Humanistic Burden of Paroxysmal Nocturnal Hemoglobinuria from the Patient Perspective: Results from a Cross-Sectional Study

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Introduction and Objective

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare blood condition, caused by complement-mediated hemolysis with chronic anemia and fatigue, that negatively impact patient's health-related quality of life (HRQoL) and substantially reduces survival[1,2,3].
- Currently approved first-line treatments include complement 5 inhibitors (C5i) such as eculizumab and ravulizumab[2] which contributed to improvements in morbidity and survival[4,5].
- Despite receiving C5i treatment, many patients continue experiencing persistent anemia, various symptoms (e.g., fatigue, dyspnea, abdominal pain etc.), poor HRQoL, and require blood transfusions[6,7].
- The aim of this study was to assess the humanistic burden of PNH among patients treated with C5i.

Methods

- Data were drawn from the Adelphi PNH Disease Specific Programme™, a cross-sectional survey of PNH-treating physicians and their patients from Canada, France, Germany, Italy, Japan, Spain, and the United States (data collected January-July 2022).
- Patients filled self-completion forms comprising demographics, PNH-related signs/symptoms, and patient-reported outcome measures including:
  - FACIT-Fatigue (Functional Assessment of Chronic Illness Therapy - Fatigue, recall period 7 days, score ranging 0-52).
  - SF-36 (mental and physical component summary scores (MCS, PCS) were calculated).
  - EQ-5D-5L and EQ-5D VAS (visual analogue scale) - score ranging 0-100. EQ-5D utility score were calculated using the United Kingdom (UK) tariffs - score ranging 0-1.
  - Lower scores indicate worse outcomes for all measures.
- Physicians reported based on medical charts, patients' current treatment, dates of diagnosis and treatment initiation.
- Descriptive analysis was conducted for the entire cohort; bivariate analysis was conducted to determine any differences between males and females.

Results

Patient characteristics

- A total of 143 C5i-treated PNH patients (77.6%: eculizumab and 22.4%: ravulizumab) were included in the analysis. Demographics of the overall cohort and by gender are in **Table 1**. No significant difference was observed between male and female.

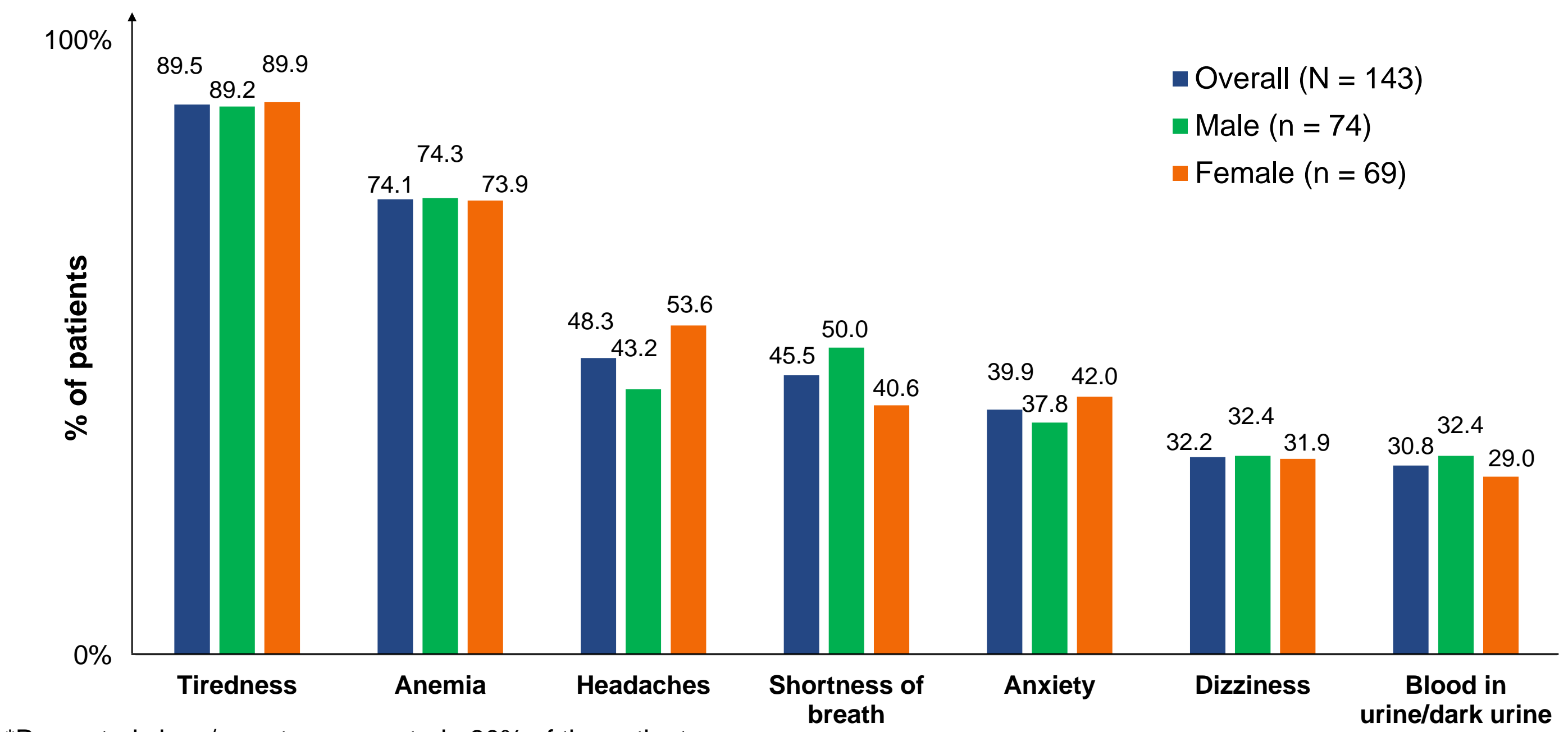**Table 1. Patients' demographics at the time of survey**

