Associations Between Physical Activity Levels and Bleeding Frequency in People with Mild, Moderate, and Severe Hemophilia A (HA): A Preliminary Analysis of the CHESS II Study

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SUMMARY

- Bleeding frequency and progressive joint damage correlate with increasing hemophilia A (HA) disease severity;[1] however, the relationship between bleeding tendency and level of engagement in physical activities is not currently well understood in persons with hemophilia A (PwHA).[2,3]
- Martin AP, et al. (2020) found that the required level of clotting factor (F)VIII/IX to avoid a bleeding episode in PwHA increased with higher risk physical activities.[4]
- This retrospective study examined physical activity and bleeding frequency in PwHA without current FVIII inhibitors who participated in the Cost of Haemophilia in Europe: a Socio-economic Survey (CHESS) II study.
- Our results suggest a possible association between higher bleeding frequency and increased participation in sports and recreational activities in people with moderate and severe HA.

INTRODUCTION

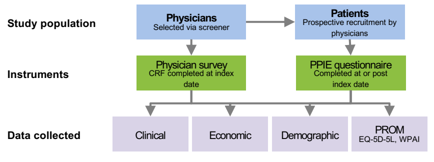
- HA is a congenital bleeding disorder caused by a deficiency in clotting FVIII.[5]
- The CHESS study,[6] and its follow-up, CHESS II, are burden-of-illness studies designed to evaluate the economic and disease burden associated with living with HA.
- The current interim analysis evaluated CHESS II data in order to examine the relationship between physical activity and bleeding frequency in adults with HA without current FVIII inhibitors.

METHODS

CHESS II is a real-world, retrospective, and cross-sectional European study.

- Male participants (aged ≥18 years) were enrolled across eight European countries: Denmark, France, Germany, Italy, the Netherlands, Romania, Spain, and the UK.
- Informed consent was obtained from all participants, and the study was approved by the University of Chester ethical committee.
- The current analysis draws on 12 months of retrospective CHESS II data in adults with mild, moderate, or severe HA, defined according to endogenous FVIII (IU/dL).

Figure 1. CHESS II study design.


Study population
Physicians
Selected via screener
Patients
Prospective recruitment by physicians
Instruments
Physician survey
CRF completed at index date
PPIE questionnaire
Completed at or post index date
Data collected
Clinical
Economic
Demographic
PROM
EQ-5D-5L, WPAI

CRF, case report form; EQ-5D-5L, the 5-level EuroQol 5D questionnaire; PPIE, Patient Public Involvement Engagement; PROMs, patient-reported outcome measurements; WPAI, Work Productivity and Activity Impairment questionnaire.

METHODS (continued)

- A web-based Case Report Form, containing information about the patient's medical history and consultations, was completed by the physician; a paper-based patient and public involvement engagement questionnaire, covering non-medical costs, work impairment, and health status, was completed by the patient (**Figure 1**).
- Data on bleed frequency reported by hemophilia specialists were analyzed along with physical activity levels reported on patient-completed forms.
- In the current study, patient-reported activity level was classified as 'none' or 'any', based on participation in any recreation- and fitness-based activity such as jogging, cycling, or team sport, among others, but excluding activities such as walking and gardening.
- Problem joints,[7] target joints,[8] and annualized bleed rates were reported by physicians.

RESULTS

Demographics and characteristics did not differ according to activity levels.

- Of 787 patients profiled in the interim CHESS dataset, 41% (*n* = 258) of the 628 PwHA who were recruited had data on physical activity recorded.
- Mean age and body mass index (BMI) were similar across disease severity groups; age of patients tended to be higher in those with no activity than those with activity.
- Of this cohort, 16% (*n* = 41), 28% (*n* = 72), and 56% (*n* = 145) had mild (FVIII/IX activity >5% to <40%), moderate (1% to ≤5%), and severe HA (<1%), respectively (**Table 1**).
- Persons with severe HA were more likely to have no activity; they also received more treatment and had more affected joints than those with mild or moderate HA.

Table 1. Baseline demographics and clinical characteristics of people with mild, moderate, and severe HA, by activity level.

