Original Article

An observational study of the demographic, clinical, and diffusion-weighted magnetic resonance imaging characteristics of patients with musculoskeletal infections

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Abstract

Introduction: Musculoskeletal infections have been emerging nowadays. Its early diagnosis is warranted as it may lead to disabling sequelae. Recently, the use of diffusion-weighted magnetic resonance imaging (DWMRI) provided additional pulse sequences enabling better diagnosis and needs to be explored for diagnosing musculoskeletal infections. Thus, we conducted this study with an aim to discuss demographic, clinical, and DWMRI findings of the spectrum of musculoskeletal infections, emphasizing the apparent diffusion coefficient (ADC) map for this domain of infections.

Methods: A retrospective observational study was carried out in the department of radiodiagnosis of a tertiary care hospital. The study was performed on 50 patients who were suspected cases of musculoskeletal infections. All the patients underwent basic investigations, ultrasound, magnetic resonance imaging, and diffusion-weighted imaging with ADC mapping. The data were entered into MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Results: Maximum patients were in the age group of 11–20 years (40%) with 58% males and 42% females. Lower limb infections were common, especially the involvement of the hip joint. Pain and swelling were the most common symptoms as seen in 96% and 88% of the patients respectively. DWMRI was able to diagnose and lay down significantly different ADC values for different musculoskeletal infections. The mean ADC values were higher for acute infections and lower for chronic infections.

Conclusions: DWMRI holds an important role in the investigation profile for musculoskeletal infections and must be used wherever deemed necessary to avoid unnecessary referrals and treatments.

Keywords: Apparent diffusion coefficient, diffusion-weighted imaging, joint effusion, musculoskeletal infections

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INTRODUCTION

Musculoskeletal infections are being increasingly encountered in the medical practice that may involve bones, muscles, joints, cartilage, or nearby soft tissues.[1] The nonspecific clinical picture causes the diagnostic dilemma and even the laboratory findings show nonspecific picture. The delay in its diagnosis because of its diagnostic dilemma causes disabling sequelae by degenerating the bones and

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the muscles. The spreading infections also infect the surrounding area and thereby also decrease the esthetic appearance and the quality of life of the patients.

The role of imaging investigations has been explored for an early diagnosis of the musculoskeletal infections. Imaging investigations, including radiography, computed tomography (CT), scintigraphy, and magnetic resonance imaging (MRI) are often performed to help arrive at the diagnosis.

Although X-Ray is the earliest and the simplest investigation performed it suffers from the limitation of identifying an infection only after it is around 2 weeks old. The reason being at least 50% of the bone needs to be involved and destroyed by an underlying osteomyelitis for any prominent changes to be visible on the radiographs.[2] In addition, X-rays cannot visualize the specific soft-tissue involvement. On the other hand, MRI plays an important role in defining the nature and extent of the musculoskeletal infection.[3] MRI has a number of advantages compared with all other imaging modalities. It is extremely sensitive and gives an accurate map of the anatomical distribution of the infection. It has a 100% negative predictive value, and a normal MRI removes all doubts of an infection.[4] MRI holds the power to discern the soft tissues very minutely.

However, even MRI may cause a diagnostic dilemma by giving a similar picture of infectious and many other noninfectious diseases that may produce similar imaging findings on routine MR sequences. Even the use of contrast is to be avoided in certain patients with diabetes or renal impairment.

In such cases, the role of diffusion-weighted magnetic resonance imaging (DWMRI) was explored and it has been found to show some additional pulse sequences that enable it to play a significant role in detection, differentiation, and characterization of the spectrum of musculoskeletal infections from other lesions. Hence, overall DWMRI holds superiority in terms of detecting the Brownian motion of water molecules within a voxel of tissues.[5,6]

DWMRI uses the concept of apparent diffusion coefficient (ADC) mapping whereby the local cellular environment and extracellular water are adjudged. Low ADC values represent high cellular concentrations and low extracellular water levels. There is a dearth of literature discussing the role of DWMRI in musculoskeletal infections. Thus, in this study, we discuss the imaging findings of the spectrum of musculoskeletal infections, emphasizing the role of DWMRI in this domain.

