ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

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Investigation of the Relationship Between Hemophilia Joint Health Score and Haemophilia Early Arthropathy Detection with Ultrasound Score in Hemophilic Arthropathy

Hemofilik Artropatide Hemofili Eklem Sağlığı Skoru ve Hemofili Erken Artropati Taraması Ultrason Skoru Arasındaki İlişkinin Araştırılması

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ABSTRACT Objective: Hemophilia is classified according to the factor VIII or IX level as severe, moderate and mild. The Hemophilia Joint Health Score (HJHS) and Haemophilia Early Arthropathy Detection with Ultrasound (HEAD-US) score used in recent years contribute significantly to the early diagnosis of arthropathy, which continues to be an important problem in severe hemophilia. It was aimed to investigate the compatibility between HJHS and HEAD-US scores. **Material and Methods:** The demographic and disease-related data, HJHS 2.1 and HEAD-US scores of the participants who participated in the Workshop of the Hemophilia Federation in 2020 were recorded. **Results:** The mean age of 32 participants was 20.6 (minimum: 15-maximum: 31). Twenty three were diagnosed as Hemophilia A, 8 were Hemophilia B, 1 was Von Willebrand disease. HJHS score of 30 patients was 6.7±6.2 (minimum: 0-maximum: 22). The mean of HEAD-US was 14.3±11.5 (minimum: 0-maximum: 34). HJHS and HEAD-US scores were compatible with each other (p=0.002). Arthropathy was present in 33 joints of 21 patients. There was a statistical significance between patients with and without arthropathy with both the HJHS and the HEAD-US scores (0.006 and 0.005 respectively). The most common arthropathy is in the right knee. HJHS and HEAD-US scores are compatible in both knee and elbow joints. Nonetheless, it is incompatible in both ankles. HJHS and HEAD-US scores were discordant in 21 joints of 7 patients. These joints were right ankle (n=7), left ankle (n=6), left elbow (n=4), right elbow (n=2) and right knee (n=2). **Conclusion:** A correlation was found between the HJHS and HEAD-US scores. HEAD-US is more sensitive than HJHS in detecting the early stage of arthropathy in the ankle joint. These scores should be done routinely to all patients for manifesting treatment deficiencies and incompatibilities.

Keywords: Hemophilia A; Hemophilia B; arthropathy

ÖZET Amaç: Hemofili, faktör VIII veya IX düzeyine göre ağır, orta ve hafif olarak sınıflandırılır. Son yıllarda kullanılan, Hemofili Eklem Sağlığı Skoru [Hemophilia Joint Health Score (HJHS)] ve Hemofili Erken Artropati Taraması [Haemophilia Early Arthropathy Detection with Ultrasound (HEAD-US)], ultrason skoru ağır hemofilide önemli bir sorun olmaya devam eden artropatinin erken teşhisine önemli katkı sağlamaktadır. Bu çalışmada, HJHS ve HEAD-US skorları arasındaki uyumluluğun araştırılması amaçlanmıştır. **Gereç ve Yöntemler:** 2020 yılında Hemofili Federasyonu Çalıştayına katılan katılımcıların, demografik ve hastalık ilişkili verileri HJHS 2,1 ve HEAD-US puanları kaydedilmiştir. **Bulgular:** Otuz iki katılımcının ortalama yaşı 20,6 (minimum: 15-maksimum: 31) idi. Yirmi üçü Hemofili A, 8'i Hemofili B, 1'i Von Willebrand hastalığı tanılıydı. Otuz hastanın ortalama HJHS skoru 6,7 (minimum: 0-maksimum: 22) idi. Ortalama HEAD-US skoru 14,3 (minimum: 0-maksimum: 34) idi. HJHS ve HEAD-US skorları birbiriyle uyumluydu (p=0,002). Yirmi bir hastanın 33 ekleminde artropati mevcuttu. Hem HJHS hem de HEAD-US skorları ile (sırasıyla p=0,006 ve p=0,005) artropatisi olan ve olmayan hastalar arasında, istatistiksel anlamlılık vardı. Artropati en sık sağ dizdeydi. HJHS ve HEAD-US skorları, hem diz hem de dirsek eklemlerinde uyumlu, her 2 ayak bileğinde ise uyumsuzdu. Yedi hastanın 21 ekleminde HJHS ve HEAD-US skorları uyumsuzdu. Bu eklemler; sağ ayak bileği (n=7), sol ayak bileği (n=6), sol dirsek (n=4), sağ dirsek (n=2) ve sağ diz (n=2) idi. **Sonuç:** HJHS ve HEAD-US skorları arasında bir korelasyon saptanmıştır. HEAD-US, ayak bileği ekleminde artropatinin erken evresini tespit etmede HJHS'den daha hassastır. Bu skorlar, tedavi eksikliklerinin ve uyumsuzluklarının ortaya çıkması için tüm hastalara rutin olarak uygulanmalıdır.

