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Are biomechanical factors, meniscal pathology, and physical activity risk factors for bone marrow lesions at the knee? A systematic review☆

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ABSTRACT

Objective: To systematically review the literature to determine whether biomechanical factors, meniscal pathology, and physical activity are risk factors for bone marrow lesions (BMLs) at the knee identified from magnetic resonance imaging in pre-osteoarthritis and osteoarthritis populations.
Methods: Electronic searches of MEDLINE and EMBASE were performed from January 1, 1996 to October 31, 2012 using the keywords of bone marrow lesion(s), bone marrow (o)edema, osteoarthritis, and knee. Studies examining biomechanical factors, meniscal pathology, or physical activity in relation to the presence, incidence, or change in BMLs at the knee were included. Two independent reviewers extracted the data and assessed the methodological quality of selected studies. Due to the heterogeneity of the studies, we performed a best evidence synthesis.
Results: Fifteen studies were included in this review, of which 9 were considered high quality. The study populations were heterogeneous in terms of the symptoms and radiographic knee osteoarthritis. There was strong evidence for relationships of mechanical knee alignment and meniscal pathology with BMLs in osteoarthritis populations. There was a paucity of evidence for a relationship between physical activity and BMLs.
Conclusion: Despite the heterogeneity of included studies, these data suggest that mechanical knee alignment and meniscal pathology are risk factors for BMLs in knee osteoarthritis. It suggests that BMLs in individuals with osteoarthritis are more susceptible to mechanical knee alignment. Given the role of BMLs in the pathogenesis of knee osteoarthritis, identifying strategies to modify these risk factors will be important in slowing the progression and reducing the burden of knee osteoarthritis.

Introduction

Osteoarthritis (OA) is a significant public health problem [1,2]. It is the most common single cause of pain and disability in the elderly [1,2]. Most current management strategies for OA focus on relieving symptoms. There is no treatment that affects the progression of the disease although several drugs and nutriceuticals have been evaluated in clinical trials to determine whether they are potential disease modifying OA drugs [3]. Thus a major focus of work in OA is to identify and understand the mechanisms underlying modifiable risk factors so that effective preventive and therapeutic strategies can be developed.

OA is a chronic disease involving the whole joint. Bone marrow lesions (BMLs), which can be detected from magnetic resonance imaging (MRI), have been identified in both symptomatic [4–7] and asymptomatic [8–10] populations. They are associated with symptoms [4] and structural changes in knee OA including the severity and progression of radiographic knee OA [7], the prevalence and severity of cartilage defects [8–11] and increased cartilage loss [6,7]. It has been shown that BMLs may be the consequence of episodes of subchondral ischemia [12], and subchondral ischemia may cause OA by impairing the supply of nutrients and oxygen to the overlying cartilage plate [13–15], or reducing the strength of the bony foundation of articular cartilage [14,15].

The natural history of BMLs in pre-OA and OA populations may be different. For example, recent data suggest that in pre-OA populations BMLs have a fluctuating course with up to 50% resolving within 2 years [16], which is higher than described in OA populations, where they tend to persist [7]. A wide range of risk factors for BMLs have been identified. This may, in part,

