Concordance between Haemo-QOL and the Hemophilia Activities List (HAL) in Assessing Hemophilia A Impact on Quality of Life

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Background

Hemophilia A is a congenital bleeding disorder characterized by deficient or dysfunctional factor VIII. The estimated global prevalence of hemophilia A is approximately 17.1 per 100,000 males.[1] In Taiwan, the prevalence has been reported as 8.58 per 100,000 males.[2] Clinically, hemophilia A manifests as spontaneous or trauma-induced bleeding, often occurring in soft tissues, joints, and muscles. If left untreated, recurrent bleeding episodes can result in severe pain, swelling, and permanent joint damage.[3] In addition to physical complications, hemophilia patients face significant economic burdens. In Taiwan, the mean medical costs per hemophilia A patient were estimated to be 99,335 USD in 2017.[4] These burdens of illness substantially impair patients' physical functioning and overall quality of life (QoL).[5,6]

To assess the impact of hemophilia on various aspects of life, two instruments have been developed: the Haemo-QoL questionnaire and the Hemophilia Activities List (HAL). The Haemo-QoL questionnaire is primarily used to assess the impact of hemophilia on emotional well-being, physical functioning, social interactions, and treatment-related experiences.[7] The Hemophilia Activities List (HAL) focuses on patients' functional abilities in daily activities, such as mobility, self-care, and participation in sports and household tasks. However, the relationship between these instruments and their ability to capture specific domains remains unclear.[8]

Objective

This study aimed to evaluate the concordance between Haemo-QoL and HAL in assessing the impact of hemophilia A on daily life.

Method

Data Source

This cross-sectional study retrospectively analyzed data from the Taiwan Society of Thrombosis and Hemostasis (TSTH) in 2023. The TSTH manages clinical information on hemophilia patients recruited from hemophilia treatment centers across Taiwan. Healthcare professionals at the treatment centers assess patient care using the Haemo-QoL and HAL questionnaires each year, and the results from both assessments are systematically collected in the TSTH database.

Study Subject

Inclusion Criteria: Patients with a diagnosis of hemophilia A who completed both the Haemo-QoL and HAL assessments were included in this study.

Exclusion Criteria: Patients under 18 years old were excluded.

Materials

The **Haemo-QoL questionnaire** consisted of 46 items, divided into 10 domains. The higher the score was, the poorer the quality of life was. Responses were scored as follows: never=1, seldom=2, sometimes=3, often=4, all the time=5. Negatively worded items follow this scale. However, positively worded items were reverse-coded to align with this scoring system (i.e., all the time=1, never=5). These values were summed to calculate the raw scores for each subscale. Raw scores could be transformed into a scale from 0 to 100 for easier comparison. The transformation formula was as follows:

$$\text{Transformed scale score} = 100 \times \frac{\text{Raw score} - \text{Minimal possible raw score}}{\text{Maximal possible raw score} - \text{Minimal possible raw score}}$$

The **HAL** consisted of 42 items. Scores for the HAL were calculated across 7 functional domains, with three additional component scores reflecting activities involving the upper extremities, basic activities involving the lower extremities, and complex lower extremity activities. The scoring system represented levels of functional limitation, with 1 indicating "Impossible" and 6 indicating "Never problems". After calculating raw scores, normalization was applied to convert them to a 0 to 100 scale, where 0 reflected the worst functional status and 100 reflected the best possible functional status. The normalization formula is as follows:

$$\text{Normalization score} = 100 - \left(\frac{\text{Raw score} - \text{Number of valid response}}{5 \times \text{Number of valid response}}\right) \times 100$$

Table 1 Haemo-QoL Domains

Haemo-QoL domain 1 (QD1)	Physical Health
Haemo-QoL domain 2 (QD2)	Feeling
Haemo-QoL domain 3 (QD3)	View of Themselves
Haemo-QoL domain 4 (QD4)	Sports and Leisure
Haemo-QoL domain 5 (QD5)	Work and School
Haemo-QoL domain 6 (QD6)	Dealing With Hemophilia
Haemo-QoL domain 7 (QD7)	Treatment
Haemo-QoL domain 8 (QD8)	Thought about Future
Haemo-QoL domain 9 (QD9)	Family Planning
Haemo-QoL domain 10 (QD10)	Partnership and Sexuality