METHODS

An observational cross-sectional study was carried out in the department of radiodiagnosis of a tertiary care hospital over a period of 18 months. The ethical clearance was obtained from the Institutional Ethical Committee (1072). The study was performed on 50 patients who were suspected cases of musculoskeletal infection. The patients were suspected of musculoskeletal infections based on the clinical presentations comprising of joint, muscle, or bone pain, swelling, redness, and sometimes fever or other constitutional signs of infection.[7] Patients having any intraocular metallic foreign body, cochlear implants, implants near vital organs, and other contraindications to MRI were excluded from the study. Even uncooperative patient or patients having spine infections were not included in the study.

The sample size was based on the study of Romeih *et al*.[7] who observed that ADC of benign soft tissue tumor (STT) was $1.43 \pm 0.56 \times 10^{-3}$ mm^2/s, respectively. Taking this value as reference, the minimum required sample size with precision error of 15% and 1% level of significance is 38 patients. To reduce margin of error, the total sample size taken was 50.

The patients were explained about the study and informed consent was taken from them. The demographic history and clinical details of the patients were noted. The limb and the area infected were recorded in the study pro forma. The patients underwent blood investigations which included complete blood counts and inflammatory markers (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]).

MRI scans were carried out on 1.5 Tesla MR Imaging machine (Achieva by Philips Medical Systems.). The localizer was taken in all three planes after proper positioning of the patient. The standard MRI protocol followed in the study comprised of T2W, T1W, STIR Axial, T2W, STIR Coronal, and T2W sagittal sequences. Other relevant investigations included SKIAGRAM of the affected part to see any underlying soft-tissue mass, calcification, and skeletal abnormalities of the affected part and CHEST X-RAY, wherever indicated, with regards to the provisional diagnosis.

Diffusion-weighted images were obtained in the axial planes, 3–4 mm slice thickness, 1 mm intersection gap, FOV 250 mm, TR/TE/TI-3459/63/180 ms, EPI factor 45. The diffusion sensitizing gradient was applied in all three orthogonal planes (X, Y, Z) using b values (0 and 800).

ADC maps were automatically calculated by MRI machine software and included in the sequence. Whenever required T1-weighted images with and without fat saturation were performed after the administration of 10 ml of gadopentetate dimeglumine contrast.

Statistical analysis

Categorical variables were presented in number and percentage (%) and continuous variables will be presented as mean ± standard deviation and median. The normality of data was tested by Kolmogorov–Smirnov test. If the normality is rejected then nonparametric test was used; Chi-square test was used for comparison. The data were entered into MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0 (IBM manufacturer, Chicago, USA).

RESULTS

Maximum patients were in the age group of 11–20 years (40%) with 58% males and 42% females. The lower limb was involved in 76% of cases and upper limb in 24% of cases. The common areas involved were hip joints (40%) followed by legs, ankle, and knees. Total leucocyte counts were increased in 35 (70%) patients, ESR and CRP were increased in 34 (68%) patients each [Table 1].

Pain and swelling were the most common symptoms as seen in 96% and 88% of the patients respectively.

Ultrasonography showed nonspecific findings such as soft tissue edema or collection, subperiosteal collection, synovial thickening, joint effusion, or increased color Doppler flow. The final diagnosis was made on MRI findings as shown in Table 2. The combination of T1W, T2W, and STIR images (in the background of clinical findings) identified cases of acute osteomyelitis (n = 9), chronic osteomyelitis (n = 8), tubercular Hip (n = 8), infective arthritis (n = 7), sacroilietis (n = 6), tenosynovitis with cellulitis (n = 4), myositis (n = 2), tendinitis (n = 2), chronic infective synovitis (n = 1), cellulitis (n = 1), and acute infective synovitis (n = 2).

DW-MRI findings of the lesions showed that the lesions that were predominantly hypointense on DW-MRI was hyperintense on ADC mapping [Table 3].

After comparing the DWMRI findings with the MRI, the mean ADC values of each of the entities were estimated. There was a significant difference in the ADC values of different musculoskeletal infections as shown in Table 4. Some of the representative diagnosed cases with DW-MRI are shown in Figures 1-4.

