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Systematic evaluation of hemophilic arthropathy in Lithuania

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ABSTRACT

Introduction: in patients with hemophilia, recurrent hemarthroses often lead to irreversible joint destruction. Thus, the condition of joints represents the adequacy of hemophilia management.
Aim: to evaluate the condition of joints with several standardized noninvasive methods in patients with hemophilia A and B in Lithuania.
Methods: structural joint damage was evaluated applying the World Federation of Hemophilia (Gilbert) scale and Hemophilia Joint Health Score. Functional joint status was assessed using performance-based tools (Functional Independence Score in Hemophilia, Keitel Functional Test and 6-minute Walk Test) and self-assessment questionnaire (Hemophilia Activities List). Two assessments were carried out with the interval of one year, and the outcomes were compared.
Results: twenty-one pediatric and 21 adult patients were enrolled into the study. 81.0% of children received prophylaxis, while the adults were mostly treated on-demand (61.9%). At baseline, mean HJHS score for children was as low as 6.6. In adults, structural joint damage was more advanced: mean total HJHS score was 30.1, and mean WHF-PES was 23.2. The results of performance-based and self-assessed functional evaluation in adults were lower than those in children. Over a year, the condition of joints worsened more markedly in adults than in children. In adults, strong correlation existed between FISH and HAL, as well as between both tools of physical examination.
Conclusion: the condition of joints in Lithuanian pediatric patients with hemophilia is satisfactory. The joints of adults are more affected, and the damage progresses more quickly. The role of physical activity is beneficial, but needs to be investigated further.
Keywords: hemophilia, bleeding, joint damage, hemarthrosis, prophylaxis, on-demand treatment

Introduction

Spontaneous or traumatic bleeding is the most common manifestation of hemophilia. 90% of bleeding events occur in the musculoskeletal system and in 80% of these cases hemorrhage sites include joints [1]. Recurrent intra-articular bleeding (hemarthrosis) induces synovial hypertrophy and cartilage damage and results in gradual, but irreversible joint destruction (hemophilic arthropathy) [2]. It usually starts in childhood, but clinical signs show up around the second decade of life [3]. Bleeding related joint damage is associated with persisting pain and leads to the loss of function and long-term physical and psychosocial impairment [4].

Hemophilia can be well controlled with regular infusions of the deficient clotting factor either for the treatment of hemorrhagic episodes, or prophylactically [5]. However, on-demand treatment does not provide sufficient control of recurrent joint bleeding and leads to more severe joint damage [6]. On the contrary, prophylaxis reduces the number and severity of hemarthroses, ultimately resulting in a better joint preservation [7, 8].

The extent of musculoskeletal damage reflects the efficacy of hemophilia control. Hence, there is a need for accurate and sensitive methods for the assessment of joint damage [9]. To enable the international cooperation and research it is essential to standardize the evaluation methods, especially in the light of the disease rareness [10].

There are several different schemes for the evaluation of physical joint condition. One of the first schemes known as Gilbert score was proposed by World Federation of Hemophilia (WFH) [11]. However, it is not sensitive enough to detect early joint alterations and is not suitable for children [12]. To resolve these issues, an instrument to evaluate mild joint changes known as Hemophilia Joint Health Score (HJHS) was developed. The evaluation showed promising accuracy results in children and adolescents [13, 14].

While WFH (Gilbert) and HJHS schemes estimate the degree of structural changes, other tools were developed for the assessment of the functional capability of hemophilia patients. These tools are based either on self-assessment questionnaires (Hemophilia Activities List [HAL]) or objective performance evaluation methods (Functional Independence Score in Hemophilia [FISH]) [15, 16]. Also, tests measuring functional capacities in patients with other chronic conditions are feasible for hemophilia patients as well (Keitel Functional Test [KFT], 6-minute Walk Test [6MWT]) [17, 18].

The aim of this study was to evaluate the condition of joints using several standardized noninvasive methods in patients (children and adults) with hemophilia A and B in Lithuania.

Materials and Methods

This prospective study was conducted in Lithuania at three health care centers: Children‘s Hospital, Affiliate of Vilnius University Hospital Santaros Klinikos (Vilnius), Lithuanian Sports University (Kaunas) and Jurando Physiotherapy Center (Klaipeda). The study continued for two years.

