

Multislice spiral computed tomography imaging in evaluating hemophilic arthropathy

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Abstract

Background: Certain hemophilia patients are unable to cooperate with or afford magnetic resonance imaging (MRI) examinations. The purpose of our study was to explore the value of multislice spiral computed tomography (MSCT) in evaluating hemophilic arthropathy (HA).

Methods: Thirty-eight patients with 73 joints of HA were consecutively selected from January 2016 to May 2018 for this prospective study. All 73 joints were examined by X-ray, CT, and MRI within 2 days. The MRI scores of the joints were determined by the International Prophylaxis Study Group (IPSG) standard. The CT findings were quantified according to the IPSG standard, except for cartilage injury, which was quantified by joint space narrowing using the X-ray Pettersson score. The CT and MRI scores were compared by the paired Wilcoxon signed-rank test. The correlations between the CT score of joint space narrowing and MRI score of cartilage injury and the total CT and MRI scores were analyzed by Spearman rank correlation. The kappa test was used to compare the consistency of CT and MRI scores.

Results: MRI was superior to CT based on the scores for small amount of effusion ($P < 0.05$), synovial hypertrophy and hemosiderin deposition in the mild groups ($P < 0.05$). The CT and MRI scores were not significantly different for moderate and massive effusion, synovial hypertrophy, and hemosiderin deposition in the moderate and severe groups, bone erosion or cystic changes ($P > 0.05$), and there was a high degree of consistency between the two scores ($\text{kappa} > 0.81$). The consistency between the Pettersson scores of joint space narrowing on CT and the IPSG scores of cartilage injury on MRI was high ($\text{kappa} = 0.774$, $P < 0.05$).

Conclusion: The image scores of MSCT are generally consistent with MRI except for mild synovitis, which can be used as an alternative for the evaluation of HA.

Keywords: Hemophilia; Arthritis; Magnetic resonance imaging; Computed tomography; Radiography; Comparative evaluation

Introduction

Hemophilic arthropathy (HA) is a series of pathological changes in the joint synovial membrane, cartilage, and subchondral bone caused by repeated bleeding in the joints, mainly in the knee, elbow, and ankle.^[1] Joint deformity is a common clinical manifestation of hemophilic patients and is the main cause of disability. Imaging examinations play an important role in evaluating HA. Previous studies on HA mainly focused on X-ray, ultrasound and magnetic resonance imaging (MRI), while the application of computed tomography (CT) has only occasionally been described in case reports on hemophilic pseudotumor.^[2] X-ray imaging can only locate late-stage hemophilic joints that already have bone changes.^[3] Ultrasound examinations fail to assess cartilage

and bone destruction in deep joints and are operator-dependent, leading to poor quantitative assessment and reproducibility.^[4] MRI is recognized as the gold standard for the comprehensive evaluation of joints.^[5,6] At present, the most widely used method is the International Prophylaxis Study Group (IPSG) score, which was established in 2012^[7] and is more simplified and practical than other available methods. However, because of the high cost, long scanning time, need for sedation in children, and prohibited use for certain patients (eg, patients with metal implants), MRI is not suitable for routine screening.^[8] In China, more than 70% of hemophilic patients over 30 years old have joint deformities, and 12.8% of hemophilic children under 12 years old have joint deformities.^[9] Placing limbs in radiofrequency coils is

Access this article online

Quick Response Code:



Website:
www.cmj.org

DOI:
10.1097/CM9.0000000000000876

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Chinese Medical Journal 2020;133(14)

Received: 16-03-2020 Edited by: Qiang Shi

difficult when joint dysfunction occurs, which limits the application of MRI.^[10] In addition, MRI is not easily accessible for many patients worldwide, and some patients may face financial challenges associated with MRI. Therefore, MRI is seldomly reported as an evaluation method for HA in certain countries, such as China, where X-ray and ultrasound remain the main examination methods for HA.

With the continuous advancements in CT technology, image quality, and low-dose technology, CT examinations for HA joints are becoming feasible. In addition, thin-layer isotropic high-resolution CT imaging can display images in any two-dimensional direction, and the resolution of bone, cartilage, and peri-articular soft tissue is clinically acceptable.^[11-16] However, few reported studies have evaluated CT for the diagnosis and quantification of HA. Therefore, we evaluated HA patients with multislice spiral computed tomography (MSCT) and compared the results with MRI. We hypothesize that MSCT examination is an alternative to MRI for diagnosing HA patients.

