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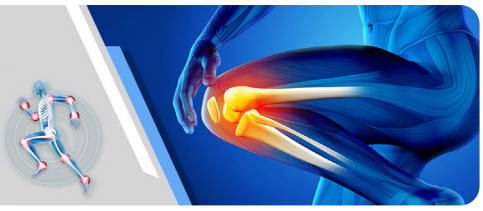

Prevalence of Bone Edema-like Lesions in Patients with Knee Osteoarthritis

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Abstract

Context: The presence of subchondral Bone Edema-Like Lesions (BELs) in patients with Knee Osteoarthritis (OA) is associated with increased pain and a faster progression of OA. However, the exact prevalence of BELs is controversial due to contradicting findings reported in previous studies.

Aim: To evaluate the prevalence of BELs by Magnetic Resonance Imaging (MRI), in patients with adjacent full-thickness cartilage loss of the knee.

Settings and Design: Single center cross-sectional study.

Methods: We evaluated 100 consecutive MRI studies of patients with Kellgren and Lawrence grade IV knee osteoarthritis from April 2019 to May 2019. The primary outcome of the study was to evaluate the prevalence of BELs. The secondary outcome was to evaluate the association of BELs with the demographic characteristics of patients including age, sex, body mass index, presence of osteophytes, and previous diagnosis of osteoporosis or osteopenia.

Results: All patients had pain at the time of MRI evaluation. The average age was 66.5 ± 10.1 years and the average body mass index was 27.3 ± 5.1 kg/m². A total of 86 patients (86%) had BELs on the evaluated MRI, with both male and female patients being equally affected (P=0.405). No demographic characteristic showed a significant association with the presence of BELs. However, while not statistically significant, male patients, patients with obesity, and patients with osteophytes had an increased risk of having BELs.

Conclusion: The majority of patients with symptomatic grade IV knee osteoarthritis have BELs on MRI evaluation. No demographic characteristic was associated with a greater risk of presenting BELs.

Keywords: Bone Edema-Like Lesions; Bone Marrow Edema; Knee; Magnetic Resonance Imaging; Osteoarthritis

Introduction

The presence of subchondral Bone Edema-Like Lesions (BELs) in patients with Knee Osteoarthritis (OA) is associated with increased pain and a faster progression of OA [1-4]. Despite being non-specific for knee OA, BELs are a common finding in patients with symptomatic knee OA, especially in areas with greater cartilage loss [3]. The exact prevalence of BELs is controversial due to contradicting findings reported in previous studies [1, 3-11]. A good understanding of the relationship between BELs, symptoms, and the severity of OA would be important while keeping an eye on available therapeutic interventions and their global impact on knee OA. The osteochondral unit

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as a whole (including the subchondral bone, bone cartilage interface, and articular cartilage) has been suggested as the primary responsible for OA [12-14]. Its three components are highly interconnected and whenever one of them is affected, the others also are. BELs are an imaging finding, observed as an area of increased signal of intensity in fluid sensitive magnetic resonance imaging (MRI). BELs are not well understood even though it is commonly identified in different musculoskeletal pathologies. Felson et al. [2] were the first to describe the important relationship of BELs with knee OA, revealing a poorer prognosis of OA when BELs were present. Since that discovery, this relationship has been extensively studied reporting greater pain and a faster progression to total knee replacement when present, reinforcing the idea that future OA therapies could target BELs [1,4-11,15,16]. In order to propose BELs as a treatment target, we first need to understand it better. Previous studies have reported BELs are present in 13.7% to 82% of patients with knee OA, especially in male, overweight, and older patients [1,3,5-7,9,10]. But other studies have stated there is no association between demographic characteristics and the presence of BELs [5,11,17]. Due to the broad range of prevalence reported and the controversial associations with demographic characteristics, we conducted a study to better understand the relationship between BELs and knee OA. The purpose of this cross-sectional study was to evaluate the prevalence of BELs in 100 patients with symptomatic knee OA and describe the association of BELs with patient demographic characteristics.