Table 2 HAL Domains

HAL domain 1 (HD1)	Lying / Sitting / Kneeling / Standing
HAL domain 2 (HD2)	Functions of the Legs
HAL domain 3 (HD3)	Functions of the Arms
HAL domain 4 (HD4)	Use of Transportation
HAL domain 5 (HD5)	Self Care
HAL domain 6 (HD6)	Household Tasks
HAL domain 7 (HD7)	Leisure Activities and Sports
HAL domain 8 (HD8)	Upper Extremity Activities
HAL domain 9 (HD9)	Basic Lower Extremity Activities
HAL domain 10 (HD10)	Complex Lower Extremity Activities

References:
1. Bullinger M, von Mackensen S, Fischer K, Khair K, Petersen C, Ravens-Sieberer U, Rocino A, Sagnier P, Tusell JM, van den Berg M, Vicariot M. Pilot testing of the 'Haemo-QoL' quality of life questionnaire for haemophiliac children in six European countries. Haemophilia. 2002 Mar;8 Suppl 2:47-54.
2. Van Genderen FR, Van Meeteren NLU, Van der Bom JG, Heijnen L, De Kleijn P, Van denBerg HM, Helders PJM. Functional consequences of haemophilia in adults: the development of the Haemophilia Activities List. Haemophilia 2004; 10: 565-71.

Statistical Analysis

Concordance is a concept frequently employed in medical research to evaluate the degree of agreement between different assessment instruments. One common method used to assess agreement between measurements of continuous variables is the Bland-Altman analysis, which graphically displays the differences between the two instruments' measurements against their average values. This allows for the identification of any bias (i.e., the mean difference between the two instruments) and the calculation of 95% limits of agreement. When the differences between the two instruments' measurements fell within these 95% limits, it indicated a high degree of concordance.

Descriptive analyses were performed to estimate the Haemo-QoL and HAL scores, followed by Kendall's tau-b correlation analysis to assess the association between corresponding domain scores from the Haemo-QoL and HAL questionnaires. Bland-Altman plots were generated to visualize the agreement and identify any potential biases between the total scores and domain scores of these two instruments. Statistical significance was set at a p-value of less than 0.05 for all analyses. Data processing and visualization were performed using GraphPad Prism 9, which provided the graphical outputs necessary for our Bland-Altman plots, and SPSS was used for calculating the correlation coefficients and descriptive statistics.

Results

Twenty-four hemophilia A patients completed both Haemo-QoL and HAL assessments. The mean age of patients was 36.7. The findings of our study indicated a significant relationship between the total HAL score and the total Haemo-Qol score. (p=0.001, tau_b= -0.485) (Table 5). Correlation coefficients between corresponding domains ranged from 0.023 to -0.658, with some domains showing stronger association than others. Bland-Altman plots and the calculated 95% limits of agreement range indicated that the findings supported the moderate correlation coefficients observed between the corresponding domains of the two instruments (Figure 1-6).

Table 3
Total and subscale scores of Haemo-QoL

Domain	Mean (SD)
Haemo-QoL total score (QT)	33.27 (17.197)
Physical Health (QD1)	29.81 (24.158)
Feeling(QD2)	23.86 (27.579)
View of Themselves (QD3)	50.74 (17.634)
Sports and Leisure (QD4)	43.70 (26.333)
Work and School (QD5)	25.25 (19.035)
Dealing With Haemophilia (QD6)	24.38 (23.338)
Treatment (QD7)	44.81 (18.826)
Thought about Future (QD8)	32.59 (26.068)
Family Planning (QD9)	16.68 (24.944)
Partnership and Sexuality (QD10)	24.07 (31.636)

The score range is from 0 to 100.

