 1. Physician-reported characteristics

	All patients (n=56)	FC I (n=14)	FC II/III (n=42)
Patient age, mean (sd)	38.2 (17.6)	40.3 (13.0)	37.5 (19.0)
Patient sex, n (%)			
Male	39 (70)	11 (79)	28 (67)
CHD subtype, n (%)			
Eisenmenger syndrome	5 (9)	-	5 (12)
PAH associated with systemic-to-pulmonary shunts	9 (16)	1 (7)	8 (19)
PAH with small/coincidental defects	1 (2)	1(7)	-
PAH after corrective cardiac surgery	24 (43)	7 (50)	17 (40)
Palliated single ventricle	17 (30)	5 (36)	12 (29)
NYHA Functional Classification, n (%)			
Class I – No limitation of usual physical activity	14 (25)	14 (100)	-
Class II – Mild limitation of physical activity	38 (68)	-	38 (90)
Class III – Marked limitation of physical activity	4 (7)	-	4 (10)
Class IV – Unable to perform any physical activity	-	-	-
BMI, mean (sd)	26.3 (4.8)	23.2 (2.8)	27.3(4.9)
Ethnicity, n (%)			
White/Caucasian	45 (80	13 (93)	32 (76)
African American	7 (12)	-	7 (17)
Hispanic/Latino	2 (4)	-	2 (5)
Other	2 (4)	1 (7)	1 (2)

Body mass index, BMI; congenital heart disease, CHD; New York Heart Association, NYHA; pulmonary arterial hypertension, PAH; standard deviation, sd.

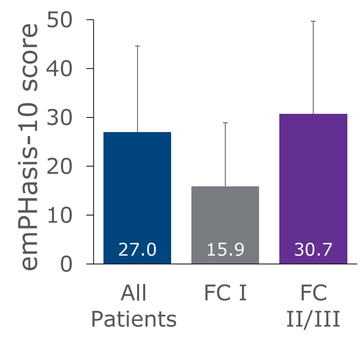
Figure 1. EQ-5D-5L health related quality of life measures



--- Age-matched United States EQ-5D population norms[7]

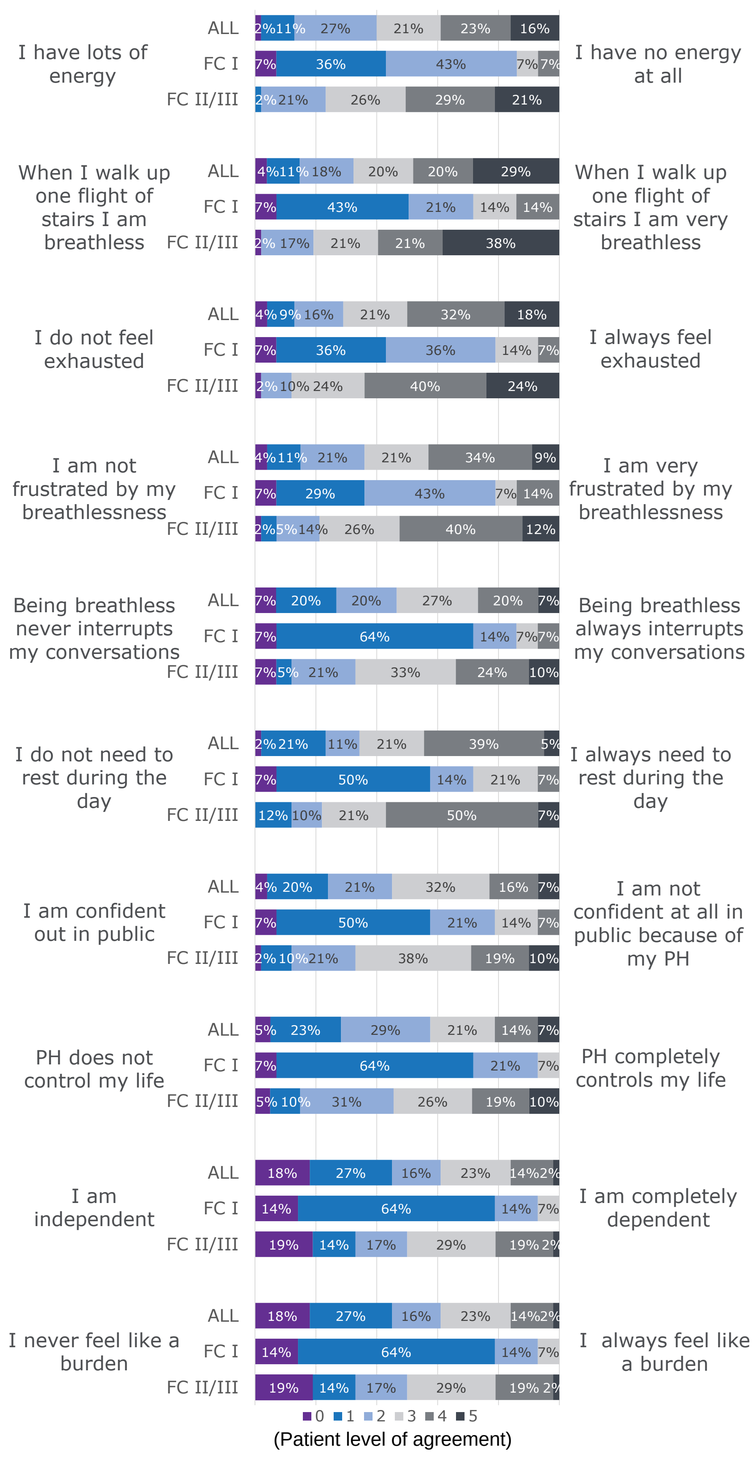
In both the EQ-5D-VAS (Figure 1a) and EQ-5D-utility scores (Figure 1b), there was a significant association of FC with quality of life (p=0.03 and p<0.0001, respectively). Patients with higher FC reported worse quality of life, which was notably below matched population norms for these measures.