Table 1: Demographic and clinical characteristics of the study patients

Demographic and clinical parameters	Number of patients (n=50), n (%)
Gender distribution	
Male	29 (58)
Female	21 (42)
Age group	
0-10	4 (8.00)
11-20	20 (40.00)
21-30	9 (18.00)
31-40	7 (14.00)
41-50	7 (14.00)
51-60	3 (6.00)
Limbs	
Lower limb	38 (76.00)
Upper limb	12 (24.00)
Area involved	
Hip joints	20 (40.00)
Leg	8 (16.00)
Ankle	5 (10.00)
Knee	4 (8.00)
Thigh	3 (6.00)
Shoulder	2 (4.00)
Pelvis	2 (4.00)
Forearm	1 (2.00)
Hand	1 (2.00)
Elbow	1 (2.00)
Foot	1 (2.00)
Wrist	1 (2.00)
Sternoclavicular joint	1 (2.00)
TLC	
<11,000	15 (30.00)
>11,000	35 (70.00)
ESR	
<15	16 (32.00)
>15	34 (68.00)
CRP	
<150	16 (32.00)
>150	34 (68.00)

TLC – Total leukocyte count; ESR – Erythrocyte sedimentation rate; CRP – C-reactive protein

DISCUSSION

Musculoskeletal infections are on a rise and their clinical presentations mimic each other. It becomes imperative to have increased differentiating features for better diagnosis and management. The current study was an attempt to study the overall clinical and diagnostic profile of patients with musculoskeletal infections.

In the present study, the most common age group was 11–20 years accounting for 40% of the cases. There was a slight male preponderance (58%) in the study. The young population is affected with no definite predilection for the age group and the gender. Comparable to the study, Okubo *et al.* conducted a study on acute osteomyelitis and stated that most of the subjects were younger than 20 years of age; however, there was slight female preponderance in their study with ratio of 1.8:1.6.[6] Even in few other studies, though there was no specific predilection for gender in

Table 2: Magnetic resonance imaging findings among the study patients

Diagnosis	T1W		T2W			STIR	
	HYPO	HYPO to intermediate	Hyper	Hypo	Intermediate to hyper	Hyper	Hypo
Acute osteomyelitis	8	1	8	0	1	9	0
Chronic osteomyelitis	7	1	4	3	1	4	4
Tubercular hip	8	0	6	0	2	8	0
Infective arthritis	7	0	6	1	0	6	1
Sacroilietis	4	2	3	2	1	4	2
Tenosynovitis with cellulitis	3	1	4	0	0	4	0
Myositis	2	0	2	0	0	2	0
Tendinitis	2	0	2	0	0	2	0
Chronic infective synovitis	0	1	0	1	0	1	0
Cellulitis	1	0	1	0	0	1	0
Acute infective synovitis	2	0	2	0	0	2	0
Total	44	6	38	7	5	43	7

STIR – Short tau inversion recovery

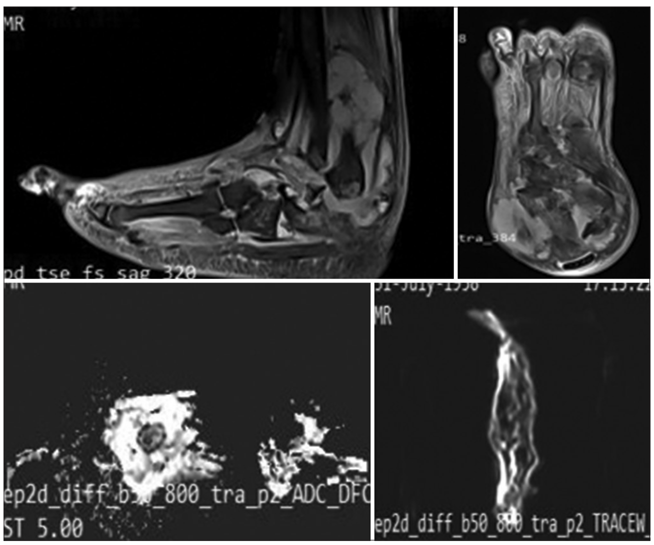

Figure 1: A case showing multiple small abscesses extending along the muscles and tendons with involvement of the underlying bones. The arrow marked shows diffusion restriction in one of the abscesses. The case was diagnosed as osteomyelitis (ADC 1.2). ADC – Apparent diffusion coefficient