Materials and Methods

This cross-sectional study was conducted at a single institution. A trained radiologist in musculoskeletal diseases evaluated consecutive knee MRIs of patients 50 years old or older, with a previous diagnosis of osteoarthritis grade IV Kellgren and Lawrence, starting in April 2019. The first 100 MRIs with full thickness cartilage loss either on the femur or the tibia, were included in the study. All MRIs with a total knee replacement were excluded. MRIs were collected at the Hospital for Special Surgery, a musculoskeletal specialized referral hospital in New York City. The starting point was arbitrarily selected in order to obtain an unbiased sample of patients. Demographic data including age, sex, Body Mass Index (BMI), and history of osteoporosis was collected from the electronic medical record of patients included in the study. The study was performed according to the Good Clinical Practice guidelines and the Declaration of Helsinki. The study was approved by the internal ethics committee and the internal review board of the Hospital for Special Surgery with the following registration number #2019-0818-AM1.

Magnetic Resonance Imaging Evaluation

BELs were defined as an area of increased signal of intensity located in the subchondral bone on Short Tau Inversion Recovery (STIR) images (Figure 1) [18]. BELs had to be located in the subchondral bone adjacent to the full-thickness cartilage loss to be considered related to OA. MRIs were also evaluated for the presence or absence of osteophytes defined as a focal bony outgrowth extending from a cortical surface in the knee joint. All MRI studies were analyzed by a fellowship-trained radiologist in musculoskeletal diseases, as well as a research fellow for the presence of BELs in any of the femoral condyles or tibial plateau. MRIs were performed using a 1.5-T or 3.0-T superconducting magnet (GE Medical Systems; Milwaukee, WI) using a standardized protocol. MRI was performed using 2-dimensional fast-spin echo images acquired along 3 anatomic planes (sagittal, coronal, axial) (time of repetition/time of echo [TR/TE], 4000 to 6000/25 to 30 ms; echo train length, 8 to 16; bandwidth, 32 to 62.5kHz over entire frequency range; acquisition matrix, 512 x 256-416; 1 or 2 number of excitations (NEX); field of view, 15 to 16 cm; slice thickness, 3.5 mm with no gap). Additional sagittal and coronals inversion recovery sequences were obtained (TR/TE, 5000 to 8000/18; echo train length, 8 to 16; time of inversion, 150 to 180; bandwidth 32 to 62.5; 256 x192, 1 or 2 NEX; field of view, 16 to 18 cm; slice thickness, 3.5 to 4.0 cm).

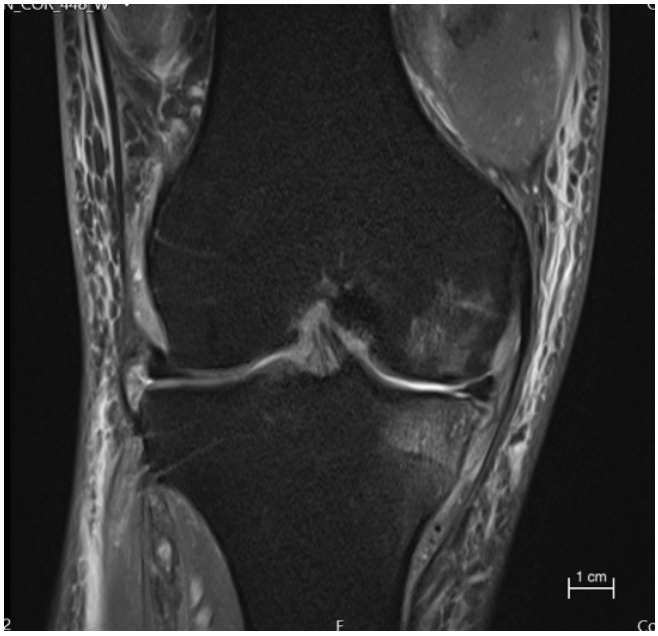

Figure 1: Magnetic resonance imaging of a 59-year-old male patient with knee osteoarthritis. This coronal STIR image demonstrates focal subchondral bone edema-like lesion in the medial femoral condyle and tibia.

Statistical Analysis

Continuous data with a normal distribution were expressed in terms of means and standard deviations, categorical data as frequencies and percentages. We calculated univariate Prevalence Odds Ratios (POR) and Prevalence Ratios (PR) to assess the association of BELs and demographic characteristics of the patients. If the proportion of cases

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was greater than 10%, PR was chosen over POR to prevent overestimation [19]. Two-tailed tests were used for all statistical analyses, with a P-value set to <0.05 to indicate statistical significance. Statistical analysis was performed using RStudio 2021.09.01 (PBC).

