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Review Article

Hemophilic Arthropathy: Basic Records for Proper Joint and Musculoskeletal Health Care in Patients with Hemophilia

Querol-Giner F, Perez-Alenda S and Querol-Fuentes F*

Physiotherapy Department, University of Valencia, Spain

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Corresponding author:
Felipe Querol Fuentes,
Physiotherapy Department, University of Valencia, C / Gasc Oliag N 3, 46010 Valencia, Spain, Tel: +34 963983853;
Email: Felipe.Querol@uv.es

ABSTRACT

Hemophilia is a genetic disease, classified as a rare disease and affects approximately 1 in every 5,000 live births male. It is classified as severe, moderate and mild depending on the percentages of plasma circulating coagulation factors. It is characterized by hemorrhagic episodes that, in the absence of treatment, occur spontaneously in muscles and joints, causing hemophilic arthropathy and greatly influencing quality of life.

Joint health care in the hemophilia patient involves, in addition to factor replacement therapy, very strict monitoring to detect early signs of the joint degenerative process caused by even subclinical hemorrhages.

The World Federation of Haemophilia establishes health recommendations that include the use of specific forms for clinical and radiological evaluation that allow the evolutionary control of the disease.

The objective of this work is the description of the medical care that patients receive or should receive and the universal use forms that allow the control of joint health.

It concludes by pointing out the importance of care and the unification of criteria for the evolutionary control of the disease.

INTRODUCTION

Hemophilia is a genetic coagulation disorder that continues to affect approximately 1 in 5,000 live births and is characterized by bleeding involving the musculoskeletal system with serious implications for physical activity and quality of life [1-4].

Two realities directly related to joint health are identified in hemophilia in today's world: 1) populations of hemophilia (PWH) patients who have access to factor replacement therapy and 2) those who do not have adequate hematological treatment. In both populations, musculoskeletal disorders are the most frequent and limiting daily life activities and quality of life.

There are also two health care needs for the patient with hemophilia:

1) The first need, for the evolutionary control of the disease, the provision of regulated assistance in medical consultation in Haemophilia Centers by multidisciplinary teams led by hematologists.

2) And the second need, the possibility of early care after an acute bleeding episode.

Some tools, although with specific interest in the pharmacokinetics of coagulation factors, also monitor acute bleeding processes and physical activity, some examples

are: FlorioTM, WAPPS Hemo (Population Pharmacokinetic Service accessible on the web - Hemophilia), Haemoassist® and MyPKFiT™ [5-7].

Considering, as a minimum, the inevitable possibility of accidental musculoskeletal injuries, hemarthrosis and muscular hematomas, which mainly lead to hemophilic arthropathy, the objective of this work is to show care protocols that affect the criteria of joint health care.

The following section describes the specific data that is recorded and is summarized on specific forms. The results and conclusions of the use of unified forms are obvious, since they have useful records for health control.

BASIC RECORDS, FORMS AND SCORES

First, we consider the attention in consultation and the two possibilities that represent the need of the patient with hemophilia.

Attention in medical consultation

Attendance at the hospital or point of care of the patient with hemophilia can only be for two reasons:

1) An acute bleeding problem (Figure 1) or

2) The systematic clinical review program (1 or 2 times a year in severe hemophilia) for the global evolutionary control of the disease. In either case, a minimum data protocol to be recorded must be considered [8].

The minimum data collected for the consideration of clinical discharge from hemarthrosis are shown in Table 1 and the Table 2 shows, briefly, the items to register, the concept and the details (Table 1).

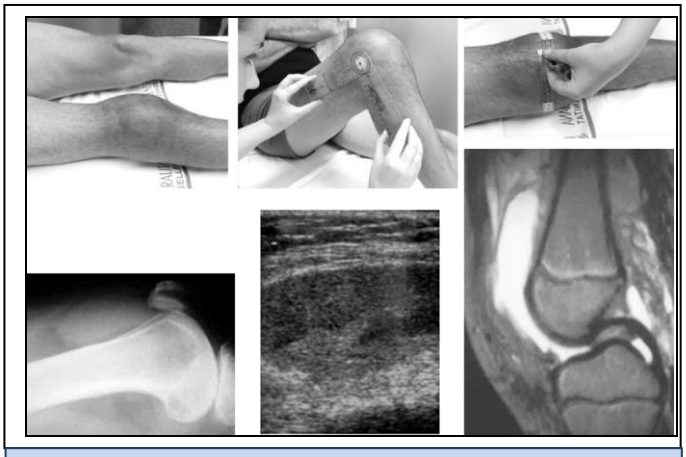


Figure 1: Acute hemorrhagic process: clinical evaluation of the ROM, swelling and evaluation by radiological, echographic and MR images.