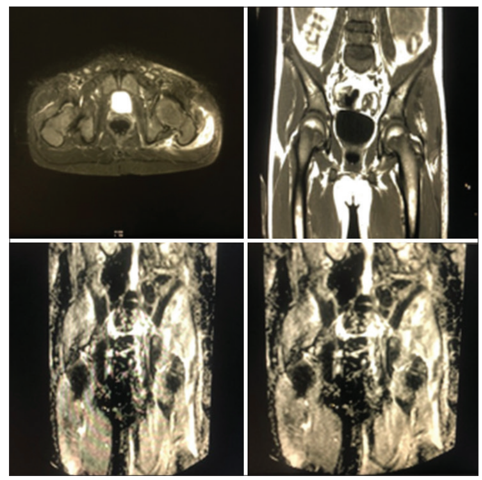

Figure 2: A case of cellulitis showing diffusion restriction with ADC of 2. ADC – Apparent diffusion coefficient

musculoskeletal infections, the most commonly affected individuals were either children or young adults.[8-10] As seen in infections, pain and swelling were the most common symptoms in our patients. However, the vagueness of the symptoms prevents a definite diagnosis in the cases of musculoskeletal infections.

In our study, the most common area involved in musculoskeletal infections was the hip followed by the legs. Previous literature also reports the hip and legs involvement as the most common. India is a country where tuberculosis (TB) has high occurrence; this shows in the studies where TB involvement of the spine, hip, and the long bones was on a predominant basis.[11]

The role of radiological investigations becomes significant in these cases. DW-MRI is one of the best radiological investigations currently being investigated for this tough category of musculoskeletal infections. We matched the DW-MRI diagnosis and estimated a mean ADC values for the individual entities. The findings showed a significant difference between the mean ADC values of different entities. Although there was some overlap, with the clinical background one may use the DWMRI findings and ADC values to differentiate the lesions. Similar evidence has been seen in the study to Kumar *et al*.[5] who gave a range of ADC for various musculoskeletal infections.

The utility of DWMRI relies on the principle of Brownian motion giving it an edge to differentiate various normal and abnormal regions such as showing dark signal for normal bone and light signal for edema and osteomyelitis due to increased extracellular water levels. Among the two (acute and chronic osteomyelitis), DWMRI helps to differentiate as it showed lower ADC for chronic and higher ADC for acute osteomyelitis (ADC = 1.44 vs. 1.18). It is due to the fact that the sequestrum (necrotic bone) shows a lower ADC than ischemic bone (but not dead bone) and thus

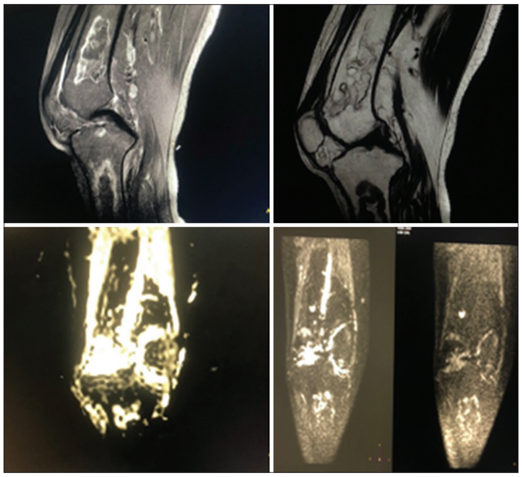

Figure 3: A case of chronic osteomyelitis with bony infarcts showing no significant diffusion restriction

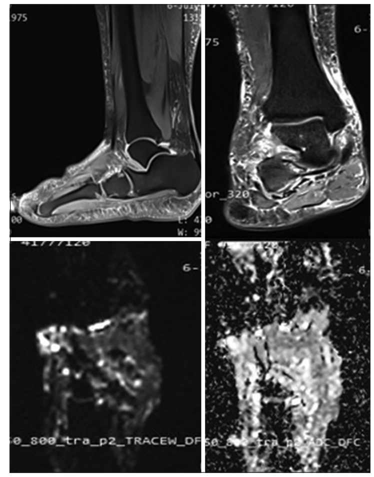

Figure 4: A case of subcutaneous edema showing diffusion restriction however the ADC value obtained was higher >2 which helps it to distinguish from a case of cellulitis. ADC – Apparent diffusion coefficient