Anahtar Kelimeler: Hemofili A; Hemofili B; artropati

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Hemophilia is classified according to the factor VIII or IX level as severe, moderate and mild. Despite the rapid advances in hemophilia care, arthropathy is the most common cause of morbidity today, especially in severe hemophilia.[1] Knee, elbow and ankle are the most common joints.[2] In the pathogenesis of hemophilic arthropathy, recurrent intra-articular bleeding causes early effusion, deposition of hemosiderin, and synovial hypertrophy. In chronic period, destructive changes such as cartilage loss, bone tissue erosions, and formation of subchondral cysts are observed.[3,4]

Although the findings are more evident in symptomatic patients, osteochondral damage caused by subclinical bleeding in asymptomatic patients can not be detected by physical examination often. Further tools are needed to detect osteochondral changes in this condition.[5,6]

Joint health assessment should be performed every six months in children and once a year in adults for the early detection of potential problems in hemophilia patients. Of the patients, 90% were shown to have changes in their joints when evaluated with radiological and physical examination scores. Joint health is evaluated both by clinical examination and by using radiological scores. Physical examination assessment is an easily accessible and cost-effective, effective assessment method, which is often used to measure structural and functional joint damage. Scales such as World Federation of Hemophilia (WFH) Gilbert score, Colorado Physical Examination Scale, Hemophilia Joint Health Score (HJHS), Functional Independence Score in Hemophilia are used.[7,8] Detecting radiological changes in the joints have become more difficult with primary prophylaxis. Radiological evaluations such as Petterson Score, MRI Denver Score and Hemophilia Early Arthropathy Detection with Ultrasound (HEAD-US) attempted to detect early changes in the joints.[9-11]

Radiographic evaluation with Petterson Score is not successful in showing arthropathic changes in early stages.[12] WFH Gilbert Score does not give reliable results, especially in the pediatric age group and in patients undergoing radioisotope therapy.[13] It shows poor correlation with HJHS and Magnetic Resonance Imaging (MRI).[14,15] For this reason, more recent methods such as the HJHS joint score and the HEAD-US radiological score, which have been used in recent years, make an important contribution to the early detection of arthropathy.

In this study, it was aimed to investigate the compatibility between HJHS used in physical evaluation and HEAD-US scores used in radiological evaluation.

MATERIAL AND METHODS

The demographic data, treatments and hemophilic arthropathy histories of the individuals who participated in the Workshop of the Hemophilia Federation in 2020 were recorded using HJHS 2.1 and ultrasonography (GE LOGIQ E and linear probe 4-12, GE Healtcare, USA). Approval was obtained from patients or, if necessary, their legal representative. The study was performed in accordance with the Declaration of Helsinki Principles.

PATIENTS

The median age of 32 participants was 20.6 (minimum: 15-maximum: 31). Twenty three were diagnosed with Hemophilia A, 8 were Hemophilia B, 1 was Von Willebrand Disease (vWH). Twenty nine patients were receiving prophylaxis and 3 were receiving treatment as they had bleeding. Twenty patients were using recombinant products, 8 patients were using clinical study drugs and 4 patients were using plasma-derived factor products. Eight patients had a history of radioisotope synovectomy therapy, and one patient had a history of orthopedic surgery.