Table 1: Data recorded for the evolutionary control of hemarthrosis and the consideration and score 0 points equivalent to the normality and resolution of the acute process.

Pain:	0: NO
Swelling	0: Not observed
Active ROM without pain:	0: Value in degrees without discomfort equal to degrees as in the state prior to hemarthrosis
Effort / walking without pain:	0: As in the situation before the problem
Discharged from acute process by echography:	Return to PREVIOUS SITUATION or CHRONICITY CONSIDERATION (of the new image) with the requirement of a new SCORE (HEAD-US)

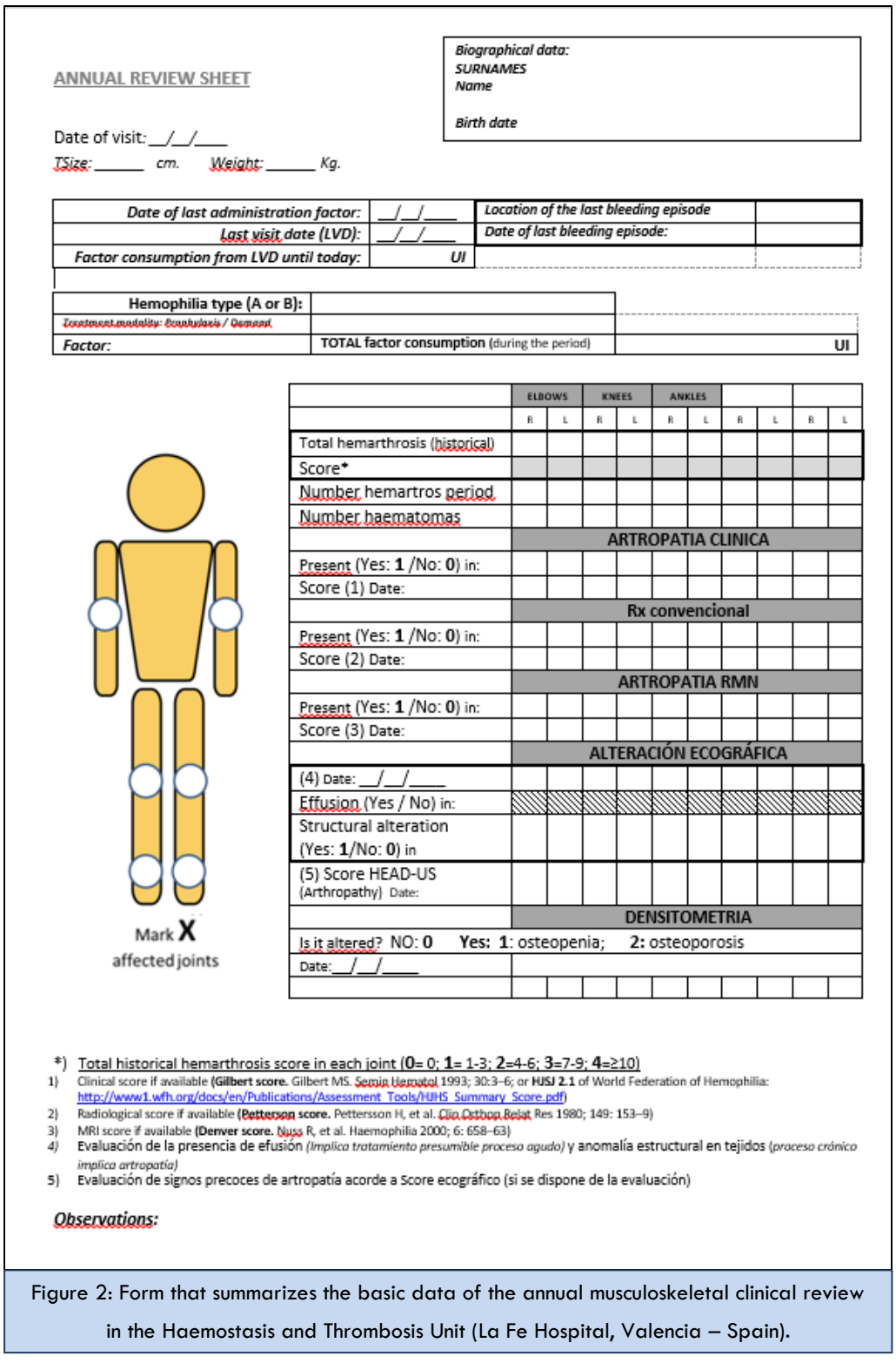
Table 2: Basic concepts of a standard program, which target the musculoskeletal health of the hemophilia patient.