Figure 2. emPHasis-10 health-related quality of life measure



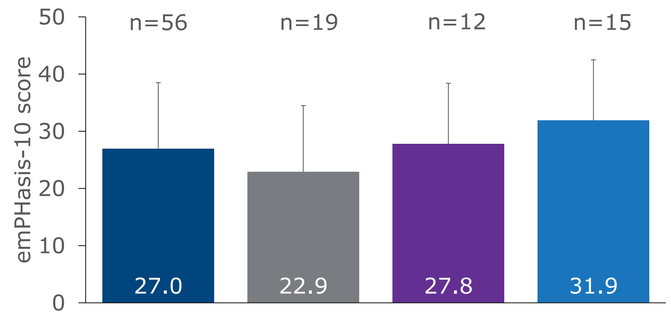
The PAH-specific emPHasis-10 measure also showed significantly worse HRQoL for those with a higher FC (p<0.0001). This difference was larger than the reported minimally important difference (MID) of 6.0 points[8] (Figure 2).

Figure 3. emPHasis 10 breakdown



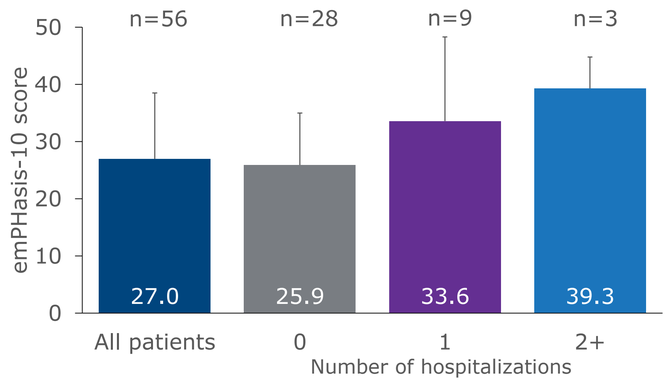
Those with FC II/III PAH-CHD frequently report being adversely affected to a large degree by their disease across a wide range of areas of daily life (Figure 3).

Figure 4. Association of time to diagnosis on health-related quality of life



Patients who had a longer time between first symptoms and a diagnosis of PAH reported worse current HRQoL, as measured on the emPHasis-10 scale (Figure 4).

Figure 5. Association of PAH-related hospitalization number on health-related quality of life



Note: number of hospitalizations not known for all patients

Higher numbers of PAH-related hospitalizations were significantly correlated with worse emPHasis-10 scores (r^2=0.17, p<0.0001), with each additional hospitalization being associated with a worsening of 6.3 points, more than the MID of 6.0 points (Figure 5).

CONCLUSIONS

- **HRQoL burden increases with higher FC classification, showing differences larger than the reported MID**
- **A longer time to diagnosis and a higher number of PAH-related hospitalizations were associated with poorer HRQoL**
- **Results demonstrate the importance of regular HRQoL assessment across the PAH-CHD disease trajectory**
- **Ongoing inclusion of HRQoL measures, as an end point in clinical trials, will help improve the understanding of drug therapy and their impact on patient's QoL**

LIMITATIONS

- This DSP survey consisted of patients with a physician-confirmed diagnosis of PAH-CHD, diagnosis via right heart catheterization was not required for inclusion in the survey. It is therefore possible that included patients may have had a PAH misdiagnosis.
- Physicians were asked to provide data for a consecutive series of patients to avoid selection bias, but no formal patient selection verification procedures were in place.
- Participating patients may not reflect the general PAH-CHD population as those visiting their physician are more often are more likely to be included, and may be more severely affected.

References

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