	Mild HA (*n* = 41)		Moderate HA (*n* = 72)		Severe HA (*n* = 145)	
	No activity (*n* = 17)	Any activity (*n* = 24)	No activity (*n* = 35)	Any activity (*n* = 37)	No activity (*n* = 80)	Any activity (*n* = 65)
Mean (SD) age, years	41.29 (17.47)	36.79 (12.76)	44.03 (17.51)	35.59 (12.60)	40.41 (15.46)	33.74 (12.55)
Mean (SD) BMI, kg/m²	24.19 (1.93)	24.81 (2.45)	25.18 (3.44)	24.71 (2.40)	24.90 (2.83)	24.36 (2.19)
Treatment strategy, *n* (%)						
No treatment	9 (53)	16 (67)	20 (57)	25 (68)	0 (0)	0 (0)
On-demand	8 (47)	6 (25)	11 (31)	11 (30)	29 (36)	29 (45)
Prophylaxis	0 (0)	2 (8)	4 (11)	1 (3)	51 (64)	36 (55)
Problem joints, *n* (%)	4 (24)	4 (17)	14 (40)	14 (38)	36 (45)	32 (49)
Target joints, *n* (%)	1 (6)	1 (4)	6 (17)	5 (14)	32 (40)	35 (54)

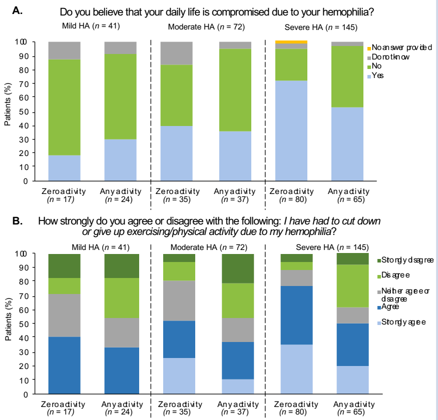
BMI, body mass index; HA, hemophilia A; SD, standard deviation.

RESULTS (continued)

HA impacts patients' lives to a certain extent regardless of disease severity.

- The majority of patients with severe HA believe their daily life is compromised due to their HA (**Figure 2A**).
- PwHA reported having to cut down or give up exercising/physical activity regardless of disease severity (**Figure 2B**).

Figure 2. Impact of HA on A. daily life, and B. exercise/physical activity.

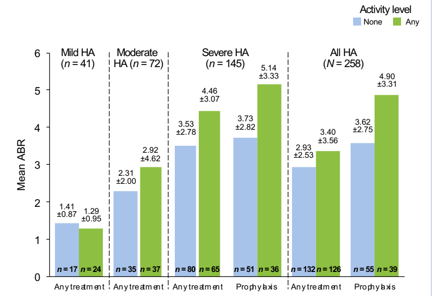

A.
Do you believe that your daily life is compromised due to your hemophilia?
Mild HA (n = 41)
Moderate HA (n = 72)
Severe HA (n = 145)
Patients (%)
No answer provided
Do not know
No
Yes
Zero activity (n = 17)
Any activity (n = 24)
Zero activity (n = 35)
Any activity (n = 37)
Zero activity (n = 80)
Any activity (n = 65)
B.
How strongly do you agree or disagree with the following: I have had to cut down or give up exercising/physical activity due to my hemophilia?
Strongly disagree
Disagree
Neither agree or disagree
Agree
Strongly agree

HA, hemophilia A.

RESULTS (continued)

Increased participation in sports and recreational activities appears to be associated with increased bleeding frequency in moderate and severe HA (Figure 3).

Figure 3. Activity levels and mean ABR (±SD) in people with mild, moderate, and severe HA.


Activity level
None
Any
Mean ABR
Mild HA (n = 41)
Moderate HA (n = 72)
Severe HA (n = 145)
All HA (N = 258)
1.41 ±0.87
1.29 ±0.95
2.31 ±2.00
2.92 ±4.62
3.53 ±2.78
4.46 ±3.07
3.73 ±2.82
5.14 ±3.33
2.93 ±2.53
3.40 ±3.56
3.62 ±2.75
4.90 ±3.31
n = 17
n = 24
n = 35
n = 37
n = 80
n = 65
n = 51
n = 36
n = 132
n = 126
n = 55
n = 39
Any treatment
Any treatment
Any treatment
Prophylaxis
Any treatment
Prophylaxis

ABR, annualized bleed rate; HA, hemophilia A; SD, standard deviation.

CONCLUSIONS

- **A considerable proportion of patients feel that they have had to cut down or give up exercise/physical activity due to HA, and believe their life is compromised by HA.**
- **In people with moderate and severe HA, the data suggest a trend towards increased bleeding frequency in patients with greater participation in sports and recreational activities, regardless of treatment strategy.**
- **Limitations of the study include the variability of the endpoints, the cross-sectional study design, and potential for recall bias. Consensus regarding a preferred tool for assessing activity is lacking,[9] thus the categorization of activity levels used should be carefully considered when interpreting these results.**
- **Strengths of the study include the sample size, particularly the size of the mild and moderate HA cohorts.**
- **While these real-life data help to define the burden associated with activity and bleeding risk in PwHA, it is also important to note that they are descriptive only; thus prospective studies using validated tools are needed in the future to further quantify risks.**

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