The study was approved by Lithuanian Bioethics Committee. Written informed consent was obtained from all study subjects or their parents.

Subjects

Patients diagnosed with hemophilia A or B, both children and adults, were eligible for the study. According to the database of Children’s Hospital, Affiliate of Vilnius University Hospital Santaros Klinikos and Lithuanian Hemophilia Society, there are 150 patients with hemophilia in Lithuania. All of them were invited to participate in the study via the webpage www.hemofilija.lt. Subjects who experienced an acute bleeding episode within 2 weeks or those with

other accompanying congenital blood clotting disorders were not eligible.

Assessments

Four physiotherapists assessed clinical joint condition using the following tests: WFH (Gilbert) score (only for adults), HJHS, FISH, KFT, and 6MWT.

Two assessments were carried out one year apart (in 2014 and 2015) and each time subjects were examined by the same physiotherapists. During the first visit, physiotherapists provided detailed individual recommendations for physical exercises and self-management.

The WFH (Gilbert) score measures the health of the joints most commonly affected by bleeding in hemophilia (knees, ankles and elbows), with regard to their structure and function [11]. It encompasses 4 sections: estimation of pain (0-3 points), bleeding (0-3 points), physical examination (0-12 points), and radiographic examination (0-13). Radiographic evaluation was omitted in this study. Physical examination score (PES) contains the following parameters: swelling, muscle atrophy, axial deformity, crepitus, range of motion, flexion contracture and instability. A PES of zero denotes normal joints; 68 points correspond to the worst level of arthropathy [11].

The HJHS (version 2.1) is an 11-item scoring tool for assessing joint impairment, primarily in children aged 4–18 years. Six index joints (elbows, knees and ankles) are assessed on the following 8 parameters: swelling (0–3), duration of swelling (0–1), muscle atrophy (0–2), crepitus on motion (0–2), flexion loss (0–3), extension loss (0–3), pain (0–2) and strength (0–4), and a total score is calculated as the sum of all joint scores. Also, the gait is evaluated (0-4) assessing 4 skills: walking, stairs, running, and hopping on one leg. Total HJHS score ranges from 0 to 124 (maximal impairment) [13].

The FISH is an objective performance-based assessment instrument to measure the functional independence of patients [16]. It evaluates 8 items of activity divided into three categories: self-care (eating, grooming, bathing and dressing), transfer (chair and squatting) and mobility (walking, going up stairs and running). Activities are graded from 1 to 4; the total score may range from 8 to 32 points with 32 indicating the highest level of functional independence [16].

The 6MWT is a self-paced walking test used to assess functional capacity in patients with chronic conditions. The main outcome is the distance that a subject can walk in 6 minutes. Subjects are instructed to walk between two cones positioned 30 meters apart as fast as possible (without running) at a steady pace for 6 minutes. Before and after the 6MWT, blood pressure and heart rate are measured [17].

The KFT examines joint functional performance by assessing 24 simple movement patterns for both upper and lower extremities. Joint range of motion and muscular activity is evaluated in 3 sites: hands and wrists (9 items), shoulders (2 items) and lower limbs. 15 items are assessed bilaterally (the other 9 notably assess walking or change of position) and an overall score is awarded to them. The scores for each of the items are different, varying from 0 to 2 up to 0 to 6. The minimum total score is 4 (normal), and the maximum score 100 (severe) [18]. An adapted and approved version of the KFT with 21 movement patterns and a maximum value of 95 points corresponding to normal functional ability is used in Lithuania [19].

The Hemophilia Activities List is a hemophilia-specific self-assessment questionnaire which measures the impact of hemophilia on self-perceived functional abilities in adults (HAL) or children (PedHAL) [15, 20]. The questionnaire contains multiple choice questions in 7 domains: lying/sitting/kneeling/standing, functions of the legs,

functions of the arms, use of transportation, self-care, household tasks, leisure activities and sports. Overall score, as well as scores for each of the domains, and for three components (activities involving the upper extremities, basic activities involving the lower extremities and complex activities involving the lower extremities) were calculated. Normalized scores for the domains, components and full questionnaire range from 0 to 100, where 100 represent the best possible functional status [15]. Adult patients and children over eight years of age completed the questionnaire themselves. For younger children (aged 4-7 years), a parent/proxy version of PedHAL was completed by parents.