Methods

Ethical approval

This study was approved by the Ethics Committee of People's Hospital of Zhengzhou University, Henan Provincial People's Hospital ([2017] No. 49). Informed consent was obtained from all patients or their relatives before the study.

Patients

Seventy-three HA joints from 38 patients were selected for this prospective study. The patients were selected consecutively between January 2016 and May 2018 in the People's Hospital of Zhengzhou University, Henan Provincial People's Hospital. The inclusion criteria included the following: (1) patients with a history of hemophilia; (2) the presence of one or more HA by clinical or X-ray examination; (3) the image data of X-ray, MSCT, and MRI acquired within 2 days. The exclusion criteria included the following: (1) arthritis caused by other causes; (2) having a history of other blood system diseases; and (3) poor image quality that cannot meet the diagnostic requirements. All patients were male and aged 7 to 46 years old, with an average age of 15.7 ± 8.3 years; all

patients were diagnosed with hemophilia A by clinical laboratory examinations. The course of hemophilia varied from 3 to 46 years. Among these patients, a total of 42 knees, 19 ankle joints, five elbow joints, and seven hip joints were included in this study. The duration of bleeding was different among the 38 patients.

Inspection methods

Anteroposterior and lateral view radiography examinations were performed (Definium 6000, GE Healthcare, Waukesha, USA) on all joints. All joints were scanned by a 64-slice spiral CT scanner (Discovery CT 750 HD, GE Medical Systems, Waukesha, USA) with the following: low dose, high resolution, 80 to 100 kV, automatic milliamperes-second technique, 0.35 s/rot, bone and standard reconstruction, slice thickness and interval of 0.625 mm, and noise reduction with adaptive statistical iterative reconstruction. During the scan, the exposure range was strictly limited to the distribution of each joint, and the other body parts were protected by lead garments; the principle of as low as reasonably achievable was adopted. The total scanning time was less than 1 min.

MRI scans were acquired with a 3.0 T scanner (MAGNETOM Prisma, Siemens, Erlangen, Germany) and 16-channel knee, ankle, and body coils (for elbow and hip joints). T1 weighted imaging (T1WI) and proton density-weighted image-fat suppression (PDWI-FS) scans were acquired with the turbo spin-echo sequence. Sagittal, coronal, and axial scans were acquired for the knee, elbow, and ankle joints, and coronal and axial scans were acquired for the hip joints. The parameters are shown in Table 1.

Observation indicators and grouping

The 73 joints were divided into three groups to reflect the severity of the joint disease according to the X-ray Pettersson scoring standard^[17]: 0 points: mild group; <4 points: moderate group; and ≥ 4 points: severe group. Corresponding comparative studies between CT and MRI were then conducted based on this grouping.

The MRI scores of all joints were analyzed according to the IPSPG standard established in 2012.^[7] As a comparison

Table 1: Magnetic resonance imaging scan parameters for different joints.

Parameters	Knee	Ankle	Elbow	Hip
T1WI				
TR (ms)	310	416	498	521
TE (ms)	11	11	10	10
PDWI-FS				
TR (ms)	4200	4180	3000	3000
TE (ms)	36	33	22	50
Matrix (pixel \times pixel)	384 \times 384	320 \times 320	320 \times 320	512 \times 512
FOV (cm \times cm)	16 \times 16	15 \times 15	15 \times 15	38 \times 38

All joints had the same layer thickness (3.5 mm), layer spacing (0.4 mm), and number of excitation (1). T1WI: T1 weighted imaging; TR: Repetition time; TE: Echo time; PDWI-FS: Proton density weighted image-fat suppression; FOV: Field of view.

with the MRI scores, the quantitative CT scores of effusion/hemarthrosis, synovial hypertrophy, hemosiderin deposition, bone erosion, and cystic degeneration were evaluated with the IPSG scoring system. Because CT cannot directly show the degree of cartilage injury as 1 to 4 points, we scored joint space narrowing according to the Pettersson score as a reference to indirectly reflect the articular cartilage injury on CT images. The CT scores of cartilage injury were divided into normal, 1 point (joint space >1 mm) and 2 points (joint space ≤ 1 mm).