	N	Overall	Male	Female
Age (years)*, mean (SD), median	143	48.2 (14.7), 47.0	48.9 (14.1), 47.0	47.5 (15.4), 46.0
Sex*, n (%) Male Female	143	74 (51.7) 69 (48.3)	74 (100.0) -	- 69 (100.0)
Time since diagnosis (years)#, mean (SD), median	142&	2.5 (2.8), 1.7	2.4 (2.4), 1.6	2.7 (3.2), 1.9
Duration since starting C5i therapy (years)#, mean (SD), median	140&	1.8 (2.1), 1.1	1.8 (1.9), 1.1	1.9 (2.2), 1.1

C5I: Complement 5 Inhibitors; N: Sample Size; SD: Standard Deviation
*Data obtained through patient self-completion forms; #Data obtained through physician survey based on medical charts; &Missing data excluded from overall base (N = 143)

Patient reported signs and symptoms at the time of survey

- The most common were tiredness (lack of energy) (89.5%), anemia (74.1%), headache (48.3%), shortness of breath (45.5%) and anxiety (39.9%) with no significant difference between male and female (**Figure 1**).
- A majority of patients (60.6%) reported tiredness as most bothersome symptom. Patients were also bothered by their ongoing anemia (16.9%).
  - There was no significant difference reported between male and female patients experiencing tiredness (65.5% & 55.1%) and anemia (15.1% & 18.8%).

Figure 1. Patient reported signs/symptoms at the time of survey*: overall and by gender

*Presented signs/symptoms reported >30% of the patients

FACIT-Fatigue results

- The mean (SD) FACIT-Fatigue score was 36.3 (10.1), which was lower than the general population score of 43.5 (8.3)[8]; with no significant difference between male and female.
- On specific FACIT-Fatigue items, 23.9% of patients had trouble doing their usual activities, 11.2% experienced limitations with social activities and 9.8% required daytime sleep.

SF-36 results

- Patients had low physical and mental status as shown by PCS and MCS scores lower than the general population score of 50.0 (10.0)[9,10] (**Figure 2**); no significant difference between male and female scores.