Demographic data and disease characteristics of subjects were extracted from their medical records.

Statistics

The descriptive statistics were applied for the data analysis. The results were presented as mean and median values (± SD). The data of the first and the second measurements were compared applying the Wilcoxon signed-rank test and McNemar test. Non-parametric Spearman's correlation coefficient was used to evaluate the correlation between different outcome assessment instruments (between HJHS and Gilbert scores for adults and between FISH and HAL scales for children and adults). Correlation coefficient equal or exceeding 0.80 was considered to indicate a very strong correlation, falling within the interval of 0.60 – 0.79 was considered to indicate a strong correlation, while values of 0.40 – 0.59 were considered as moderate and values of 0.2– 0.39 as a weak correlation [21]. The significance level for all tests was set on α=0.05.

Results

Twenty-one pediatric and 21 adult subjects were enrolled into this study. Mean age (± standard deviation [SD]) of children was 9.8±4.5 years, and mean age of adult subjects was 32.8±9.8 years. Nineteen children and 19 adults (90.5%) attended the second evaluation after approximately one year. Those who did not attend the second evaluation were excluded from comparative analysis. At the time of the first evaluation two children were younger than four years, these children were eliminated from PedHAL analysis. The majority of subjects had severe hemophilia A. Two adult subjects had hemophilia A with inhibitors. Most of the children (81.0%) received prophylaxis treatment while the adults were mostly treated on-demand (61.9%). The demographic and clinical characteristics of subjects are shown in Table 1.

Table 1. Baseline demographic and clinical characteristics of study subjects

Characteristics	Children N=21	Adults N=21
Age, years		
mean ± SD	9.8 ± 4.5	32.8 ± 9.8
min-max	3-17	20-50
Type of hemophilia, n (%)		
hemophilia A	19 (90.5)	16 (76.2)
hemophilia A with inhibitors	0	2 (9.5)
hemophilia B	2 (9.5)	3 (14.3)
Severity of hemophilia, n (%)		
mild	1 (4.8)	0
moderate	3 (14.3)	3 (14.3)
severe	17 (81.0)	18 (85.7)
Treatment regimen, n (%)		
on-demand	4 (19.0)	13 (61.9)
prophylaxis	17 (81.0)	8 (38.1)
primary prophylaxis	6 (28.6)	0
secondary prophylaxis	11 (52.4)	8 (38.1)
Joint condition, mean ± SD		
WFH PES score	N/A	23.2±10.5
HJHS total score	6.6±7.6	30.1±15.7
FISH total score	31.0±3.5	27.4±3.8
6MWT	431.2±61.8	393.3±70.8
KFT score	89.7±11.5	78.3± 14.3
Modified KFT score	41.8±7.2	38.4±6.2
HAL/PedHAL	87.3±14.4	70.1±16.9

WFH, World Federation of Hemophilia; PES, Physical Evaluation Score; HJHS, Hemophilia Joint Health Score; FISH, Functional Independence Score in Hemophilia; 6MWT, Six-Minute Walk Test; KFT, Keitel Functional Test; HAL, Hemophilia Activities List; PedHAL, Pediatric Hemophilia Activities List

In adults, the mean WFH PES for all joints was 23.2. The mean sum of pain, bleeding and physical examination was 30.5. The HJHS total score was 30.1 (range, 6 to 64). As expected, HJHS score in pediatric subjects was lower, with the mean value of 6.6 (range, 0 to 21) (Table 2). The most affected joints were left elbow and ankles in children (scores above 1) and right ankle and knees in adults (scores above 5).

Performance-based functional ability scores (FISH) almost reached maximal values in children and were only slightly decreased in adults (mean values 31.0 and 27.4, respectively, the normal function score being 32). During 6MWT, children walked on average 38 meters further than adults. The mean distance was 431.2 meters in children and 393.3 meters in adults. The outcomes of KFT showed that the joint functionality of patients with hemophilia is reduced. Mean KTF score was 89.7 in children and 78.3 in adults.