Items	Concepts	Details
Date	Of the current visit	To establish control
Review period	Date of the last routine check-up	It is essential to know the number of bleeding episodes that occurred in the period
Routine check	The existence or absence of musculoskeletal problems with factor requirements is noted in the period since the last routine review visit	Problems (if any) in the joints or areas where they have existed are detailed
Hemophilia type and severity	A or B and severe, moderate or mild	It is common to highlight this, as well as verify the type of commercial factor that is used
Treatment modality	On demand or prophylaxis	The dose and frequency are usually indicated.
Data last factor administration	Dose, date and time	Essential in severe hemophilia to safely perform exploratory maneuvers
Current size and weight	Control of obesity	Important for measuring body mass index and dietary and physical activity recommendations
Physical activity	Minimum: sedentary or active	Use of forms is recommended, for example FISH (Functional Independence Score in Hemophilia), IPAQ short version (International Physical Activity Questionnaire)
Sport	If you do it regularly and what	Frequency of sports practice
Clinical score	Date	Score type (HJHS, Gilbert, etc.) and its global score
Score Rx	Last date (if available)	Pettersson score (global score of the 6 key joints)
Ultrasound score	Date	HEAD-US or basic protocol of ultrasound normality yes or no
Score MR	Last date (if available)	Denver score or at least indicate the presence / absence of injury
Densitometry	Date (if available)	At a minimum note normality, osteopenia or osteoporosis

Regarding the medical review and specifically related to joint and musculoskeletal health, the data is recorded by a physical therapist or a doctor specializing in rehabilitation and physical medicine. A basic summary of the

records in the medical record is shown in Table 2, and the forms / scores recommended by the World Federation of Hemophilia (WFH) are described below (Table 2).

Some centers use graphic forms that provide a summary of each joint and a visual impression of the joint overall. Figure 2 shows the annual revision form used by the Hemostasis and Thrombosis Unit of the LA FE Polytechnic and University Hospital in Valencia (Spain) [9] (Figure 2).



ANNUAL REVIEW SHEET

Biographical data:
SURNAMES
Name

Birth date

Date of visit: __/__/____

TSize: _____ *cm.* *Weight:* _____ *Kg.*

Date of last administration factor:	__/__/____	*Location of the last bleeding episode*	
Last visit date (LVD):	__/__/____	*Date of last bleeding episode:*	
Factor consumption from LVD until today:	*UI*		

Hemophilia type (A or B):		
~~Treatment modality: Prophylaxis / Demand~~		
Factor:	**TOTAL factor consumption** (during the period)	**UI**

	ELBOWS		KNEES		ANKLES					
	R	L	R	L	R	L	R	L	R	L
Total hemarthrosis (historical)										
Score*										
Number hemartros period										
Number haematomas										
	ARTROPATIA CLINICA									
Present (Yes: **1** /No: **0**) in:										
Score (1) Date:										
	Rx convencional									
Present (Yes: **1** /No: **0**) in:										
Score (2) Date:										
	ARTROPATIA RMN									
Present (Yes: **1** /No: **0**) in:										
Score (3) Date:										
	ALTERACIÓN ECOGRÁFICA									
(4) Date: __/__/____										
Effusion (Yes / No) in:										
Structural alteration (Yes: **1**/No: **0**) in										
(5) Score HEAD-US (Arthropathy) Date:										
	DENSITOMETRIA									
Is it altered? NO: **0** **Yes: 1**: osteopenia; **2:** osteoporosis										
Date: __/__/____										

Mark **X** affected joints

*) Total historical hemarthrosis score in each joint (**0**= 0; **1**= 1-3; **2**=4-6; **3**=7-9; **4**=≥10)

