Association of obesity and systemic factors with bone marrow lesions at the knee: A systematic review

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ABSTRACT

Objective: The objective of this study was to systematically review the literature to determine whether obesity and systemic factors, including age, gender, heritability, dietary factors, smoking, serum and urine biomarkers of cartilage or bone metabolism, bone-related factors, and medication, are associated with knee bone marrow lesions (BMLs) identified on magnetic resonance imaging in asymptomatic pre-osteoarthritis and osteoarthritis populations.
Methods: Electronic searches of MEDLINE and EMBASE were performed from January 1, 1996 to September 30, 2012 using the following keywords: bone marrow lesion(s), bone marrow (o)edema, osteoarthritis, and knee. Studies examining obesity and non-biomechanical factors in relation to the presence, incidence, or change in BMLs were included. Two independent reviewers extracted data and assessed methodological quality of selected studies. Due to the heterogeneity of the studies, we performed a best evidence synthesis.
Results: Among 30 studies, 17 were considered high quality. The study populations were heterogeneous in terms of symptoms and radiographic knee osteoarthritis. There was strong evidence for an association between serum lipids and BMLs and no association between age and BMLs. There was moderate evidence for a relationship between obesity and BMLs. There was limited evidence for gender, smoking, C-telopeptide of type I collagen, anti-bone-resorptive treatments, licofelone, and chondroitin sulfate. There was a paucity of evidence for heritability and conflicting evidence for dietary fatty acids.
Conclusion: There is strong evidence for serum lipids and moderate evidence for obesity as risk factors for knee BMLs. Given the role of BMLs in the pathogenesis of knee osteoarthritis, identification of modifiable risk factors of BMLs and therapeutic interventions targeting BMLs has the potential to reduce the burden of knee osteoarthritis.

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Introduction

Bone marrow lesions (BMLs) have an important role in the pathogenesis of osteoarthritis (OA). They are present in both symptomatic [1–3] and asymptomatic [4,5] populations. BMLs have been shown to be associated with knee pain [1] and structural progression of disease including knee joint replacement [6]. Histologically, BMLs consist of varied pathologies including osteonecrosis, edema, fibrosis, trabecular abnormalities, and bony remodeling [7], and they may be a consequence of subchondral ischemia [8]. This may contribute to the risk of OA by reducing the integrity of subchondral bone [9,10] and/or impairing the supply of nutrients and oxygen to the overlying cartilage plate [9–11].

While BMLs have been associated with knee trauma [12,13] and biomechanical factors such as mechanical knee alignment and meniscal pathology [14,15], increasing evidence suggests that they are also associated with obesity [5,16] and non-biomechanical systemic factors such as dietary components [17,18], serum lipids [19], and osteo-protective medications [20]. BMLs seen in early and

late OA may result from different risk factors and reflect varied pathological processes; in well-established OA, biomechanical factors such as mechanical knee alignment or meniscal pathology may play a more prominent role than systemic factors [14,15]. Understanding this is important, as BMLs may be potential targets for the prevention and treatment of knee OA.

No systematic review has been performed examining the association of obesity and non-biomechanical systemic factors (age, gender, heritability, dietary factors, smoking, serum and urine biomarkers of cartilage or bone metabolism, bone-related factors, and medication) with BMLs. We systematically reviewed the literature to examine the relationship between these factors and knee BMLs identified on magnetic resonance imaging (MRI) in OA and asymptomatic pre-OA populations.

Patients and methods

This systematic review was conducted according to the 2009 PRISMA guidelines [21].

Identification and selection of literature

Electronic searches of MEDLINE and EMBASE were performed to identify studies from January 1, 1996 to September 30, 2012. No studies described risk factors for knee BMLs prior to 1996. The following keywords were used: bone marrow lesion(s), bone marrow (o)edema, osteoarthritis, and knee. The search was restricted to studies on human published in English. Studies examining obesity and non-biomechanical factors in relation to BMLs at the knee were included. The references from the identified studies were scrutinized for additional relevant studies.