Observation methods

The thin-layer axial CT images were transferred to Workstation ADW 4.5 CT for post-processing reconstruction in the coronal and sagittal directions and compared with the T1WI and PDWI-FS images of the corresponding MRI. Effusion exceeding 45 HU (Hounsfield unit) indicated the presence of hemorrhage. A hyperplastic synovial membrane that showed mottled or patchy density with a CT value over 50 HU suggested hemosiderin deposition.

For standardization, all X-ray, CT, and MRI images were evaluated and quantified by two professional musculoskeletal radiologists (with 11 and 21 years of work experience, respectively) trained in assessing hemophilia imaging who were blinded to the clinical data. Inconsistent scores were resolved through discussion.

Statistical analysis

SPSS 23.0 software (SPSS Inc., Chicago, USA) was used to statistically analyze the scores. Spearman rank correlation test was used to analyze the correlation between the CT scores of joint space narrowing and the MRI scores of joint cartilage injury and between the total CT and MRI scores. The non-parametric paired Wilcoxon signed-rank test was used to compare CT and MRI scores for other indicators. The Kappa test was used to compare the consistency of CT and MRI scores, $0.61 \leq$ Kappa value ≤ 0.80 means strong consistency, $0.81 \leq$ Kappa value ≤ 1.00 means very strong consistency. A value of $P < 0.05$ was considered statistically significant.

Results

Grouping HA joints

According to the Pettersson scoring system, the radiographs of 73 joints were scored; 58 joints (79%) were in the moderate and severe group, and 15 joints (21%) were in the mild group.

Comparison of the IPSG scores between CT and MRI

The detection rates of MRI and CT were compared, and the CT detection rate of a small effusion/hemarthrosis was 25/48 (52%), the MRI score was higher than the CT score (1 point *vs.* 0 point, $Z = -4.796$, $P < 0.05$). The CT and MRI scores of 20 joints with moderate and massive effusion/hemarthrosis were consistent, their scores were the same, including 2 points for 11 joints and 3 points for nine joints. There was no effusion/hemarthrosis in the

remaining five joints. Representative images of moderate effusion are shown in Figure 1.

The synovial hypertrophy and hemosiderin deposition IPSG scores of MRI were higher than those of CT in the mild group (all $P < 0.05$). However, the CT and MRI scores were not significantly different between the moderate and severe groups (all $P > 0.05$), and there was a very high degree of consistency between the two scores (all kappa > 0.81) [Table 2]. Representative images of a moderate amount of hemosiderin deposition are shown in Figures 2 and 3. Five joints with mild synovial hyperplasia all had a 1-point MRI score, but a 0-point CT score, including three joints in the mild group and two joints in the severe group. Similarly, ten joints with mild hemosiderin deposition all had a 1-point MRI score, but a 0-point CT score, including six joints in the mild group, two joints in the moderate group and two joints in the severe group. In the moderate group, one joint with medium hemosiderin deposition had a 2-point MRI score but was mistakenly rated as 1 point by CT due to the heterogenous and dispersed distribution of the hemosiderin deposition.

The IPSG scores of bone erosion and cystic degeneration were not significantly different between CT and MRI in all groups (all $P > 0.05$), and there was a very high degree of consistency between the two scores (all kappa > 0.81) [Table 3]. Representative images of bone erosion and cystic degeneration are shown in Figures 1 and 3. In addition, the number of lesions detected by CT was higher than or equal to that detected by MRI, and the minimum diameter of the cysts measured by CT was 0.8 mm while that of MRI was 1.3 mm. The bone erosion of one severe osteoporotic joint in the mild group was misjudged by CT as 0 points instead of 1 point. In the moderate group, the bone erosion of two joints was judged as 1 point by CT, but MRI showed no lesion. Three joints in the moderate group also showed cystic changes on CT, whereas MRI did not show lesions. In the severe group, the bone cystic change of one joint was misdiagnosed as 1 point instead of two points due to incomplete MRI findings.

Of the 73 joints, we found that scores of 0, 1, or 2 points on CT of joint space narrowing corresponded to scores of 0 to 2, 2 to 4, or 3 to 4 points on MRI of joint cartilage injury, respectively [Table 4]. Spearman rank correlation analysis showed that a strong positive correlation existed between the two scores ($r = 0.905$, $P < 0.05$), and the Kappa test showed the consistency between the two scores was high (kappa = 0.774, $P < 0.05$).

