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Prevalence and risk factors of low bone mineral density in psoriatic arthritis: A systematic review

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ABSTRACT

Objective: Prevalence and impact of low bone mineral density (BMD) in psoriatic arthritis (PsA) is not well understood. We aimed to synthesize current evidence regarding the prevalence, impact, and risk factors for low BMD and fractures in PsA.

Methods: A systematic literature search limited to human studies was conducted without language restriction. Data on BMD, prevalence of osteoporosis, osteopenia and fractures, risk factors, morbidity, and mortality due to low BMD in PsA patients were collected.

Result: A total of 21 studies (16 case–control, 4 cross-sectional, and 1 prospective cohort) were reviewed after screening 639 titles and abstracts. In all, 17 studies compared PsA patients with one or more control group (four normal controls, five psoriasis, and eight other rheumatic diseases with or without healthy controls). The number of PsA patients in the studies ranged from 8 to 2212 with a mean (standard deviation) age of 35 (10) to 63.4 (6.2), and mean PsA duration of 2.25–13.65 years. Reported prevalence of osteoporosis varied from 1.4% to 68.8%. Low BMD was identified as a significant problem in 13 of the 21 studies. Age, female sex, postmenopausal status, PsA duration, presence of erosions, and cumulative steroid dose were associated with lower BMD. Fractures (12–40%) were associated with postmenopausal status and axial disease. No studies reported on hospitalization and mortality due to low BMD.

Conclusion: This systematic review synthesizes current evidence on BMD and its impact in PsA. High likelihood of bias and inconsistent results suggest a need for well-designed longitudinal studies on bone health in PsA.

Introduction

Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease affecting both peripheral and axial joints in patients with psoriasis [1,2]. The skeletal manifestations of PsA comprise of focal bone resorption in the form of erosions, and new bone formation (ankylosis, periostitis, and syndesmophytes) [1,2]. Moreover, patients with PsA may have concomitant osteoarthritis and diffuse idiopathic skeletal hyperostosis (DISH) [3], conditions associated with new bone formation. The effect of PsA on bone mineral density (BMD) is not well understood.

Osteoporosis is a systemic skeletal disease characterized by diminished bone mass, compromised bone strength and micro-architectural deterioration of bone tissue with increased risk for fragility fractures (fractures caused by minimal or low trauma such

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as a fall from a standing height or less) [4,5]. In the general population, osteoporosis affects one in two women and one in five men [6,7]. BMD, as measured by dual-energy x-ray absorptiometry (DXA), is typically used for the diagnosis of osteoporosis in men and women over the age of 50 [8]. A definition of osteoporosis in postmenopausal women was given by the World Health Organization working group in 1994 as the BMD *T*-score at the hip and/or the spine of more than 2.5 standard deviations (sd) below the mean peak bone mass (i.e., *T*-score < -2.5) of young healthy women [9]. In men and in women over the age of 50 years if *T*-score is between -1 and -2.5 standard deviations below the average density of a young woman, the term low bone density (formerly osteopenia) is applied, recognizing that osteopenia technically refers only to postmenopausal women with low bone mass [4]. In women younger than 50 years and not postmenopausal, BMD is considered normal unless the *T*-score is less than -2. These criteria are widely accepted for the diagnosis in older adults and to make decisions in conjunction with risk factors on therapeutic intervention in patients with osteoporosis [8,10].

Abnormal calcification of spinal ligaments as well as new bone formation in the spine and peripheral joints are hallmarks of PsA [6]. This may increase BMD as measured by DXA in spite of the presence of osteoporosis and poor bone quality. Thus, BMD may not be a sensitive marker for diagnosing osteoporosis in PsA.

Spontaneous and minimal trauma fractures are very common in patients with low BMD and osteoporosis, causing considerable morbidity and disability [11]. Inflammation-mediated bone loss, limited physical activity (which directly correlates with disease activity), renal impairment (associated with many rheumatic diseases that may lead to secondary hyperparathyroidism), and treatment with disease modifying drugs such as methotrexate and glucocorticoids, all potentially contribute toward increasing the risk of low BMD in the rheumatic diseases [12]. PsA patients have chronic inflammation and altered bone remodeling [13] and suffer from chronic fatigue, immobility due to pain and impaired joint movement [14,15]. Studies have also recognized the presence of chronic renal disease in addition to other systemic comorbidities in severe psoriasis and PsA [16]. However, little is known about the occurrence of low BMD-related fragility fractures in PsA. Some studies show normal BMD levels in PsA patients but increased fractures with longer duration of disease [17]. Studies on bone microarchitecture and bone quality in PsA are sparse, and there is no conclusive evidence to support compromised bone quality in these patients [18]. A preliminary review of studies evaluating BMD in PsA provides inconsistent and conflicting results [19–24].