HJHS

HJHS is designed to track changes in joints and evaluate the effectiveness of treatments over time in children aged 4-18 years with or without mild joint disorders, and is also recommended for use in the adult population. Knee, elbow and foot ankle are evaluated bilaterally. There are 8 subheadings in each joint: swelling, swelling time, muscle atrophy, muscle strength, crepitation, flexion and extension loss and pain. In the HJHS 2.1 version and the worst score of the each joint may get is 20. Finally,

the global gait score is added and the total joint health score can be up to 124. As this score increases, joint health is considered to be worse physically.[16]

HEAD-US

Ultrasonography is fast, easily accessible and cost effective. With these aspects, it is a suitable method for the recognition and follow-up of hemophilic arthropathy. It was standardized for this purpose in 2013 by Martinoli et al. Six joints are evaluated, both knee, elbow and foot ankle. A score of 0-8 is obtained by scoring synovial hypertrophy (0-2 points), cartilage damage (0-4 points) and bone damage (0-2 points) for each joint. As the arthropathy worsens, the score obtained increases.[10]

STATISTICAL ANALYSIS

SPSS 20.0 package program was used for statistics. Descriptive statistics of the data are presented as n (%) and if the variable is normally distributed, the mean±standard deviation, otherwise the median (minimum-maximum). The test for normal distribution was performed using the Shapiro-Wilk test. t-test or Mann Whitney-U test was applied according to whether the variables have normal distribution or not. A value of $p<0.05$ was considered as statistically significant.

RESULTS

The HJHS score of 30 patients was measured and the mean was 6.7 (minimum: 0-maximum: 22). The HEAD-US score could be applied to 20 of 30 patients and median score was 14.3 (minimum: 0-maximum: 34). The HJHS and HEAD-US scores were statistically correlated as in Figure 1 ($p=0.002$).

A history of arthropathy was present in 33 joints of 21 patients. HJHS and HEAD-US scores of patients with and without arthropathy history are shown in Table 1. Mean HJHS and HEAD-US scores of 33 joints with arthropathy history are shown in Table 2.

According to Table 2, the most common history of arthropathy is in the right knee. HJHS and HEAD-US scores are compatible in both knee and elbow joints. However, it is discordant in both ankles.

HJHS and HEAD-US scores were discordant in 21 joints of 7 patients. These joints were right ankle (n=7) (33.3%), left ankle (n=6) (28.5%), left elbow (n=4) (19.0%), right elbow (n=2) (9.6%) and right knee (n=2) (9.6%).

DISCUSSION

Correlation between HJHS that is a clinical assessment scale and HEAD-US which was evaluated ra-

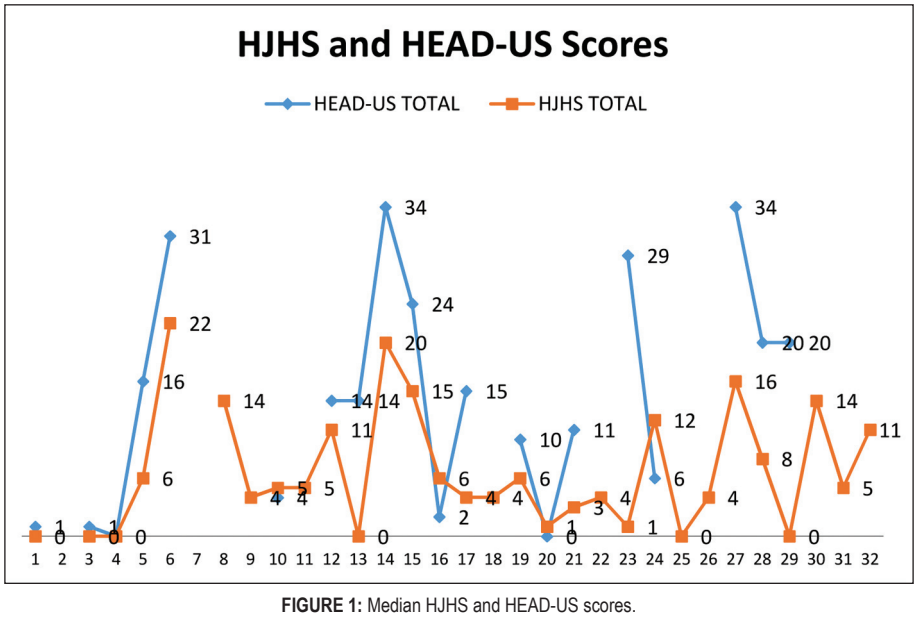

FIGURE 1: Median HJHS and HEAD-US scores.
HJHS: Hemophilia joint health score; HEAD-US: Haemophilia early arthropathy detection with ultrasound.

TABLE 1: HJHS and HEAD-US scores of patients with and without a history of arthropathy.