Although the total CT and MRI scores of the 73 joints were different, Spearman rank correlation analysis showed that the two scores had a strong positive correlation ($r = 0.975$, $P < 0.05$), and the correlations in the moderate ($r = 0.974$, $P < 0.05$) and severe ($r = 0.971$, $P < 0.05$) groups were stronger than those in the mild group ($r = 0.773$, $P < 0.05$).

Discussion

The imaging quality of CT was dramatically improved after 64-row CT became available. Moreover, CT images



Figure 1: The right knee of a 14-year-old boy with hemophilia A. (A) Lateral X-ray showed joint swelling, osteoporosis, and local low density in the posterior patella; this patient was assigned to the moderate group. (B and C) Sagittal T1WI and PDWI-FS MRI showed moderate joint effusion, low signal with mild line-like hemosiderin deposits and subchondral bone cyst of the patella. (D and E) The sagittal reconstructed CT showed the same degree of effusion, hemosiderin deposits (higher density, arrows) and a clearer patella cyst than the MRI. The IPSG CT scores were the same as the MRI scores. CT: Computed tomography; IPSG: International prophylaxis study group; MRI: Magnetic resonance imaging; PDWI-FS: Proton density weighted image-fat suppression; T1WI: T1 weighted imaging.

Table 2: Comparison of synovial hypertrophy and hemosiderin deposition detected by computed tomography and magnetic resonance imaging in different joints, n.

Items	IPSG score								Z*	P*	Kappa
	0 point		1 point		2 points		3 points				
	CT	MRI	CT	MRI	CT	MRI	CT	MRI			
Synovial hypertrophy											
Mild group	8	5	5	8	2	2	-	-	-2.236	0.025	-
Moderate group	2	2	11	11	6	6	13	13	0	1.000	1.000
Severe group	2	0	5	7	4	4	15	15	-1.414	0.157	0.870
Hemosiderin deposition											
Mild group	14	8	1	7	-	-	-	-	-2.449	0.014	-
Moderate group	9	7	7	8	6	7	10	10	-1.732	0.083	0.916
Severe group	3	1	4	6	5	5	14	14	-1.414	0.157	0.879

* Wilcoxon signed ranks test of IPSG score between CT and MRI in each group. Kappa: The value of Kappa test of IPSG score between CT and MRI in each group. IPGS: International prophylaxis study group; CT: Computed tomography; MRI: Magnetic resonance imaging; -: Not applicable.



Figure 2: The right elbow of a 12-year-old boy with hemophilia A. (A) Anteroposterior of X-ray showed osteoporosis and an enlarged bone end; this patient was assigned to the moderate group. (B) The PDWI-FS MRI showed a moderate amount of hemosiderin deposition around the joint, and the IPSP score was 2 points. (C) The coronal reconstructed CT image showed high density in the corresponding position (arrow) on MRI, and the IPSP score of hemosiderin deposition on CT was also 2 points. CT: Computed tomography; IPSP: International prophylaxis study group; MRI: Magnetic resonance imaging; PDWI-FS: Proton density weighted image-fat suppression.