Inclusion and exclusion criteria

Overall, 193 studies were identified by the initial search, with 5 additional studies identified from the references of these studies. A total of 103 studies were excluded as 49 were duplicates and 54 were reviews, letters, or posters, only examined imaging methods of BMLs, or examined the associations between previous trauma or injury and BMLs. Thus 95 studies were screened, from which 58 were excluded as they did not describe risk factors for BMLs, examined the association of BMLs with progression or symptoms of OA, or examined the relationship between patellofemoral pathology and BMLs. Of the 37 studies that investigated factors associated with the presence, incidence, or changes in knee BMLs using MRI, 25 examined obesity and non-biomechanical factors and were included in this review (Fig.).

Data extraction

The characteristics of included studies were tabulated including study population, country, radiographic knee OA, symptoms, age, number and female percentage of participants, follow-up duration, MRI sequences for BML assessment, quality score (Table 1), outcomes, and results (Tables 2–4).
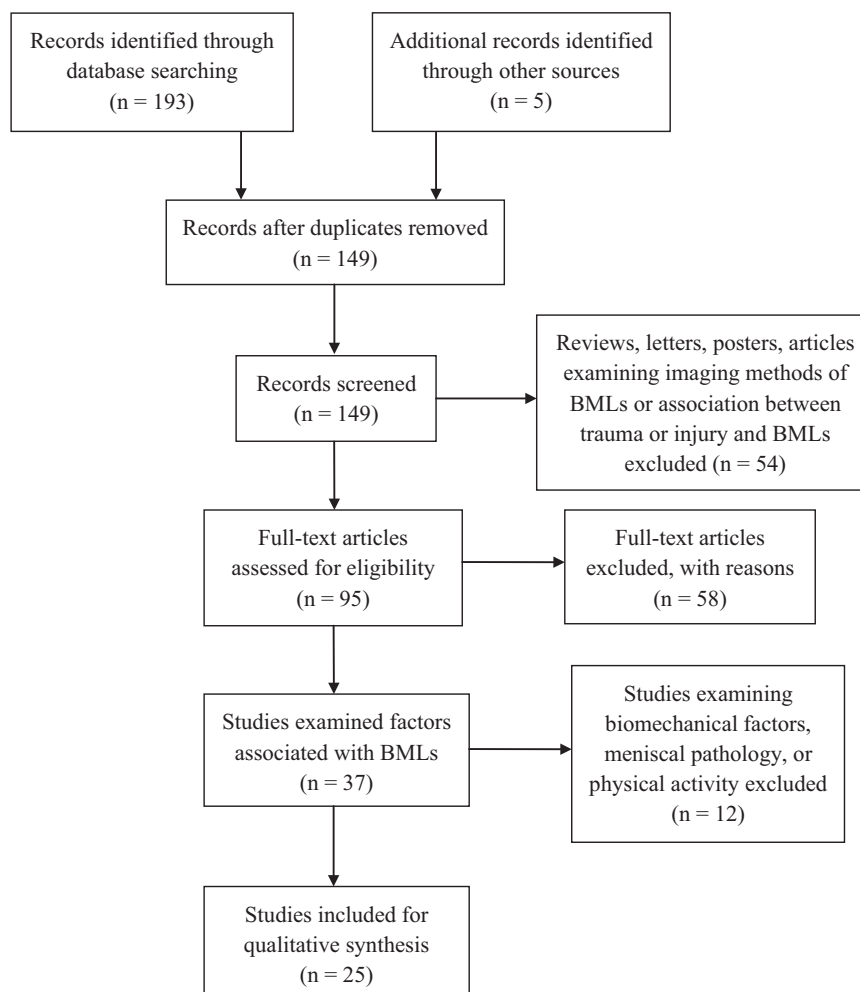

Fig. Flow diagram of included and excluded studies according to the PRISMA statement.