**Figure 2. SF-36 PCS and MCS scores: overall and by gender**
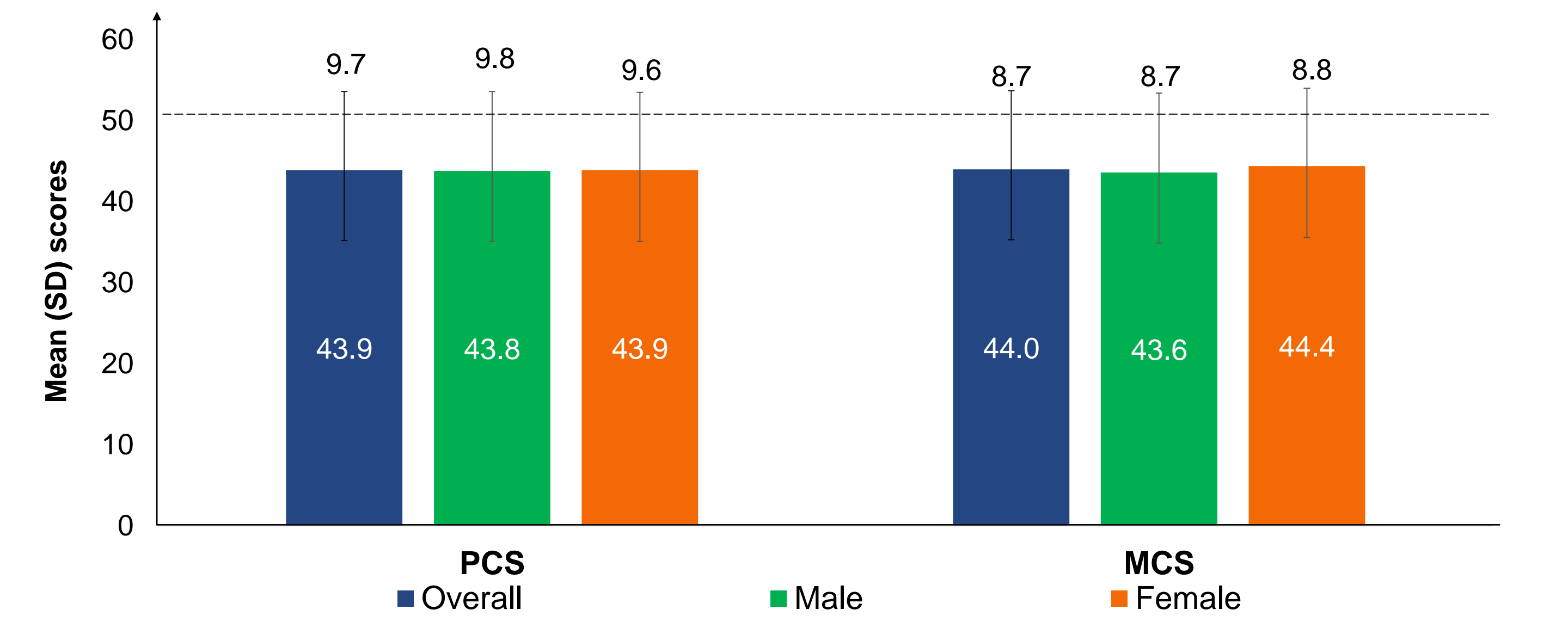
MCS: Mental Component Summary Score; PCS: Physical Component Summary Score; SD: Standard Deviation. Dotted line indicates general population mean (SD) score: 50 (10)[9,10]

EQ-5D results

- In the EQ-5D-5L[11], the most affected dimensions on which patients reported moderate-severe problems were anxiety/depression, usual activities, and pain/discomfort (**Figure 3**).

Figure 3. EQ-5D-5L dimensions: % of patients reporting moderate-severe problems: overall and by gender
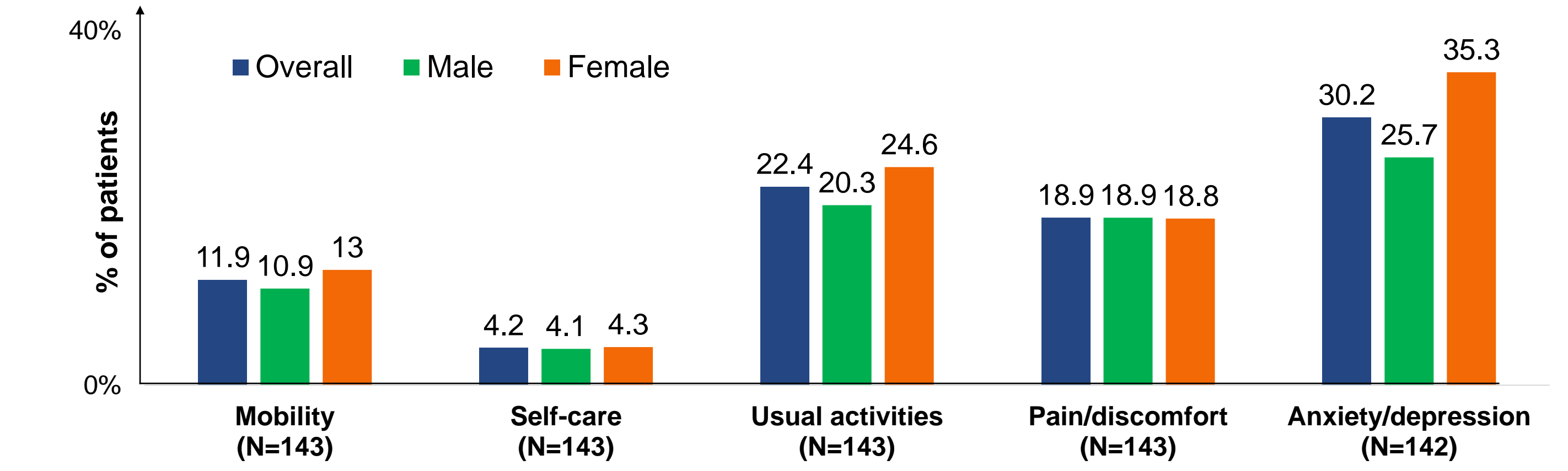
% of overall patients reporting no-slight problems: mobility (88.1%), self-care (95.8%), usual activities (77.7%), pain/discomfort (81.1%), anxiety/depression (69.7%). No patients reported very severe problems.