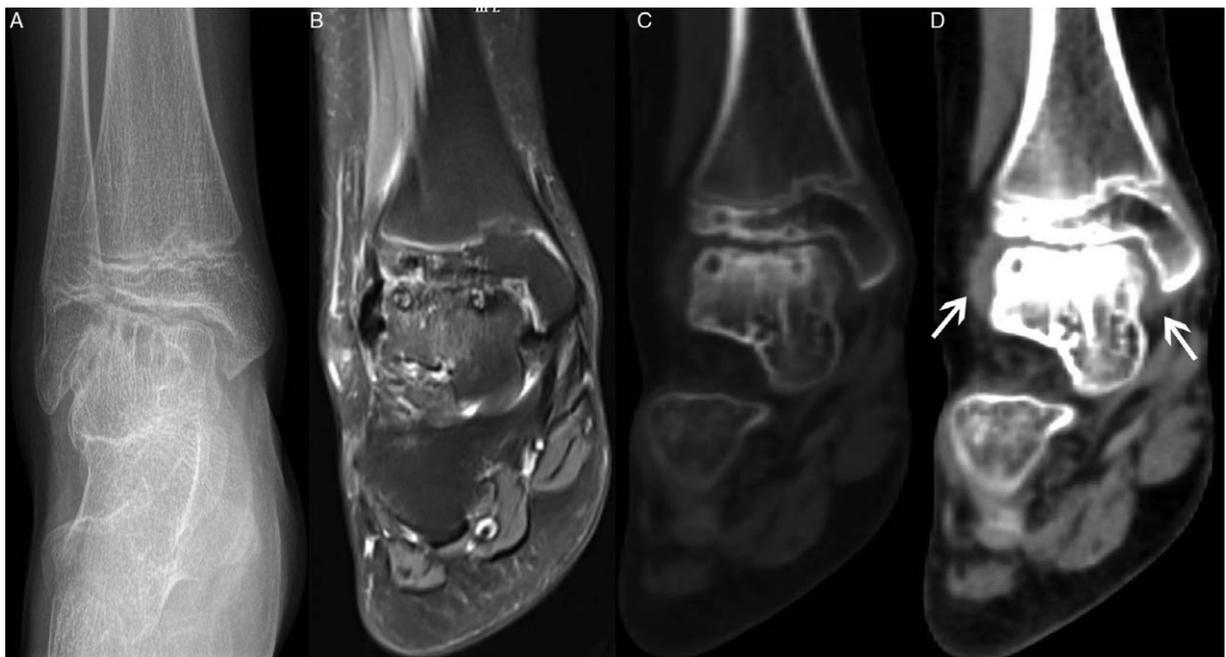


Figure 3: The right ankle of a 10-year-old boy with hemophilia A. (A) Anteroposterior of X-ray showed osteoporosis, enlarged bone end, irregular subchondral surfaces, local narrowing of joint spaces and cystic changes below the articular surface of the talus; this patient was assigned to the severe group. (B) The PDWI-FS MRI showed a moderate amount of hemosiderin deposition around the joint, unclear development of the articular surface and joint space, and subchondral bone cysts of the tibia and talus. (C and D) The coronal reconstructed CT images showed the same degree of hemosiderin deposits (higher density, arrows), clearer cysts of tibia and talus and clearer articular surface than the MRI. The IPSP CT scores were the same as the MRI scores. CT: Computed tomography; IPSP: International prophylaxis study group; MRI: Magnetic resonance imaging; PDWI-FS: Proton density weighted image-fat suppression.

can now be collected with a low radiation dose, and the trunk or sensitive organs can be well protected during CT scans of the limb joints. Therefore, the value of CT for imaging HA needs to be re-evaluated. In this study, the value of CT was evaluated by comparing CT with the internationally recognized MRI standards. The results supported our hypothesis that for certain hemophilia patients who are unable to undergo or afford MRI

examination, low-dose CT is considered a quick and cost-effective alternative.

In this study, the CT scores were inferior to the MRI scores for small amount of effusion/hemarthrosis, synovial hypertrophy and hemosiderin deposition, which has little clinical significance, and a small amount of effusion/hemarthrosis can be gradually absorbed. We believed that

Table 3: Comparison of bone erosion and cystic degeneration detected by computed tomography and magnetic resonance imaging in different joints, n.

Items	IPSG score						Z*	P*	Kappa
	0 point		1 point		2 points				
	CT	MRI	CT	MRI	CT	MRI			
Bone erosion									
Mild group	11	10	4	5	-	-	-1.000	0.317	0.842
Moderate group	10	12	15	13	7	7	-1.414	0.157	0.903
Severe group	-	-	5	5	21	21	0	1.000	1.000
Bone cystic degeneration									
Mild group	13	13	1	1	1	1	0	1.000	1.000
Moderate group	9	12	7	4	16	16	-1.732	0.083	0.848
Severe group	-	-	1	2	25	24	-1.000	0.317	1.000

* Wilcoxon signed ranks test of IPSG score between CT and MRI in each group. Kappa: The value of Kappa test of IPSG score between CT and MRI in each group. -: Not applicable; IPSG: International prophylaxis study group; CT: Computed tomography; MRI: Magnetic resonance imaging.

Table 4: Comparison of computed tomography scores of joint space narrowing and magnetic resonance imaging scores of joint cartilage injury, n.