Table 3: Diffusion weighted magnetic resonance imaging of the study patients

	Hyper	Hypo
DWMRI		
Acute osteomyelitis	9	0
Chronic/chronic active osteomyelitis	4	4
Tubercular hip	8	0
Infective arthritis	6	1
Sacroiliitis	4	2
Tenosynovitis with cellulitis	4	0
Myositis	2	0
Tendinitis	2	0
Chronic infective synovitis	0	1
Cellulitis	1	0
Acute infective synovitis	2	0
ADC mapping		
Acute osteomyelitis	0	9
Chronic osteomyelitis	4	4
Tubercular hip	0	8
Infective arthritis	1	6
Sacroilietis	2	4
Tenosynovitis with cellulitis	0	4
Myositis	0	2
Tendinitis	0	2
Chronic infective synovitis	1	0
Cellulitis	0	1
Acute infective synovitis	0	2

DWMRI – Diffusion-weighted magnetic resonance imaging; ADC – Apparent diffusion coefficient

Table 4: Mean apparent diffusion coefficient values in the final diagnosis

Diagnosis	*n*	Mean ADC ($\times 10^{-3}$ mm^2/s)
Acute osteomyelitis	9	1.44±0.23
Tubercular hip	8	1.63±0.12
Infective arthritis	6	1.72±0.17
Chronic osteomyelitis	5	1.18±0.31
Sacroiliitis	4	1.53±0.31
Tenosynovitis with cellulitis	4	1.88±0.05
Tendinitis	2	1.6±0.57
Myositis	2	1.25±0.78
Cellulitis	1	2
Acute infective synovitis	2	1.55±0.07
Total	43	1.55±0.31

P: −0.018. ADC – Apparent diffusion coefficient

DWMRI becomes significant in diagnosing and detecting early stages if osteomyelitis and deciphering the stage till which the damage is being done. This helps in the better management of saving the bone and the limb and improving the patient outcome. DW-MRI also further helps differentiate the entities by demonstrating restricted diffusion in the soft tissue and intraosseous abscess.[5]

The cases of acute osteomyelitis in our study had an average ADC value of 1.44 and gave a low signal on T1 w images and high signal on T2/STIR images. Thus, as compared to the study of Kumar *et al.*[5] in which the range of ADC was between 1.1 and 1.4 the ADC value of osteomyelitis in our study was slightly on a higher side with the average value of 1.44. In the study by Lalam *et al.*,[4] it was found that in cases of chronic osteomyelitis, a low-signal intensity rim is seen in a large proportion of cases. In our study too, the cases of chronic osteomyelitis gave a low-to-intermediate signal on both T1 AND T2/STIR images. It was concluded in the study that the differentiation of chronic active from chronic inactive OM is often problematic. In active diseases, there is the presence of sequestrum, abscesses, cloacae, and subperiosteal fluid collections. Kumar *et al.*[5] said that in cases of osteomyelitis it was seen that infected bone marrow showed a low signal on T1W images and a high signal on fluid-sensitive images. In the similar study by Lalam *et al.*[4] it was found that the fluid in infection had an intermediate signal on all sequences of MRI and is inhomogeneous, unlike a nonseptic joint effusion that shows low signal on T1W and high on T2W images and is homogeneous.

The cases of infective arthritis in our study had an average ADC value of 1.7 and gave a low signal on T1 and intermediate to high signal on T2 W images. It has been explored in the study by Kumar *et al.*[5] that Septic arthritis has a complex joint fluid and thus the fluid movement may display a wide range of signals on DWMRI based on the cellular environment and relative restriction in the diffusion. The intermediate signal on T1W and T2W images may depend on the synovial thickening and the joint edema. In addition, routine MRI may confuse the noninfectious inflammatory synovitis with septic arthritis but DWMRI specifically differentiates the entities due to the different density of the tissue fluid leading to different ADC values. Furthermore, the early stages of pyogenic arthritis show a minimal inflammatory reaction and thus the ADC values may not be very low.