Results

Characteristics of the Population

Out of the 100 MRI studies included, more than half (54%) were female patients (Table 1). Even though all patients presented full-thickness cartilage loss, only 20% of patients had generalized OA affecting both the medial and lateral compartments of the knee. The medial compartment of the knee alone was the most commonly affected with OA. All patients (100%) presented knee pain at the time of the MRI evaluation, and 28% of patients had a history of diagnosed osteoporosis.

Bone Edema-Like Lesions

A total of 86 patients (86%) had BELs on the evaluated MRI study, with both male and female patients being equally affected (male 41 vs. female 45, P=0.405) (Table 1). The BMI of patients who had BELs was slightly higher than the ones that did not have BELs. However, statistically significant differences were found in any of the demographic characteristics comparing both groups (BELs vs. no BELs). If BELs were present, patients most commonly presented with edema in both the tibia and the femur concomitantly in 67% of the cases, compared to the tibia alone (21%), and the femur alone (10%).

Factors Associated with Bone Edema-like Lesion

In the univariate analysis for association, no demographic characteristic showed statistically significant association with the presence of BELs (Table 2). Despite no statistical significance, male patients (prevalence ratio 1.07; 95% Confidence Interval [CI], 0.91 to 1.25), patients with obesity (BMI >30 kg/m²) (prevalence ratio, with normal BMI as reference, 1.18; 95% CI, 0.99 to 1.41), and patients with osteophytes on MRI (prevalence ratio 1.19; 95% CI, 0.95 to 1.48) had a greater risk of presenting BELs.

Discussion

By evaluating 100 consecutive MRI studies of patients with OA of the knee, we were able to better understand the relationship between BELs and knee OA. The most important finding of this study was that up to 86% of patients with full thickness cartilage loss in the knee have BELs on MRI. In the majority of patients, BELs were observed in both femur and tibia concomitantly. No demographic characteristic showed a significant association with the presence of BELs. However, a tendency was observed showing male patients, patients with obesity, or patients with osteophytes had slightly more risk of presenting BELs. These findings help lay the basis for further prospective studies, reaffirming BELs are a common finding in knee OA. Previous studies evaluating the prevalence of BELs in patients with knee OA have reported a broad range of prevalence going from 13.7% to 82% [1,3-11,16,17]. This large variability is primarily due to the different characteristics of the populations being studied. As described by Felson et al. [1] in 2001, symptomatic patients

Table 1: Demographic Characteristics (N=100).

Characteristic	All patients (N=100)	Bone edema-like lesion (n=86)	No bone edema-like lesion (n=14)	P-value*
Sex, n (%)				0.405
Male	46 (46)	41 (47.7)	5 (35.7)	
Female	54 (54)	45 (52.3)	9 (64.3)	
Age, years	66.5 ± 10.1	67.0 ± 10.2	63.4 ± 9.5	0.213
BMI, kg/m²	27.3 ± 5.1	27.6 ± 5.2	25.4 ± 3.5	0.063
OA Location, n (%)				0.611
Medial	46 (46)	41 (47.7)	5 (35.7)	
Lateral	34 (34)	29 (33.7)	5 (35.7)	
Both	20 (20)	16 (18.6)	4 (28.6)	
Osteoporosis, n (%)	28 (28)	24 (27.9)	4 (28.6)	0.959
Bone edema-like lesion, n(%)				
Femur		10 (10)		
Tibia		18 (18)		
Both		58 (58)		

All data are expressed as mean ± SD unless otherwise specified.
BMI= Body mass index; OA= Osteoarthritis
*P-value= Bone edema-like lesion versus No bone edema-like lesion

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Table 2: Factor Associated with Bone Edema-like Lesions.