The PedHAL scale demonstrated that functional activity of children with hemophilia remains high. Almost all domain evaluations were above 90 (except "Leisure activities and sports", which was 87.3 and "Lying down/sitting/kneeling/standing", which was 89.4). The adults' scores of HAL scale were lower, the mean value being 70.1 (Table 3). Leisure activities and sports, complex lower extremity activities and functions of the legs caused the most difficulties for adult subjects (mean scores, 57.9, 59.2 and 59.2, respectively).

Table 2. Comparison of joint condition at two evaluations one year apart in children (n=19)

Assessment tools	First evaluation	Second evaluation
Joint health assessment based on physical examination		
HJHS		
HJHS total		
mean±SD	6.1±7.1	6.5±6.5
median (IQR)	2.0 (11)	4 (8)
min-max	0-21	0-21
Gait global score		
mean±SD	0.1±0.5	0.6±0.8
median (IQR)	0.0 (0)	0.0 (1)*
min-max	0-2	0-2
Joint total		
mean±SD	6.0±7.1	5.9±6.3
median (IQR)	2.0 (10)	2.0 (7)
min-max	0-21	0-21
Left elbow		
mean±SD	1.2±2.4	1.1±2.5
median (IQR)	0.0 (1)	0.0 (1)
min-max	0-10	0-11
Right elbow		
mean±SD	1.0±2.1	0.8±2.1
median (IQR)	0.0 (1)	0.0 (1)
min-max	0-9	0-9
Left knee		
mean±SD	0.5±1.0	0.5±0.8
median (IQR)	0.0 (1)	0.0 (1)
min-max	0-4	0-3
Right knee		
mean±SD	0.4±0.8	0.4±0.8
median (IQR)	0.0 (0)	0.0 (1)*
min-max	0-3	0-3
Left ankle		
mean±SD	1.2±1.8	1.1±1.8
median (IQR)	1.0 (1)	0.0 (2)
min-max	0-7	0-7
Right ankle		
mean±SD	1.8±2.4	1.8±1.9
median (IQR)	1.0 (4)	1.0 (1)
min-max	0-7	0-7
Assessment of activities and/or participation		
Objective tools		
Total FISH score		
mean±SD	31.7±0.6	31.7±1.0
median (IQR)	32.0 (1)	32.0 (0)*
min-max	30-32	28-32
6MWT, m		
mean±SD	432.3±63.2	424.1±74.4
median (IQR)	435.0 (95)	454.0 (92)
min-max	330-548	250-534
KFT score		
mean±SD	92.2±3.2	92.3±2.8
median (IQR)	93.0 (5)	94.0 (5)
min-max	85-95	87-95
Modified KFT score		
mean±SD	43.3±2.3	43.4±2.2

median (IQR)	44.0 (3)	44.0 (3)
min-max	37-45	37-45
Self-reported tools		
PedHAL		
Lying down/sitting/kneeling/standing		
mean±SD	89.9±12.0	89.8±13.8
median (IQR)	96.0 (14)	96.0 (11)
min-max	64-100	50-100
Functions of the legs		
mean±SD	93.9±8.9	92.2±11.9
median (IQR)	96.0 (7)	96.0 (8)
min-max	65-100	64-100
Functions of the arms		
mean±SD	95.1±6.8	93.8±8.1
median (IQR)	100.0 (9)	95.0 (10)
min-max	80-100	70-100
Use of transportation		
mean±SD	99.2±2.3	99.2±2.3
median (IQR)	100.0 (0)	100.0 (0)
min-max	93-100	93-100
Self-care		
mean±SD	98.1±4.7	98.2±4.7
median (IQR)	100.0 (1)	100.0 (0)
min-max	82-100	82-100
Household tasks		
mean±SD	98.7±3.0	98.4±3.8
median (IQR)	100.0 (0)	100.0 (0)
min-max	91-100	88-100
Leisure activities and sports		
mean±SD	91.4±7.9	91.4±13.0
median (IQR)	93.0 (15)	100.0 (15)
min-max	75-100	52-100
PedHAL[**] Total score		
mean±SD	89.8±9.2	92.1±7.7
median (IQR)	92.0 (14)	94.0 (11)
min-max	70-100	75-100
Adaptations and using an aid[***]		
Use of modified bike/car with adaptations, n (%)	2 (11.8)	2 (11.8)
Use of aids when carrying out certain activities, n (%)	0	0