Some soft-tissue infections may cause localized inflammatory mass. These masses on undergoing liquefactive necrosis may result in the formation of a well-defined walled-off abscess. The cases of intraosseous abscess in our study had the ADC values in the same range as described by Kumar *et al.*[5] in their study, i.e., between 0.6 and 1.1. Although routine MRI will differentiate the lesions and identify them correctly based on the low-intermediate signal on T1W images and a high T2W signal with a peripheral rim enhancement. However, it may cause confusion if any tumor shows central necrosis, and then routine MRI may not be able to discern the same. In such cases, DWMRI is slightly helpful in differentiating these two entities based on the restricted diffusion in the center of the abscess in the tumor and a restricted diffusion in the wall of the tumor as a result of high cellularity.

DWMRI can be helpful in demonstrating some restriction of diffusion in cellulitis (ADC 1.2–2.0) as simple subcutaneous edema shows increased diffusion (ADC 2.0–3.0). The case of cellulitis in our study gave a low signal on T1W image with high signal on both T2/STIR images. Kumar *et al.*[5] in their study calculated the ADC value to be in between 1.2 and 2.0. The case in our study gave an ADC value of 2 which was in range as described by a study of Kumar *et al.*[5]

The prevalence of TB has been high in developing countries as ours and it has led to increased rates of TB infection of bones: TB arthritis. The tubercular cases in our study gave a low signal on T1W images and a hyperintense signal on T2W images with few of the cases associated with joint effusion. The cases of TB arthritis usually show mild tissue swelling, periarticular osteopenia, and indistinct subarticular bone margins. The joint space may give an assessment of the stage of the disease as it may be reduced due to articular destruction, normal or wide with rare ankylosis. Lalam *et al.*[4] showed that Magnetic resonance can just add the feature of demonstrating bone marrow edema that is not seen on radiographs. As seen in our study, DWMRI can identify the joint space and determine the restriction in the movement of the water molecules and proteins. Hence. it can differentiate TB arthritis or synovitis from other infectious causes.

The fluid in the infection involving the tendon as seen in the cases of infectious tenosynovitis can be seen as a bright area on diffusion-weighted imaging and dark on the ADC map.[5] Routine MRI shows a distended and thick tendon sheath, with a varying signal of the complex fluid. The tendon itself appears ill-defined and thickened with intermediate signal intensity associated with surrounding soft tissue edema. DW-MRI is helpful in differentiating infectious tenosynovitis from noninfectious causes as the restriction in the movement of the fluid of the tendon sheath is reflected in the ADC values. The cases of tenosynovitis in our study gave a high signal on DW images with an average ADC value of 1.88. Tendon tears and erosions are also nicely identified as bright signal alterations on DW-MRI.

Other helpful findings from the study demonstrate the difference between cellulitis and simple subcutaneous edema. Cellulitis showed some restriction diffusion with the ADC value falling below 2.0 whereas as mentioned in the study conducted by Kumar *et al.*[5] subcutaneous edema has a higher ADC value, usually between 2.0 and 3.0.

The appearance of an abscess can mimic that of diabetic myonecrosis or necrotic tumors. DW-MRI can be helpful in differentiating these conditions as abscess shows central diffusion restriction whereas a tumor shows diffusion restriction in the periphery that is its walls.

DW-MRI can also help to differentiate muscle edema and hematoma (causes T2 shine through and susceptibility artifacts) from drainable abscesses as mentioned in the study by Kumar *et al.*[5]

Thus, in our study, we found out that finding on DWMRI and correlation with ADC maps and conventional images can play a vital role in the diagnosis of musculoskeletal infections and can supplement the conventional MRI findings in making a final diagnosis.

Limitations of the study

The main limitation of the study was the small sample size. Thus we recommend large multicentric studies to tackle this confusing category of diagnosis. Second, soft-tissue tumors were not included and compared with cases of musculoskeletal infections. The comparison of infectious and malignant cases of musculoskeletal lesions is recommended in the future studies that may help better validate the use of DWMRI in diagnosing musculoskeletal infections.

CONCLUSIONS

DWMRI is a novel investigation for discerning different musculoskeletal infections and it must be used wherever deemed necessary to avoid unnecessary referrals and treatments.

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Conflicts of interest
There are no conflicts of interest.

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