

Diagnosis of Hemophilic Hemarthrosis: Development of a Patient-Derived Symptom Assessment Tool Using Musculoskeletal Ultrasound (MSKUS) for Validation



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Background

- Patients with hemophilia (PWH) experience painful joint episodes which may or may not be associated with new hemarthrosis
- Point of care (POC) musculoskeletal ultrasound (MSKUS) is a valuable tool for rapidly diagnosing hemarthrosis
- Patient-derived questionnaires describing pain sensations have been suggested for diagnosing hemarthrosis
- We sought to validate a questionnaire developed by an experienced patient group, and compare it against POC-MSKUS to detect hemarthrosis

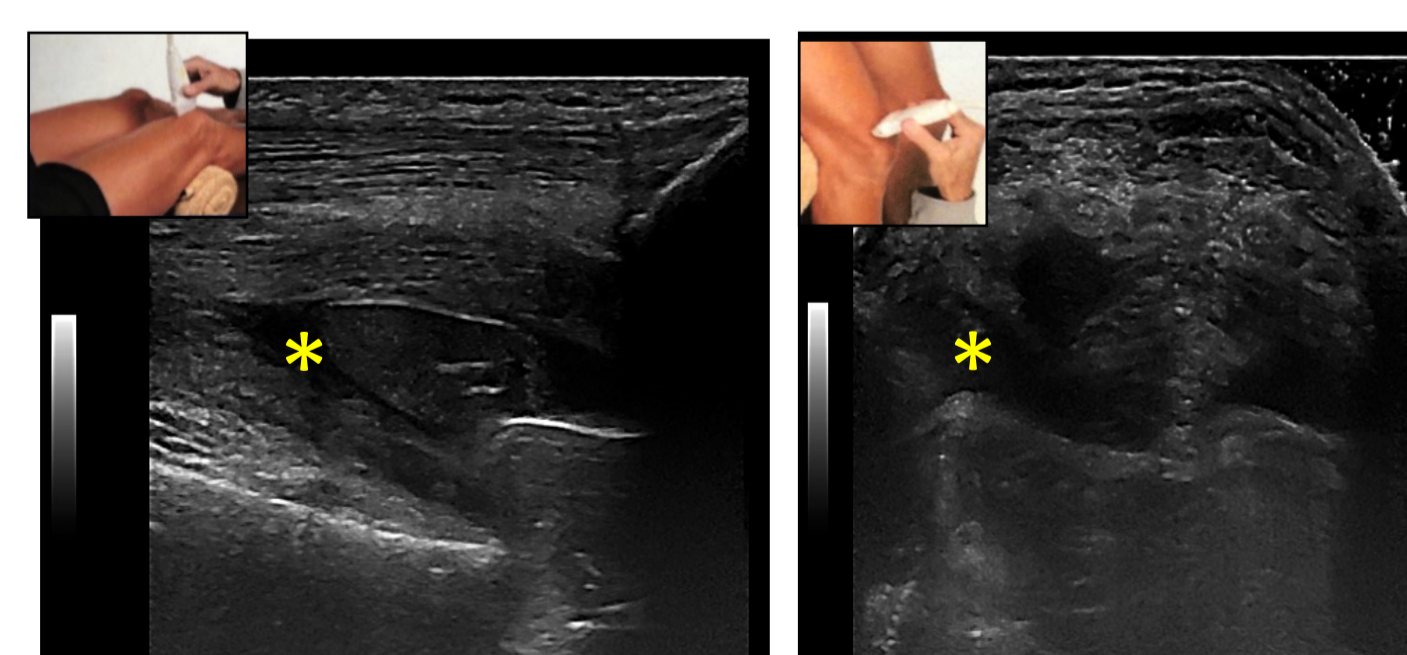
Methods

- We administered a patient-developed questionnaire comprising 20 questions (10 each associated with hemarthrosis and arthritis pain, respectively) to adult PWH experiencing acute painful episodes
- The questionnaire was developed by Mr. Page and derived from an open-text survey, sent to a group of “experienced” individuals with severe hemophilia A or B.
- Patient and providers were blinded to question assignment and the order of the questions was randomly scrambled
- The presence (or absence) of bleeding was confirmed by MSKUS
- We fitted univariate and multivariate generalized estimating equations to identify symptoms associated with hemarthrosis

Results

- Questionnaire administered to **32 patients**, presenting with **79 painful joint episodes**.
- 23 patients had Hemophilia A and the remaining had Hemophilia B
- Severe Hemophilia (Factor activity < 1%): 22 patients
- Median age : 38 years (range 21-74 years)
- POC MSKUS detected hemarthrosis in 36 (46%) episodes

Representative MSKUS images of acute joint bleeding in a patient with hemophilia



* Bleeding within joint

Supra-patellar bursa in long and short axis views showing widening of bursa, evidence of mixed echogenic signals, bursal contents that are partially compressible, consistent with clotted blood in the joint

Results

Table 1: Odds ratios (OR) relating pain associated with bleeds vs arthritic pain

Variable	OR	Lower CL	Upper CL
X19: No feeling of sponginess with movement	0.28	0.11	0.75
X5: No significant improvement after factor concentrate	0.29	0.12	0.68
X3: Irregular, non-progressive pain with movement or weight bearing	0.30	0.15	0.64
X16: Pain and discomfort in the absence of warmth or swelling	0.32	0.12	0.81
X2: Pain when flexing the muscle, or if joint, muscle nearest joint	0.35	0.14	0.83
X13: With activity, painless range of motion increases	0.38	0.15	0.95
X18: Moving through range of motion is painful, but feels moveable	0.52	0.18	1.46
X17: Limited, non-progressive swelling	1.01	0.41	2.50
X9: Little pain at rest	1.11	0.44	2.82
X6: Pain at rest	1.11	0.44	2.82
X10: Feeling of fullness in the joint	1.40	0.41	4.77
X11: Progressive swelling	1.47	0.49	4.37
X1: Rapidly Increasing pain	1.50	0.59	3.80
X12: Swelling with increasingly painful pulsing sensation leading to joint immobility	1.54	0.36	6.51
X8: Progressive loss range of motion	1.55	0.55	4.36
X4: Pain and only when the muscle or joint is flexed	1.69	0.72	3.95
X20: With activity, range of motion decreases	1.84	0.64	5.30
X15: For non-target joint, recall of an initiating incident	2.18	0.72	6.64
X7: When resting, pain eases by not moving	2.38	0.94	6.02
X14: Like a balloon swelling with water	2.84	0.75	10.77

The potential predictors of hemarthrosis pain vs arthritic pain are ranked in order of increasing odds ratios for a bleed. Red/ highlighted rows indicate questions assigned to hemarthrosis per original questionnaire

Table 2: Predictor tool to ascertain the probability of joint pain to be associated with hemarthrosis

Symptom	'Y' or 'N'	'Y' or 'N'	'Y' or 'N'
X19: No feeling of sponginess with movement.	Y	Y	N
X16: Pain and discomfort in the absence of warmth.	Y	Y	N
X5: No significant improvement after factor concentrate.	Y	N	N
X3: Irregular, non-progressive pain with movement or weight bearing.	Y	N	N
X2: Pain when flexing the muscle.	Y	N	N
Probability of hemarthrosis	6%	61%	93%

Conclusions

Objective diagnosis of hemarthrosis by MSKUS facilitated a prediction tool by informed selection of the most meaningful patient perceived indicators of arthritic versus hemarthrosis pain. The tool requires further validation and will be particularly helpful in situations where MSKUS is not readily available.