1) Clinical score if available (**Gilbert score.** Gilbert MS. Semin Hematol 1993; 30:3–6; or **HJSJ 2.1** of World Federation of Hemophilia: http://www1.wfh.org/docs/en/Publications/Assessment_Tools/HJHS_Summary_Score.pdf)
2) Radiological score if available (**Petterson score.** Pettersson H, et al. Clin Orthop Relat Res 1980; 149: 153–9)
3) MRI score if available (**Denver score.** Nuss R, et al. Haemophilia 2000; 6: 658–63)
4) Evaluación de la presencia de efusión *(Implica tratamiento presumible proceso agudo)* y anomalía estructural en tejidos *(proceso crónico implica artropatía)*
5) Evaluación de signos precoces de artropatía acorde a Score ecográfico (si se dispone de la evaluación)

Observations:

Figure 2: Form that summarizes the basic data of the annual musculoskeletal clinical review in the Haemostasis and Thrombosis Unit (La Fe Hospital, Valencia – Spain).

Subject ID #:_____ Name of Physiotherapist:_____

Assessment # : _____ Date: _____
yyyy / mm / dd

Time: _____

Hemophilia Joint Health Score 2.1 - Summary Score Sheet

	Left Elbow		Right Elbow		Left Knee		Right Knee		Left Ankle		Right Ankle	
Swelling		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Duration (swelling)		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Muscle Atrophy		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Crepitus on motion		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Flexion Loss		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Extension Loss		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Joint Pain		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Strength		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Joint Total												

Sum of Joint Totals + _____

Global Gait Score _____

(☐ NE included in Gait items)

HJHS Total Score = _____

NE = Non-Evaluable

Swelling
0 = No swelling
1 = Mild
2 = Moderate
3 = Severe

Duration
0 = No swelling or < 6 months
1 = ≥ 6 months

Muscle Atrophy
0 = None
1 = Mild
2 = Severe

Joint Pain
0 = No pain through active range of motion
1 = No pain through active range; only pain on gentle overpressure or palpation
2 = Pain through active range

Crepitus on Motion
0 = None
1 = Mild
2 = Severe

Flexion Loss
0 = < 5°
1 = 5° - 10°
2 = 11° - 20°
3 = > 20°

Extension loss
(from hyperextension)
0 = < 5°
1 = 5° - 10°
2 = 11°- 20°
3 = > 20°

Strength (Using The Daniels & Worthingham's scale)
Within available ROM
0 = Holds test position against gravity with maximum resistance (gr.5)
1 = Holds test position against gravity with moderate resistance (but breaks with maximal resistance) (gr.4)
2 = Holds test position with minimal resistance (gr. 3+), or holds test position against gravity (gr.3)
3 = Able to partially complete ROM against gravity (gr.3-/2+), or able to move through ROM gravity eliminated (gr.2), or through partial ROM gravity eliminated (gr.2-)
4 = Trace (gr.1) or no muscle contraction (gr.0)
NE = Non-evaluable

Global Gait (walking, stairs, running, hopping on 1 leg)
0 = All skills are within normal limits
1 = One skill is not within normal limits
2 = Two skills are not within normal limits
3 = Three skills are not within normal limits
4 = No skills are within normal limits
NE = Non-evaluable

NOTE: There is an accompanying instruction manual and worksheets that are required when administering the HJHS

General Comments:

_____

_____

_____

_____

Figure 3: Hemophilia Joint Health Score 2.1.

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Current clinical practice requires that the evaluation of our patients be protocolized and objectively quantify the evolutionary follow-up, schedule decisions such as hospital admission or discharge or the need for a specific therapeutic intervention or even the establishment of the degree of disability and the need for care.

Different protocols are used in hemophilia, we will summarize the best known, but all of them include parameters common to the exploration of the locomotor system (Table 3).

Table 3: Basic explorations to complete the forms recommended by the WFH.