Characteristic	Bone edema-like lesion(n=86)	No Bone edema-like lesion(n=14)	Odds Ratio(95% CI)	PR(95% CI)	P-value
Sex, n					0.405
Female	45	9	Reference	Reference	
Male	41	5	1.64 (0.51-5.30)	1.07 (0.91-1.25)	
Age, years					
50-59	24	5	Reference	Reference	
60-69	28	5	1.17 (0.30-4.52)	1.03 (0.82-1.28)	0.823
70-79	22	3	1.53 (0.33-7.15)	1.06 (0.85-1.33)	0.589
≥80	12	1	2.50 (0.26-23.86)	1.12 (0.89-1.40)	0.414
BMI kg/m²					
Normal	27	6	Reference	Reference	
Overweight	24	6	0.89 (0.25-3.13)	0.98 (0.77-1.24)	0.854
Obese	28	1	6.22 (0.70-55.15)	1.18 (0.99-1.41)	0.067
Osteoporosis, n (%)					0.959
No	62	10	Reference	Reference	
Yes	24	4	0.97 (0.28-3.38)	1.00 (0.83-1.19)	
Osteophytes, n (%)					0.062
No	22	7	Reference	Reference	
Yes	64	7	2.91 (0.92-9.23)	1.19 (0.95-1.48)	

All data are expressed as frequency (%) unless otherwise specified.
PR- Prevalence Ratio; CI- Confidence Interval; BMI- Body Mass Index; Normal BMI= 18-24 kg/m², Overweight BMI= 25-29 kg/m², Obese BMI= >30 kg/m²

with OA are more likely to have BELs on MRIs. The reported prevalence in symptomatic patients has ranged from 57-82% [1,3,7-9]. On the contrary, only 13.6-30% of asymptomatic patients have showed to have BELs [1,5]. In our study 86% of the symptomatic patients with full thickness cartilage loss had BELs. The higher prevalence was somewhat expected since all of our patients had knee pain at the time of MRI evaluation. This high prevalence in symptomatic patients suggests BELs may be an important cause of knee pain, and also reaffirms bone is something we should be aware of in patients with knee OA once treatment therapies for this condition are available. Information regarding the association of demographic characteristics and the presence of BELs in patients with knee OA is controversial. On the one hand, some studies report BELs are commonly associated with male sex, more severe OA, higher BMI, and older age. On the other hand, Davies-Tuck et al. [5], Zhao et al. [11], Zhu et al. [17], and Kornaat et al. [8] found age, gender, BMI, and severity of OA had no association with the presence or development of BELs. The findings of our study support the idea that demographic characteristics have no significant association with the presence or absence of BELs. However, despite no statistical significance, we did observe a tendency for BELs to be present in males, older (>80 years), obese, and patients that had osteophytes at the time of evaluation. Our study had several potential limitations. First of all the intrinsic characteristics of a cross-sectional study do not allow evaluating casualty. The study time point was randomly selected to avoid bias; however, it was taken from a single tertiary musculoskeletal referral institution where most patients have advanced pathologies and come for surgical treatment. The sample size might have not been powered to find significance in the association analyses, however, since it was a secondary outcome, the study was not specifically designed for that. Patients with knee OA do not routinely have MRI studies, so there might have been other acute traumas or pathologies causing BELs. But by only taking into consideration BELs that were adjacent to the areas of full-thickness cartilage loss, we avoided counting acute BELs as if they were related to OA. The diagnosis of knee OA has continued to increase in the last decade due to the aging population and the increasing obesity rates. As a result, knee OA has become one of the main contributors to the Disability Adjusted Life Years [20]. Knee OA costs around 1%-2.7% of the gross domestic product in the US, with most of the costs attributed to the total knee replacement surgery and monetary losses associated with incapacity [21]. If BELs cause knee pain and a rapid progression of OA, treating it would signify reducing symptoms and the progression of the disease. Preventing the progression of OA and alleviating the patient's symptoms may enable patients to continue working, without requiring surgery in the near future. This study reinforces that musculoskeletal physicians should be aware that BELs is commonly present in patients with knee OA regardless of

demographic characteristics ultimately emphasizing the need for effective treatments targeting BELs.

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Conflict of Interest

DK, AMI, HP, AD, AV, KC, NV, DM, and VV declare that there is no conflict of interest.

Authors Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by DK, AMI, HP, AD, AV, NV. Magnetic resonance imaging evaluation was performed by DM and VV. The first draft of the manuscript was written by DK and AMI. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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