Table 4
Total and subscale scores of HAL

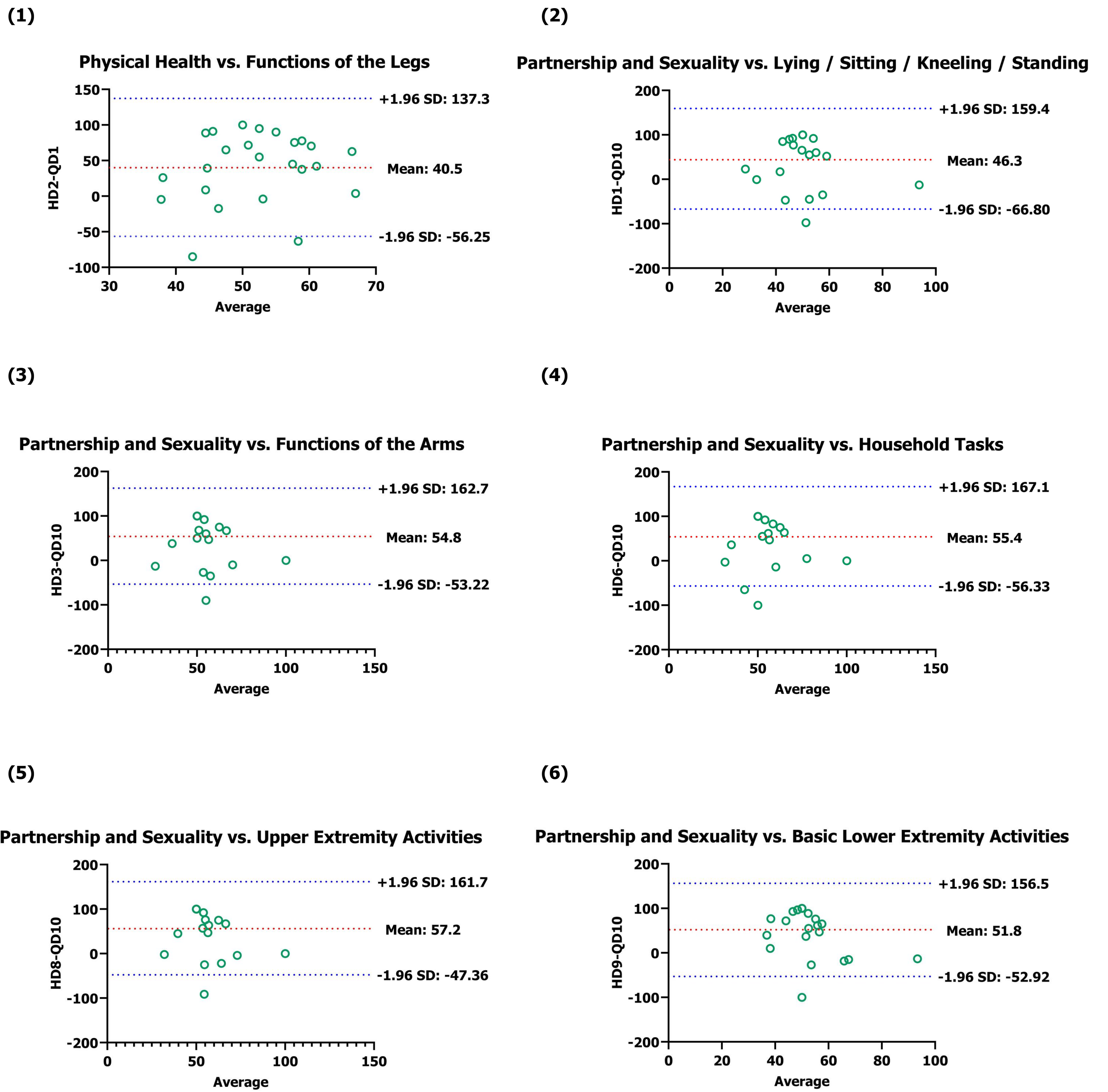| Domain	Mean (SD)
HAL total score (HT)	80.40 (26.232)
Lying / sitting / kneeling / standing (HD1)	76.02 (29.140)
Functions of the legs (HD2)	75.32 (27.051)
Functions of the arms (HD3)	83.52 (27.097)
Use of transportation (HD4)	78.40 (30.006)
Self care (HD5)	87.41 (23.709)
Household tasks (HD6)	84.07 (29.023)
Leisure activities and sports (HD7)	83.24 (26.456)
Upper Extremity Activities (HD8)	85.67 (24.943)
Basic Lower Extremity Activities (HD9)	80.75 (24.328)
Complex Lower Extremity Activities (HD10)	68.01 (33.419)

The score range is from 0 to 100.