	Explorations	Utility
1	Joint volumes	Inflammation assessment
2	Muscle volumes	Muscular trophism evaluation
3	Joint mobility	Ranges of movement (ROM): Flexo-extension and evaluation of contractures
4	Joint alignment	Assessment of axial deformities
5	Functional stability	Evaluation of ligament injuries or joint dysfunction due to bone alteration
6	Joint crepitus	Audible and/or palpable sounds during joint mobility that suggest degenerative processes
7	Pain	Assessment at rest or during mobility or charging
8	Muscle balance	Assessment of muscle strength
9	Orthosis	Verify the need for help to improve pain, mobility or gait
10	Deambulation (walking, stairs ...)	Assess the possibilities of autonomy in normal gait, stairs, monopod support, jump or race

One of the first assessments used was that Arnold and Hilgartner [10], which combined clinical and radiographics aspects. However, it was sufficiently useful for to make the hematologist aware that, having lowered the frequency of haemorraging, avoiding arthropathy would be the “principle objective”, and a certain phrase started circulating: haemophilia was “an orthopedic disease with a haematological basis”.

The WFH in its recommendations highlights the Gilbert's Core also called WFH Physical Examination and the Hemophilia Joint Health Score (HJHS in its version 2.1), this form is the most commonly used and recommended today for the individual or multiple joint evaluation both in children and adults. The numerical score of each joint can be compared to itself over time to determine if a joint is showing degenerative signs. Other assessments in use are the Colorado protocols [11-17].

The forms that we summarize below are available and can be freely consulted at: https: // elearning.wfh.org/resource/compendium-of-assessment-tools and www.ipsg.ca. It is important to remember that, regardless of the scale that we are going to use, if at the time of evaluating the patient, there had been any recent bleeding in any of the joints, this should be noted in the observations. That joint is "not testable" since the score of that joint at that time is not valid to assess arthropathy.

The objective of these scales is to describe the baseline situation of the patient in order to be able to carry out an evolutionary control over time. Said basal state should be recovered in case of new bleeding, or at least that should be our goal.

Gilbert’s core

Although it has a good correlation with the risk of bleeding and has detected its utility for the measurement of results after physical treatment, is less sensitive than the HJHS and the changes that may affect the patient's clinical situation. The score quantifies 7 concepts: swelling, muscle atrophy, axial deformity, crepitus, range of motion in deficit percentages, flexion contracture and instability. The maximum degree of arthropathy is equivalent to 12 points per joint. The pain score is considered apart (0 to 3 points) [11].

Other scales, less used, are those of Colorado. In its adult version (Colorado Adult Joint Assessment Scale), known by its acronym "CAJAS", it was designed to assess the health of the joints in adults with hemophilia due to the need for validated scales. The CAJAS scale is an evolved version of the Colorado PE-1 and Colorado PE 0.5 scales, developed in turn from the Gilbert scale, trying to improve the limitations it presented. The maximum score is 25 points for the ankles and knees and 23 for the elbows. In the pediatric version (Child PE) the score is 31, ankles and knees and 29 for elbows [15-17].

Hemophilia Joint Health Score (HJHS)

Hemophilia Joint Health Score (HJHS) is probably the most widely used scale today, incorporating items from the Gilbert scale and the Colorado scale. It was originally developed to identify the first signs of joint degeneration in children between 4 and 18 years old, being validated in this population. However, today it is generally used in both children and adults [12-14].

The HJHS 2.1 includes 8 items per joint (i.e. inflammation, duration of inflammation, muscle atrophy, crepitus in mouvement, loss of flexion, loss of extension, joint pain, and

strength) in addition to comprehensively assessing gait. Each joint has a score of 0-20 points, where 0 implies normality and 20 severe arthropathy. The gait has an evaluation of 0 to 4 points, so that we can give a value per joint or a total score that includes the 6 joints (i.e. both elbows, knees and ankles) plus the gait. The worst possible score for a patient is 124 points (Figure 3).

The second type of scales, those that try to quantify the impact of the pathology on the patient's life, are mostly represented in the bibliography by:

Hemophilia Activities List (HAL adults; PedHAL for children and parents): These are comfortable and quick scales to apply, although they have criticism regarding the reliability and validity of their results, which are still poorly documented in the bibliography. Available at: fh.org/resource/haemophilia-activities-list-hal/

Functional independence measurement for patients with hemophilia (FISH): Scale directed to patients with greater affectation. Studies show a good correlation with both the Gilbert scale and the Pettersson and Womac scale. Its internal consistency is good but it is slower to apply than HAL. Available at: https://elearning.wfh.org/resource/functional-independence-score-in-hemophilia-fish/

IPAK short form: It is a frequently used questionnaire in the general population that quantifies the level of physical activity in 7 questions, providing three levels of activity, high, moderate and low or inactive. Available at: https://journals.plos.org/plosone/article/file?type=supplementary&id=info:doi/10.1371/journal.pone.0219193.s010

DIAGNOSTIC IMAGING: CONTROL OF JOINT HEALTH

Conventional radiology

Conventional radiology. In any joint, hemarthrosis can cause structural lesions that start in the soft tissues.