- The mean (SD) EQ-5D utility and EQ-5D VAS scores are in **Figure 4 and Figure 5;** differences between male and female scores were not significant.
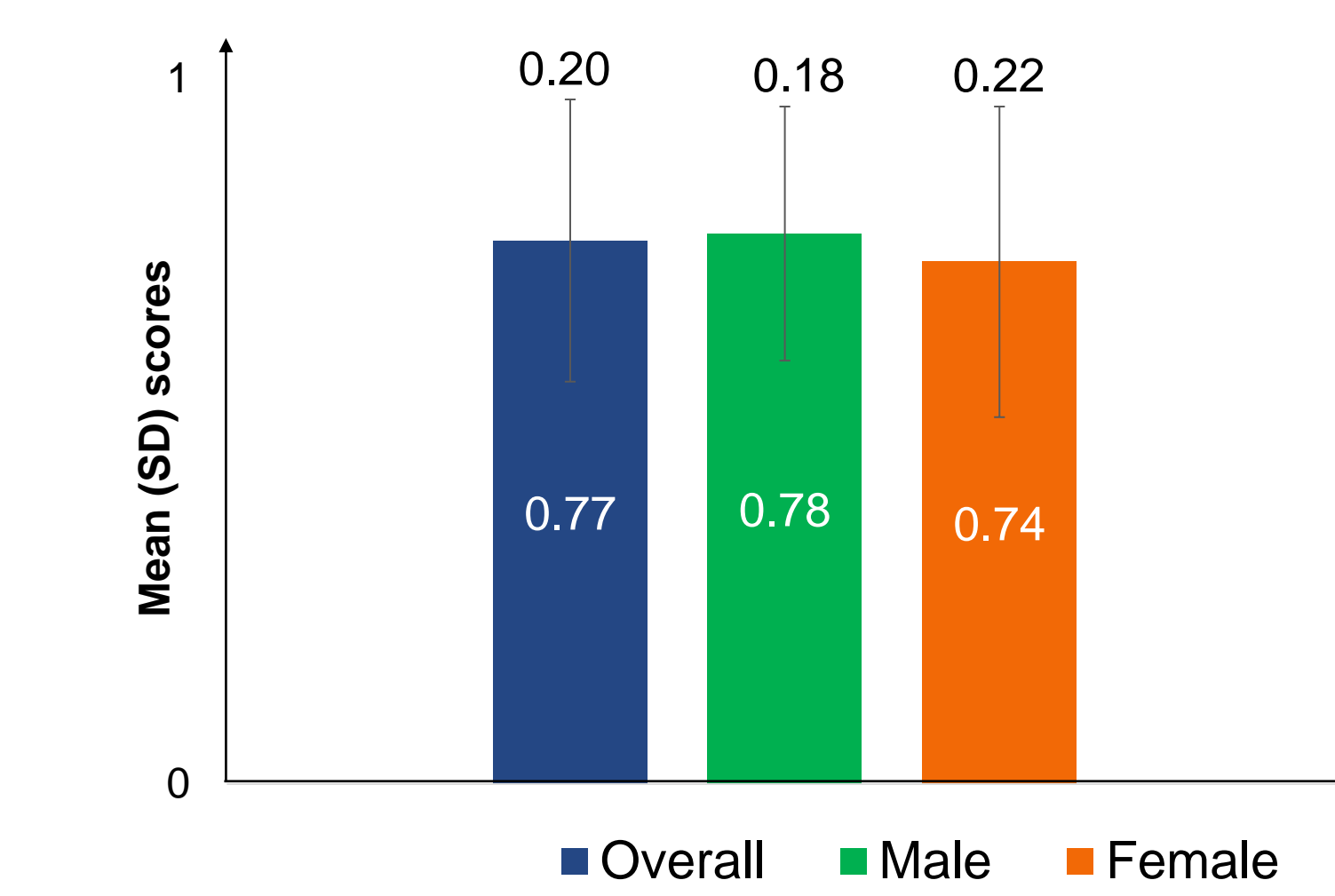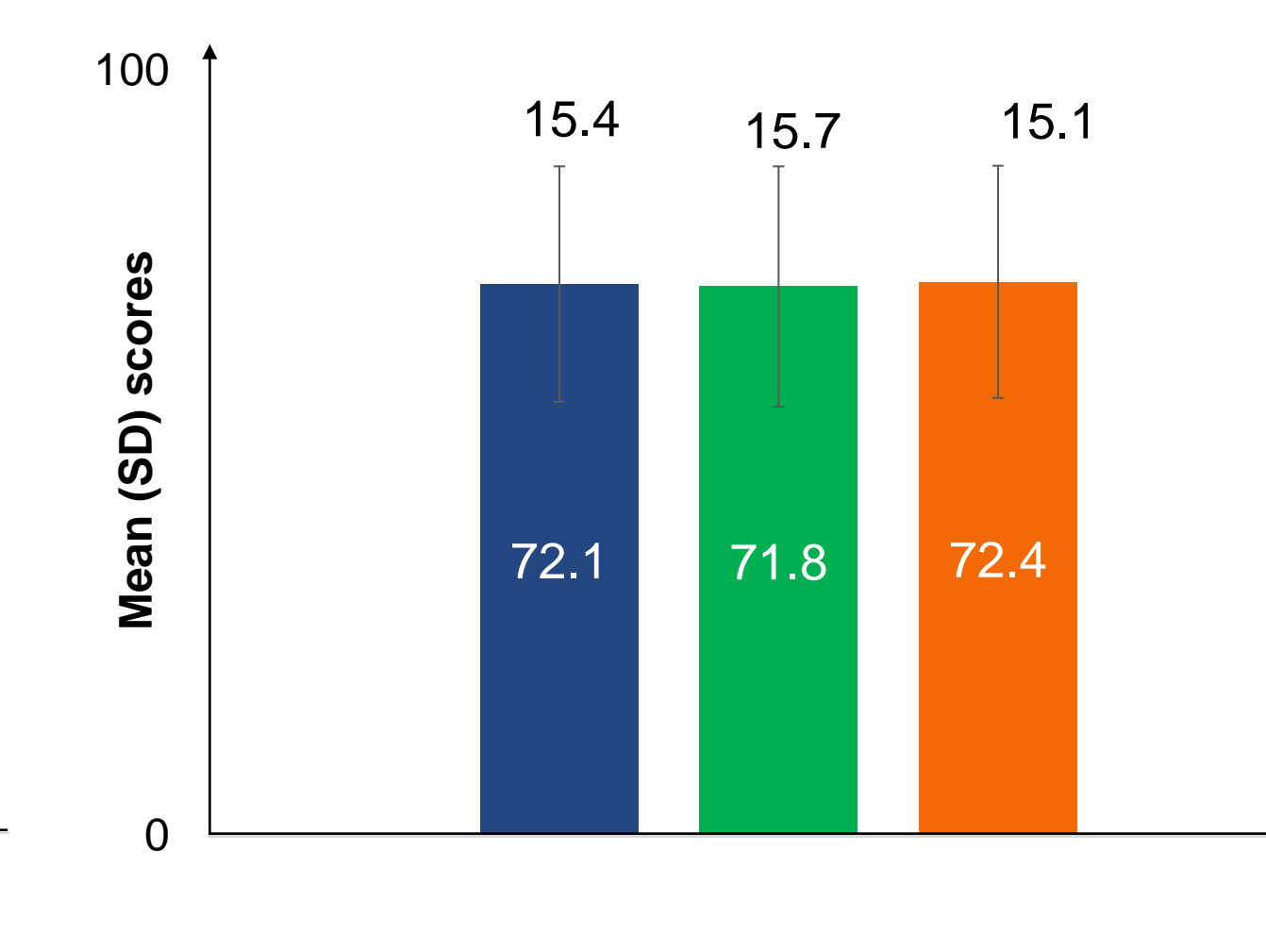
Figure 4. EQ-5D Utility scores: overall and by gender

Figure 5. EQ-5D VAS scores: overall and by gender

SD: Standard Deviation; VAS: Visual Analogue Scale

Conclusions

- Despite being treated with C5i, at the time of survey many patients continue to experience various symptoms, with fatigue being most bothersome. These have a detrimental impact on HRQoL[7,12,13].
- Patients reported low physical and mental status on SF-36, high fatigue on FACIT-fatigue, and anxiety/depression, pain/discomfort and impact on usual activities on EQ-5D.
- No significant differences in HRQoL and symptoms were seen between male and female.
- Having better therapies capable of providing comprehensive control of PNH may address the remaining clinical and humanistic burden of patients with PNH.

References

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