Aging and health status in persons leaving with hemophilia and controls without a bleeding disorder.

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PROBE® Patient Reported Outcomes Burdens and Experiences Study

INTRODUCTION

People with hemophilia (PWH) have a life expectancy disadvantage as compared to the general population but little is known about the impact of aging on health status and health-related quality of life (HRQL).

AIM

Assessing the characteristics of the association between aging, health status and HRQL in PWH and people with no bleeding disorders (PWNoBD).

METHODS

A cross-sectional, multinational study was conducted as part of the Patient Reported Outcomes, Burdens and Experiences (PROBE) project. PWH and PWNoBD were asked to complete the PROBE questionnaire. Measures of health status and HRQL were the PROBE score, the EQ-5D-5L utility index, and the EuroQol visual analog scale (EQ-VAS) of global health. The association between these measures and the participants' age was explored using a multivariable model adjusting for sex (all) and disease severity (PWH only) and stratifying by country. Age was analyzed as a continuous variable.

RESULTS

Table 1: *Characteristics of the study population*

	People with hemophilia (n = 1157)*					People with no bleeding disorders (n = 690)			
	Age category					Age category			
	18 – 44	45 – 64	65 – 74	≥ 75		18 – 44	45 – 64	65 – 74	≥ 75
n (%)**	732 (63)	331 (29)	73 (6)	21 (2)	n (%)**	335 (49)	272 (39)	71 (10)	12 (2)
Income***					Income***				
Low Middle	65 (9)	10 (3)	0 (0)	0 (0)	Low Middle	12 (4)	3 (1)	0 (0)	0 (0)
Upper Middle	302 (41)	40 (12)	2 (3)	3 (14)	Upper Middle	95 (28)	53 (19)	15 (21)	4 (33)
High	365 (50)	281 (85)	71 (97)	18 (86)	High	228 (68)	216 (79)	56 (79)	8 (67)
Male (%)	706 (96)	317 (96)	71 (97)	20 (95)	Male (%)	144 (43)	116 (43)	36 (51)	4 (33)
No. Of Comorbidities [Median (range)]	1 (0 -8)	1 (0 -9)	1 (0 – 7)	1 (0 – 4)	No. Of Comorbidities [Median (range)]	0 (0 - 6)	0 (0 - 6)	0 (0 - 5)	1.5 (0 - 3)
PROBE Score (n = 982) [median (Q1; Q3)]	0.76 (0.64; 0.85)	0.68 (0.57; 0.78)	0.71 (0.64; 0.80)	0.67 (0.52; 0.84)	PROBE Score (n = 580) [median (Q1; Q3)]	0.92 (0.83; 0.98)	0.90 (0.79; 0.96)	0.86 (0.79; 0.93)	0.75 (0.69; 0.89)
EQ-5D (n = 1109) [median (Q1; Q3)]	0.82 (0.70; 0.92)	0.75 (0.62; 0.84)	0.76 (0.63; 0.88)	0.68 (0.52; 0.86)	EQ-5D (n = 666) [median (Q1; Q3)]	0.92 (0.83; 0.98)	0.94 (0.87; 1.00)	0.94 (0.83; 1.00)	0.84 (0.50; 1.00)
VAS (n = 1228) [median (Q1; Q3)]	0.75 (0.60; 0.90)	0.70 (0.50; 0.80)	0.73 (0.60; 0.84)	0.62 (0.50; 0.80)	VAS (n = 675) [median (Q1; Q3)]	0.85 (0.75; 0.90)	0.80 (0.75; 0.90)	0.85 (0.80; 0.90)	0.80 (0.65; 0.88)
Hemophilia severity									
Mild (FL 0.05 – 0.40 IU/mL)	72 (10)	70 (21)	23 (32)	7 (33)					
Moderate (FL 0.01-0.05 IU/mL)	136 (19)	50 (15)	7 (10)	8 (38)					
Severe (FL < 0.01 IU/mL)	524 (72)	211 (64)	43 (59)	6 (29)					

*Unless otherwise specified **Row percentage (across age categories), all other percentages are within risk categories. ***This refers to the average per-capita income of the country according to the World Bank
Q1: first quartile; Q2: third quartile; PROBE = patient reported outcomes burden and experience; VAS = visual analogue scale

1157 PWH and 690 PWNoBD completed the questionnaire in 33 countries from 2016 to 2019. Eight percent of the PWH and 12% of the PWNoBD were aged ≥65 years.

Table 2: *Results of the multivariable analyses*

	PROBE Score n = 1562		EQ-5D utility index n = 1775		EQ VAS n = 1803	
Explanatory variable	Coeff*	95% CI	Coeff*	95% CI	Coeff*	95% CI
Age	-0.0010	-0.0017; -0.0004	-0.0003	-0.0012; 0.0007	0.0000	-0.0009; 0.0009
Interaction Age*PWH	-0.0015	-0.0022; -0.0008	-0.0031	-0.0041; -0.0021	-0.0030	-0.0047; -0.0014
Male sex	0.0125	-0.0145; 0.0396	0.0129	-0.0145; 0.0404	0.0061	-0.0182; 0.0304
NoBD	Ref	-	Ref	-	Ref	-
Mild	-0.0282	-0.0749; 0.0184	0.0634	-0.0028; 0.1297	0.0851	-0.0001; 0.1702
Moderate	-0.1241	-0.1668; -0.0813	-0.0461	-0.1233; 0.0312	0.0014	-0.1011; 0.1039
Severe	-0.1152	-0.1582; -0.0722	-0.0780	-0.1524; -0.0036	-0.0143	-0.0942; 0.0657
Constant	0.9130	0.8855; 0.9405	0.9166	0.8720; 0.9613	0.8161	0.7686; 0.8636

*The regression coefficients can be interpreted as the adjusted mean difference in the score. For the PROBE score and VAS, that ranges from 0 to 1, the coefficient times 100 is equal to the percentage variation in the score, with a negative sign indicating a reduction. For EQ-5D utility value, that ranges from -0.594 to 1, the coefficient needs to be reported to a scale 0-100 before being interpreted as a percentage variation.

As expected, the EQ-5D utility index and EQ-VAS did not show a variation with aging in PWNoBD, while in PWH they were reduced respectively by 0.031 (95% confidence interval [CI] 0.021-0.041) and 0.030 (95% CI 0.014-0.047) every 10 years from 18 years onwards. Aging was associated with a mean reduction in the PROBE score of 0.010 (95% CI 0.004 to 0.017) every 10 years in PWNoBD. PWH showed an additional reduction in the PROBE score of 0.015 (95% CI 0.008 to 0.022) every 10 years.

CONCLUSIONS

Aging is associated with a steeper decrease in health status and quality of life in people with hemophilia than in people with no bleeding disorders. PROBE is more sensitive than EQ5D in measuring the association of aging for the specific domains measured in both these populations.

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DISCLOSURES

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