Table 5
Correlations between total scores of Haemo-QoL, HAL, and individual domains of both instruments

	QT	QD1	QD2	QD3	QD4	QD5	QD6	QD7	QD8	QD9	QD10
HT	-0.485***	-0.559 ***	-0.493***	-0.373*	-0.045	-0.314*	-0.320*	-0.253	-0.499***	-0.189	-0.599***
HD1	-0.423 **	-0.411**	-0.392*	-0.339*	-0.117	-0.200	-0.225	-0.269	-0.369*	-0.181	-0.648***
HD2	-0.468**	-0. 611***	-0.491***	-0.358**	0.023	-0.325*	-0.300	-0.256	-0.528***	-0.183	-0.545***
HD3	-0.467**	-0.489**	-0.481**	-0.390**	-0.086	-0.285	-0.310	-0.341*	-0.472**	-0.241	-0.614***
HD4	-0.432**	-0.598***	-0.403*	-0.335*	-0.086	-0.257	-0.244	-0.245	-0.400*	-0.109	-0.482**
HD5	-0.424**	-0.516**	-0.477**	-0.419*	-0.034	-0.244	-0.166	-0.326*	-0.483**	-0.191	-0.577***
HD6	-0.474**	-0.542**	-0.549***	-0.458**	-0.064	-0.259	-0.302	-0.374*	-0.484**	-0.273	-0.647***
HD7	-0.473**	-0.524***	-0.449**	-0.405*	-0.037	-0.248	-0.323*	-0.283	-0.424**	-0.134	-0.598***
HD8	-0.447**	-0.477**	-0.459**	-0.393*	-0.068	-0.274	-0.279	-0.321*	-0.470**	-0.225	-0.621***
HD9	-0.462**	-0.459**	-0.488**	-0.384*	-0.038	-0.280	-0.217	-0.349*	-0.526***	-0.263	-0.658***
HD10	-0.424**	-0.580***	-0.386*	-0.239	-0.075	-0.252	-0.300	-0.233	-0.421**	-0.137	-0.464**

"*" indicated that the correlation is significant at the 0.05 level. "**" indicated that the correlation is significant at the 0.01 level. "***" indicated that the correlation is significant at the 0.001 level. ±0.41 to ±0.70: Suggested a moderate correlation. ±0.21 to ±0.40: Suggested a small but definite relationship.

Figure (1)-(6) Bland-Altman Plots of Domain Scores: |r|>0.6

(1) Physical Health vs. Functions of the Legs — HD2-QD1; +1.96 SD: 137.3; Mean: 40.5; -1.96 SD: -56.25

(2) Partnership and Sexuality vs. Lying / Sitting / Kneeling / Standing — HD1-QD10; +1.96 SD: 159.4; Mean: 46.3; -1.96 SD: -66.80

(3) Partnership and Sexuality vs. Functions of the Arms — HD3-QD10; +1.96 SD: 162.7; Mean: 54.8; -1.96 SD: -53.22

(4) Partnership and Sexuality vs. Household Tasks — HD6-QD10; +1.96 SD: 167.1; Mean: 55.4; -1.96 SD: -56.33

(5) Partnership and Sexuality vs. Upper Extremity Activities — HD8-QD10; +1.96 SD: 161.7; Mean: 57.2; -1.96 SD: -47.36

(6) Partnership and Sexuality vs. Basic Lower Extremity Activities — HD9-QD10; +1.96 SD: 156.5; Mean: 51.8; -1.96 SD: -52.92

Conclusions

Our research reveals a moderate negative correlation between Haemo-QoL and HAL total scores, where declining activity levels correspond with poorer quality of life. This aligns with prior research findings, which reported a negative relationship between Haemo-QoL scores and hemophilia-induced disability and arthropathy. [9] The concordance between Haemo-QoL and HAL varied across domains, highlighting their complementary roles in assessing the multifaceted impact of Hemophilia A. While both instruments provide valuable information, understanding their strengths and limitations can inform clinical practice. Utilizing both assessments can offer a more comprehensive picture of a patient's experience with Hemophilia A, leading to more tailored treatment plans and improved patient management.