HJHS, Hemophilia Joint Health Score; FISH, Functional Independence Score in Hemophilia; 6MWT, Six-Minute Walk Test; KFT, Keitel Functional Test; PedHAL, Pediatric Hemophilia Activities List; IQR, interquartile range

****p<0.05 Wilcoxon Signed Ranks Test***

***** The comparative analysis of PedHAL was made with data of 17 children***

***** McNemar Test***

Table 3. Comparison of joint condition at two evaluations one year apart in adults (n=19)

Assessment tools	First evaluation	Second evaluation
Joint health assessment based on physical examination		
HJHS		
HJHS total		
mean±SD	29.4±16.5	34.0±16.5
median (IQR)	29.0 (19)	35.0 (33)*
min-max	6-64	10-58
Gait global score		
mean±SD	1.7±1.2	2.7±1.5
median (IQR)	2.0 (2)	3.0 (3)*
min-max	0-4	0-4
Joint total		
mean±SD	27.7±15.6	31.3±15.6
median (IQR)	26.0 (18)	32.0 (30)*
min-max	6-60	9-54
Left elbow		
mean±SD	3.7±3.7	4.7±4.1
median (IQR)	4.0 (6)	4.0 (9)*
min-max	0-10	0-11
Right elbow		
mean±SD	4.0±3.8	5.5±4.3
median (IQR)	2.0 (7)	7.0 (8)*
min-max	0-11	0-11
Left knee		
mean±SD	5.5±4.2	5.7±3.7
median (IQR)	5.0 (8)	7.0 (5)
min-max	0-13	0-12
Right knee		
mean±SD	5.0±4.4	5.8±4.4
median (IQR)	5.0 (8)	6.0 (9)*
min-max	0-14	0-14
Left ankle		
mean±SD	4.3±3.1	4.8±2.7
median (IQR)	4.0 (6)	5.0 (4)
min-max	0-10	0-10
Right ankle		
mean±SD	5.3±3.3	4.7±2.8
median (IQR)	4.0 (6)	5.0 (5)
min-max	1-12	0-10
Gilbert (WFH score)		
Physical examination score (PES)		
mean±SD	22.9±10.4	26.6±10.7
median (IQR)	23.0 (16)	23.0 (21)*
min-max	6-44	8-44
PES+pain+bleeding		
mean±SD	30.4±13.4	33.3±13.2
median (IQR)	31.0 (14)	30.0 (18)*
min-max	6-58	12-61
Assessment of activities and/or participation		
Objective tools		
Total FISH score,		
mean±SD	27.5±3.9	26.7±4.7
median (IQR)	29.0 (7)	28.0 (8)
min-max	21-32	17-32

6MWT[**], m		
mean±SD	392.4±73.2	394.35±100.0
median (IQR)	370.5 (115)	380.0 (93)
min-max	300-581	265-700
KFT score		
mean±SD	78.2±13.8	78.0±14.3
median (IQR)	80.0 (18)	81.0 (19)
min-max	51-93	47-94
Modified KFT score		
mean±SD	38.6±6.0	37.9±7.1
median (IQR)	40.0 (6)	39.0 (9)
min-max	24-45	20-48
Self-reported tools		
HAL		
Lying down/sitting/kneeling/standing		
mean±SD	62.7±24.0	67.2±23.9
median (IQR)	65.0 (28.5)	70.0 (43.0)
min-max	7.5-100.0	22.5-100.0
Functions of the legs		
mean±SD	61.3±23.2	67.4±23.9
median (IQR)	62.0 (31)	73.0 (37)*
min-max	13-100	25-100
Functions of the arms		
mean±SD	70.6±21.2	77.6±20.9
median (IQR)	75.0 (30)	85.0 (25)*
min-max	25-100	30-100
Use of transportation		
mean±SD	74.7±24.6	76.3±20.9
median (IQR)	80.0 (34)	80.0 (33)
min-max	13-100	40-100
Self-care		
mean±SD	85.0±15.9	83.9±17.8
median (IQR)	92.0 (26)	84.0 (26)
min-max	52-100	36-100
Household tasks		
mean±SD	83.2±11.4	84.3±17.6
median (IQR)	83.0 (16)	90.0 (21)
min-max	63-100	30-100
Leisure activities and sports		
mean±SD	59.9±22.9	77.6±20.0
median (IQR)	62.0 (36)	80.0 (25)*
min-max	18-100	26-100
Upper Extremity Activities		
mean±SD	72.8±12.8	84.1±14.6
median (IQR)	73.0 (11)	91.0 (20)*
min-max	51-97	47-100
Basic Lower Extremity Activities		
mean±SD	79.4±15.6	70.6±25.8
median (IQR)	80.0 (21)	76.0 (26)
min-max	40-100	10-100
Complex Lower Extremity Activities		
mean±SD	60.3±23.2	62.7±23.3
median (IQR)	67.0 (33)	68.0 (32)
min-max	13-100	13-100
HAL Total score		
mean±SD	71.9±15.4	74.0±17.4
median (IQR)	73.0 (25)	77.0 (32)
min-max	37-97	31-97