The first manifestation of the image that affects bone tissue is periarticular osteopenia, the epiphysis is progressively affected (due to the increase in vascularization that produces accelerated bone maturation), irregularities of the subchondral bone and progressive destruction of the cartilage with narrowing of the joint space. Additionally, marginal erosions, subchondral cysts, and destruction of the subchondral bone can be seen.

Without adequate treatment of joint injuries, progress is made towards a final stage of hemophilic arthropathy, characterized by deformities and fibrous or bone ankylosis.

The data collected by the Pettersson Scale [18,19] are useful for the classification of hemophilic arthropathy, but ultrasound currently represents the best tool for the detection of early signs of arthropathy.

Magnetic resonance

Magnetic resonance (MRI) is the most sensitive method for detecting early changes in joint structures, whose alteration at the beginning is theoretically reversible. Identifies effusion, synovial membrane, hemosiderin, cartilage, and subchondral bone (erosions and cysts).

MRI constitutes the "gold standard" in diagnostic imaging, however, disadvantages such as the lack of availability in many hemophilia centers, the high cost, the long examination time or the need for sedation in children must be taken into account. Different scales have been published, among which it is worth mentioning the Denver protocol [20-21].

Ultrasound

Ultrasonography (US) allows the identification of the intra-articular effusion without significant differences regarding the use of MRI.

US It is the best technique for assessing vascularization, although this concept is not included in the current parameters for quantifying arthropathy. It presents a good correlation with respect to MRI to assess synovial hypertrophy.

The exploration with US It requires experience (operator dependence) and protocols to quantify effusion, synovial damage, cartilage disorders, cortical erosion, and joint margins.

As advantages we must highlight the ease of access (simple, fast, without sedation) and the low cost. It is used as a first-rate tool in the diagnosis and evolutionary control of acute hemarthrosis and also, with a basic protocol and a simple equipment, in a few minutes it allows determining alterations of the echoestructure and objectify, yes or no, joint involvement to later expand the study by specialized personnel and quantify the degree of arthropathy [22].

Currently, the committee of Image Experts works to agree on the protocols. For the evaluation of early signs of arthropathy,

the most widely used score is probably the HEAD-US [23] (Table 4).

Table 4: Ultrasound examination protocol for early signs of hemophilic arthropathy [23].

Disease activity (sinovitis)	*Score*
Hypertrophic synovium	
- Absent/Minimal	0
- Mild/moderate	1
- Severe	2
Disease damage (articular surfaces)	
Cartilage	
- Normal	0
- Echotexture abnormalities, focal partial/full-thickness loss of the articular cartilage involving <25% of the target surfaces (*)	1
- Partial/full-thickness loss of the articular cartilage involving at least ≤50% of the target surface (*)	2
- Partial/full-thickness loss of the articular cartilage involving >50% of the target surface (*)	3
- Complete cartilage destruction or absent visualization of the articular cartilage on the target bony surface (*)	4
Bone	
- Normal	0
- Mild irregularities of the subchondral bone with/without initial osteophytes around the joint	1
- Deranged subchondral bone with/without erosions and presence of prominent osteophytes around the joint	2
Total score for each joint	
(*) Note: Elbow: anterior aspect of the distal humeral epiphysis; Knee: Femoral trochlea; Ankle: anterior aspect of the talar dome.	
It is an additive scale. The total score represents the sum of the scores for the detected abnormalities. The range of values ranges from 0 (minimum) to 8 (maximum) for each joint	

The clinical evaluation, the Hemophilia Joint Health Score (HJHS) and the Haemophilia Early Arthropathy Detection with Ultrasound (HEAD-US) are probably the two fundamental tools for the control of joint health.

CONCLUSION

The prevention and treatment of musculoskeletal injuries in the patient with hemophilia and its consequence, hemophilic arthropathy, remain the main objective of the care of this pathology.

The only way to maintain joint and musculoskeletal health is evolutionary control, for which the unification of criteria in assessment protocols is required.

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