Therefore, we aimed to synthesize the evidence on prevalence and impact of low BMD in PsA patients. Specifically, through a systematic review of the published literature, we aimed to evaluate the prevalence of low BMD in PsA; prevalence of fractures in patients with PsA; risk factors for low BMD in PsA; and morbidity or hospitalization due to low BMD in PsA. The systematic review of the literature will synthesize the existing evidence and provide direction for future studies on bone health in PsA and clinical care guidelines.

Methods

Search strategy

Database searches were conducted independently by an investigator (SC) and a library information specialist. Ovid MEDLINE(R) (1946–2014), the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1981–2014), Embase (1974–2014), Cochrane Database for systematic reviews, and Cochrane Central Register of controlled trials were searched for relevant manuscripts using Medical Subject Headings (MeSH) and non-MeSH terms for PsA (psoriatic arthritis/PsA/spondyloarthritis/spondyloarthritides/spondyloarthropathies/arthritis and psoriasis/psoriatic spondyloathritis/psoriatic arthropathy) and osteoporosis (osteoporosis/bone density/osteoporotic fractures/bone mineral density/BMD/bone quality/fragility fractures/brittle bones/low bone mass/bone mineral content/thin bones/osteopenia/DXA scan/dual energy x-ray absorptiometry/bone mineral content/osteoporotic fractures/undetected vertebral fractures/fragile bones) and/or outcomes (fractures, hospitalization, morbidity and mortality, and quality of life). The search was limited to studies involving human subjects, but no language or geographic restrictions were applied. Non-English articles were translated to English by native language speakers or by using machine translation software.

Study selection for full review

Search results were combined into a single Endnote file, and duplicates were removed. Titles and abstracts were screened by two investigators (SC and AA) independently to identify articles for full qualitative review.

Inclusion criteria

Studies satisfying the following criteria were selected for detailed review and data abstraction. (1) Study population including adult PsA patients (age $\geq$ 18 years), (2) peer-reviewed observational studies with original data (case–control/cohort/cross-sectional/case-report >5 patients), (3) reporting of BMD (areal or volumetric), bone quality or fractures. Studies reporting low BMD on radiographs without BMD measurements or fractures were not included. Abstracts, case reports with less than five patients, reviews, editorials, and studies for which updated manuscripts were unavailable were excluded. The references of shortlisted articles, guidelines and reviews were hand-searched to identify relevant articles that were not captured in the original search. Any discrepancy in the decision pertaining to inclusion or exclusion of an article for full review was resolved by mutual consensus. Disagreements were resolved by an arbitrator (DDG).

Data abstraction

Data from the selected articles were abstracted by both reviewers independently. A standardized data abstraction form was used to collect information on study design, method used to measure BMD (DXA, quantitative computerized tomography, high-resolution peripheral quantitative computerized tomography, or quantitative ultrasonography), BMD values (*T*-score, *Z*-score, and/or density values in g/cm^2), prevalence of osteoporosis, osteopenia and fragility fractures, low BMD, and PsA-related risk factors which may affect the occurrence of low BMD, hospitalization, and morbidity and mortality in PsA patients due to low BMD. Where available, data were collected on low BMD-related risk factors which included age, sex, body mass index, menopausal status, use of glucocorticoids, and smoking. PsA-related patient characteristics included duration of psoriasis and PsA, disease activity measures (tender and swollen joint counts), Psoriasis area severity index (PASI), presence of axial disease, enthesitis, dactylitis, presence of inflammatory bowel disease, and laboratory measures of inflammation (erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Data on medications for PsA management including non-steroidal anti-inflammatory drugs (NSAIDs), disease modifying anti-rheumatic drugs (DMARDs) (e.g., methotrexate and corticosteroids), and tumor necrosis factor inhibitors and other biologic agents were recorded for their effect on BMD.