Adaptations and using an aid[***]		
Use of modified bike/car with adaptations, n (%)	10 (52.6)	8 (38.1)
Use of aids when carrying out certain activities, n (%)	5 (23.8)	4 (19.0)

HJHS, Hemophilia Joint Health Score; WFH, World Federation of Hemophilia; FISH, Functional Independence Score in Hemophilia; 6MWT, Six-Minute Walk Test; KFT, Keitel Functional Test; HAL, Hemophilia Activities List; IQR, interquartile range
p<0.05 Wilcoxon Signed Ranks Test
**** The comparative analysis of 6MWT was made with 17 adults***
**** McNemar Test***

As compared with the baseline, only HJHS global gait and right knee scores slightly decreased in children at the second assessment (Table 2). There were no significant alterations in the outcomes of performance-based objective or self-assessment tools.

In adults, joint damage progressed over a year (Table 3). All parameters on the WFH scale (pain, bleeding and physical examination scores) increased at the second evaluation. Total HJHS score, gait global score and all individual joint scores except left knee and both ankles also increased. While the objective activity measurements (FISH, 6MWT, and KFT) showed no differences, some of HAL domains suggested the improvement in self-perceived functional abilities. Adult subjects better evaluated their functions of legs and arms, as well as the ability to perform sports and leisure activities. Noteworthy, these domains had lowest scores at the baseline. The score of upper extremity activities was also better at the second evaluation.

In children, there was no correlation between the objective assessment (FISH) and self-reported bleeding or limitations in activities (PedHAL) (Spearman's correlation coefficient, 0.128; p=0.601). In adults, a strong correlation existed between FISH and HAL scores (Spearman's correlation coefficient, 0.598; p=0.0004) well as between both tools of physical examination (HJHS and WHF PES, Spearman's correlation coefficient, 0.897; p<0.0001).

Discussion

Our results indicated that the condition of joints in a selected sample of pediatric hemophilia patients was quite well preserved. The mean HJHS value of 6.6 was slightly higher than reported in countries with well-established primary prophylaxis [22-25]. To compare, the UK group reported mean HJHS scores of 0.4 in children < 10 years old and 4.1 in children > 10 years old receiving prophylaxis [24]. Prophylactic clotting factor replacement in Lithuania was implemented in 2007. Thus, most of children included in the current study received prophylaxis. Yet, secondary prophylaxis was more common than the primary, and four children were still on on-demand protocol. However, mean HJHS score in our study was clearly lower than presented in studies with on-demand treated children [26-28]. These findings suport the results from a comparative study of Lithuanian boys treated on-demand and Danish boys receiving prophylaxis which were extremely different: the mean HJHS score of 27.4 vs. 3.3, respectively [29].

The outcomes of performance-based instruments showed that the functionality of pediatric subjects was not considerably declined. The mean values of FISH were almost maximal and only minimal restrictions in self-care, transfer and mobility were identified. 6MWT and KFT results were similar to those of patients with chronic juvenile arthritis receiving treatment [30, 31]. PedHAL outcomes demonstrated that the limitations of children's activities were infrequent. PedHAL scores were even slightly

higher than those of prophylactically treated children with lower HJHS scores [25].