		Patient (n)	Mean (minimum-maximum)	p value
HJHS total	Arthropathy	21	8.6 (0-22)	0.006
	No arthropathy	9	2.3 (0-6)	
HEAD-US total	Arthropathy	14	19.9 (6-34)	0.005
	No artropathy	6	1.3 (0-4)	

HJHS: Hemophilia joint health score; HEAD-US: Haemophilia early arthropathy detection with ultrasound.

TABLE 2: HJHS and HEAD-US scores of 33 joints with a history of arthropathy.

	Arthropathy	n (%)	HJHS Median (minimum-maximum)	HEAD-US Median (minimum-maximum)
Right ankle	Yes	7 (21.2%)	1.7 (0-5)	6.0 (5-7)
	No		0. (0-2)	2.8 (0-7)
Left ankle	Yes	4 (12.1%)	0.7 (0-2)	5.0 (0-8)
	No		0.6 (0-4)	2.9 (0-8)
Right knee	Yes	9 (27.2%)	3.2 (0-7)	3.6 (0-8)
	No		0.9 (0-5)	0.7 (0-5)
Left knee	Yes	3 (9.0%)	4.0 (0-7)	4.0 (0-8)
	No		0.5 (0-7)	0.6 (0-6)
Right elbow	Yes	5 (15.1%)	4.0 (0-9)	5.0 (0-7)
	No		0.5 (0-4)	1.9 (0-6)
Left elbow	Yes	5 (15.1%)	2.6 (0-5)	5.2 (1-7)
	No		1.1 (0-7)	1.9 (0-7)

HJHS: Hemophilia joint health score; HEAD-US: Haemophilia early arthropathy detection with ultrasound.

diologically using ultrasonography, has been shown in different studies.[17,18] In addition to this correlation, joint findings can be detected earlier with HEAD-US. Altisent et al. also found HJHS and HEAD-US scores consistent in 91 (73%) of 126 pediatric patients.[19] In a study in which 167 patients and 976 joints were evaluated, although 14% of the patients had no history of bleeding and the HJHS score was 0, and findings of arthropathy were detected with HEAD-US.[20] In our study, the means of HJHS and HEAD-US were correlated. However, HJHS and HEAD-US scores were inconsistent in 7 (35%) of 20 patients. Our findings are compatible with the data regarding HEAD-US in the literature.

In the study of Sari et al., patients with and without arthropathy had HJHS scores of 5.7 and 10.8, respectively, and HEAD-US scores of 18.7 and 28.0, respectively. The median age of these cases is 11.7. The most common affected joints are the ankles.[21] According to Sari's study, although the median age was higher in our study, both joint scores were lower. However, as shown in Table 1, the difference between patients with and without arthropathy was significant for both scores, indicating that they were successful in demonstrating the presence of arthropathy. The most commonly affected joint was the right knee (n=9) and the least frequently affected joint was the left knee (n=3).

The reason for the few different results between HJHS and HEAD-US may be the false positives that can be seen with HEAD-US. In the study of Plut et al. that compared the findings of HEAD-US and MR, the rate of cases that could not be detected with MR but was considered false positive in favor of arthropathy with HEAD-US was 16.7. When these cases were evaluated in detail again with MRI, mild synovial hypertrophy in one elbow and two knees, small cartilage defect in two elbows and one ankle, and a small osteophyte in one knee were detected.[22]

The relatively low number of cases and the fact that the study was not prospectively and randomized planned constitute the limitations of the study.

CONCLUSION

A correlation was found between the HJHS and HEAD-US scores used in the evaluation of hemophilic arthropathy. However, HEAD-US is more sensitive than HJHS in detecting the early stage of arthropathy. In our study, this was observed in the ankle joint. If these scores are looked at once a year in the follow-up of hemophilia patients, overlooked treatment deficiencies and incompatibilities will be manifested. Therefore, it should be done routinely to all patients by hemophilia centers.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Kaan Kavaklı;* ***Design:*** *Kaan Kavaklı;* ***Control/Supervision:*** *Mehmet Can Uğur;* ***Data Collection and/or Processing:*** *Mehmet Can Uğur, İpek Tamsel, Necati Muhammet Tat;* ***Analysis and/or Interpretation:*** *Necati Muhammet Tat;* ***Literature Review:*** *Mehmet Can Uğur;* ***Writing the Article:*** *Mehmet Can Uğur;* ***Critical Review:*** *Kaan Kavaklı.*

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