CT joint space narrowing score	MRI joint cartilage injury score				
	0 point	1 point	2 points	3 points	4 points
0 point	21	4	6	-	-
1 point	-	-	14	3	4
2 points	-	-	-	1	20

-: Not applicable; CT: Computed tomography; MRI: Magnetic resonance imaging.

CT was a reliable imaging technique for evaluating the IPSG scores of medium and massive effusion/hemarthrosis, synovial hypertrophy and hemosiderin deposition in the moderate and severe groups.

For the quantitative scores of bone erosion and cystic changes, CT was better than or equal to MRI, which was different from the result of Yu *et al*^[18]; this difference may be because the resolution of the previously used 16-slice CT is lower than that of 64-slice CT, and a slice thickness of 2 mm is more likely to miss minor bone surface erosion and smaller cysts than a slice thickness of 0.625 mm. The MRI slice thickness is relatively thicker than that of CT, and some minor lesions can be missed. Therefore, in our study, CT appeared to be better than MRI for imaging bone erosion and cystic degeneration in HA patients. Clinicians can more clearly and accurately observe the bone destruction of diseased joints with CT than with MRI and thus adopt more appropriate strategies for treatment.

Our study showed that the Pettersson score of joint space narrowing on CT correlated with the IPSG MRI score of cartilage injury, and there was a high consistency between the two scores. The higher the Pettersson score for CT, the higher the IPSG score for MRI. Joint space narrowing is closely related to the loss of full thickness of cartilage. If the cartilage injury does not cause morphological changes in the cartilage, then joint space narrowing is not obvious, which can lead to an underestimation of cartilage injury with CT. Therefore, we believe that MRI is more reliable than CT for clinicians trying to observe early changes in the

cartilage. However, if the degree of cartilage destruction is severe in advanced patients, the Pettersson score of joint space narrowing on CT can be used. In short, although the total CT and MRI scores are different, these scores had a high consistency and correlation. The total CT score can reflect the characteristics of the total MRI score and the severity of the lesion; thus CT can guide clinicians to quantitatively evaluate hemophilic joints.

CT findings are closely related to clinical features, the higher the CT score is, the more serious the joint damage is. Previous literature^[19] has proven that the more serious the joint damage is, the lower the joint function will be. Eventually, joint degeneration can cause clinical symptoms and affect the quality of life.^[20] After 5-year follow-up of patients with hemophilia, Foppen *et al*^[21] found that all MRI changes except effusion were strong predictors for development of arthropathy on radiographs. MRI is inferior to CT in the display of osteoporosis. In recent years, some scholars have performed relevant research on the bone health and effects of Serum sclerostin levels on osteoporosis of HA patients,^[22,23] and the pathophysiology of HA needs to be further explored.

We recognize that our research has certain limitations. First, because the study involved patients who underwent X-ray, CT, and MRI examinations in the same period, patients who had only a single examination or two examinations for economic or other reasons could not be included in this study, thus sample size is relatively small. Second, more knees were evaluated than other joints,

which may cause statistical bias. Third, this study did not evaluate the meniscus, ligaments, and other structures in the joints. Hopefully, the technical advancements of CT can further improve the resolution of soft tissue and reduce the radiation dose from the equipment.

In conclusion, the IPSTG scores of MSCT (at least 64-slice spiral CT or above) and MRI were generally consistent except for mild synovitis, and MSCT can be used as an alternative option to MRI for the evaluation of HA patients, especially for those who are unable to undergo or afford MRI examinations. MRI might be more suitable for patients who want to detect early cartilage damage and mild synovitis.

Acknowledgements

The authors thank Dr. Ping-Chong Lei and secretary Xiang-Dong He from the Henan Hemophilia Registration and Management Center, Henan Provincial People's Hospital.

Funding

This work was supported by the grants from the National Natural Science Foundation of China (No. 81271543) and the Medical Science and Technology Research Project of Henan Province (No. 2018020470).

Conflicts of interest

None.

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How to cite this article: Zhang YX, Li MX, Wei SF, Zhang L, Cheng TM, Ge YH. Multislice spiral computed tomography imaging in evaluating hemophilic arthropathy. *Chin Med J* 2020;133:1669–1675. doi: 10.1097/CM9.0000000000000876