In our study, adults were mostly treated on-demand, therefore, joint deterioration was more remarkable. Even those few adults who received prophylactic clotting factor replacement were most likely already been affected by the previous suboptimal care. The results of structural joint evaluation were worser than those in adults treated prophylactically since childhood, but consistent with results in patients treated on-demand [32-35]. This applies also for the FISH score which was decreased to the levels reported in other studies in patients treated on on-demand protocol [34]. Mean 6MWT values were by 174 meters lower than those in healthy adults and only slightly higher than in patients with degenerative joint disease [36, 37]. Mean KFT values were also reduced and were comparable to those in patients with rheumatoid arthritis [38].

Reduced HAL scores in adult subjects indicate that their self-perceived functional abilities were rather limited. On the contrast, patients on prophylaxis, especially those on high-dose regimen, almost do not experience any restrictions in their activities [33].

Repeated evaluation of joint condition after a year revealed more changes in adult subjects than in children. In adults, significant increase was observed in both HJHS total score and WFH-PES score. On the contrary, HJHS total score in pediatric subjects did not change significantly. Also, more individual joints in adult group showed worsened condition compared to the children, implying that joint condition deteriorates more quickly in adults.

Despite worsened physical joint condition in adults, performance tests did not show meaningful alterations. The interval between the two evaluations might have been too short to reveal significant changes. On the other hand, this might indicate the positive effect of physiotherapy on patients' functional status, since after the first evaluation all subjects were given individual recommendations on physical activity and self-management. Physical exercises strengthen muscles and help to maintain their flexibility, providing better support for joints and decreasing the risk of trauma and bleeding [39, 40]. However, no data on adherence to the recommendations given were collected in this study.

Interestingly, some parameters of self-reported activity (HAL score) in adult subjects improved over a year. Due to complications associated with recurrent bleeding into joints, people with hemophilia tend to avoid physical activity. Besides, until recently, hemophilia patients were not encouraged to exercise at all. Consultations with physiotherapists and receiving an advice on careful exercising might have enhanced patients' self-esteem and this resulted in improved HAL scores.

Our study might be regarded as the first one reporting HJHS scores in adult patients treated with on-demand protocol. HJHS scale was primarily designed for pediatric evaluation and information about its application to adult population is scarce. The Dutch group reported the median HJHS score of 5.5 in 22 teenagers and young adults receiving prophylaxis [32]. In another study, which compared two prophylaxis regimens in teenagers and adults, patients treated with the intermediate-dose regimen had slightly higher HJHS scores than those receiving high-dose prophylaxis (median, 9.0 vs 7.0) [33]. In spite of suboptimal hemophilia management, adult HJHS scores in our study did not reach the maximum values. This might indicate that in the case of substantial joint damage resulting from chronic process, the HJHS score does not allow precise estimation of joint condition. The HJHS might be more feasible in adults with no severe joint damage (e.g., treated prophylactically). Although we found a strong correlation between HJHS and WFH-PES, WFH scale showed more advanced joint impairment than HJHS - the mean WFH-PES

score comprised ~34% of the possible maximum score, to compare to mean HJHS total score comprising 23% of the maximum score. WFH-PES findings were consistent with the results of studies in patients with on-demand treatment [35, 36]. Taking into account the applicability, the consistency of results across different studies, as well as the scope and significance of information provided, the WFH score might serve as the tool of the first choice for the assessment of adult patients with severe hemophilia and on-demand treatment.

This study provided valuable insights into the joint condition of hemophilia patients in Lithuania. However, there were several shortcomings in the design of the study. Less than one third of the total Lithuanian hemophilia patients were included in the study. As the invitation was placed on the website only, higher motivated patients were more likely to get enrolled. Personal encouragement from hematologists or nurses towards less responsive patients or those living further from the study centers, could have led to the greater number of participants and more adequate representation of Lithuanian hemophilia population. Also, no data were collected on the adherence to the individual recommendations on physical activity which could provide more understanding about its impact to the functional status of hemophilia patients.

Conclusion

The condition of joints in Lithuanian pediatric patients with hemophilia is satisfactory and stable demonstrating the beneficial impact of prophylaxis. The joints of adults are more affected, and the damage progresses more quickly. Regarding the consequences of hemarthroses, the management of adults with hemophilia in Lithuania is still not optimal. On-demand treatment regimen does not provide sufficient prevention of joint damage. The role of physical activity might be beneficial, but still needs to be investigated further.

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