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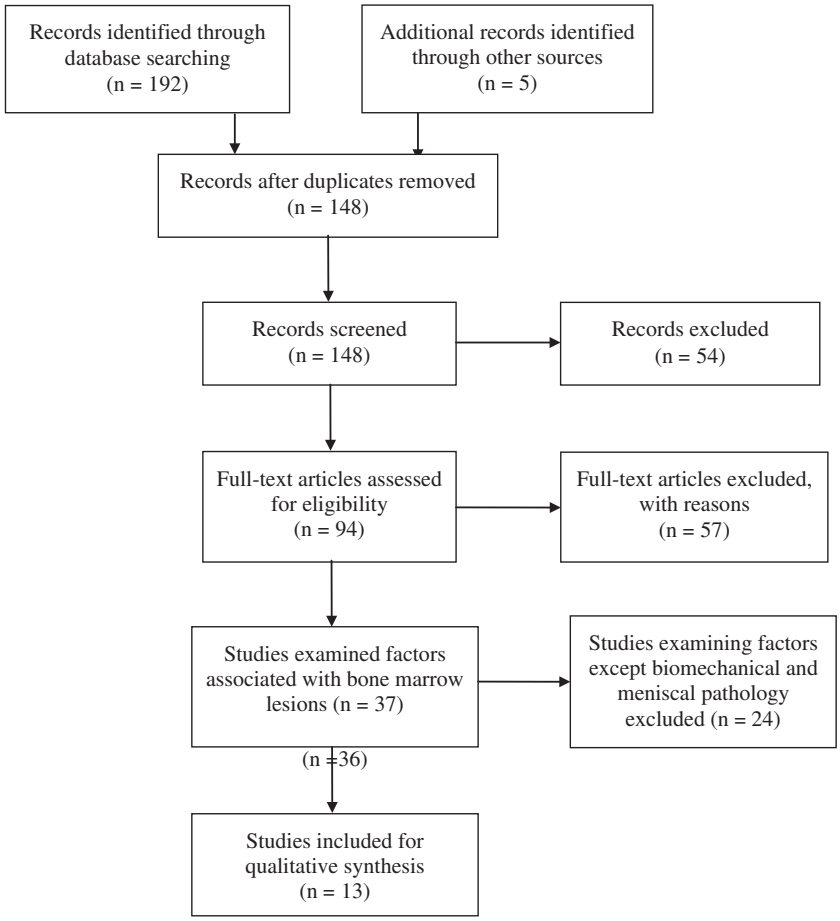

Fig. 1. Flow diagram of included and excluded studies according to the PRISMA statement.

reflect the fact that BMLs are heterogeneous, with histological examination showing that they may represent areas of osteonecrosis, fibrosis, edema, trabecular abnormalities, and bony remodeling [17]. It is likely that BMLs at different stages of OA are the consequence of different risk factors and reflect varying pathological processes in early versus late disease. BMLs are commonly described following knee trauma [18–23], however they have also been shown to be associated with a range of other factors including both biomechanical [24] and systemic factors [25,26]. The aim of this paper was to systematically review the evidence for the relationships between biomechanical factors, meniscal pathology, and physical activity and BMLs at the knee, identified from MRI in populations with and without knee OA.

Materials and methods

This systematic review was conducted according to the 2009 PRISMA guidelines [27].

Identification and selection of the literature

Electronic searches of MEDLINE and EMBASE were performed from January 1, 1996 to October 31, 2012 to identify relevant studies for this review. There were no studies describing risk factors for BMLs at the knee prior to 1996. The following keywords were used: bone marrow lesion(s), bone marrow (o)edema, osteoarthritis, and knee. Studies that described any biomechanical factors, meniscal pathology, or physical activity in relation to BMLs were included. The search was restricted to human studies published in English. The references from studies identified in the search were scrutinized for additional relevant studies.

Table 1
Criteria used to assess the methodological quality of selected cohort, case-control and cross-sectional studies

Item	Criterion	CH/CC/CS
Study population		
1	Selection before outcome was present or at uniform point	CH/CC/CS
2	Cases and controls were drawn from the same population	CC
3	Participation rate $\geq$ 80% for cases/cohort	CH/CC/CS
4	Participation rate $\geq$ 80% for controls	CC
5	Sufficient description of baseline characteristics	CH/CC/CS
Assessment of risk factor		
6	Exposure assessment was blinded	CH/CC/CS
7	Exposure was measured identical for cases and controls	CC
8	Exposure was assessed prior to the BML assessment	CH/CC/CS
Assessment of outcomes		
9	BML assessment was consistent in studied population	CH/CC/CS
10	BML was assessed reproducibly	CH/CC/CS
11	Presence of BML was according to valid definitions	CH/CC/CS
Study design		
12	Prospective design was used	CH/CC/CS
13	Follow-up time $\geq$ 2 y	CH
14	Withdrawals $\leq$ 20%	CH
Analysis and data presentation		
15	Appropriate analysis techniques were used	CH/CC/CS
16	Adjusted for at least age and gender	CH/CC/CS

Abbreviations: CH = cohort study; CC = case-control study; CS = cross-sectional study.