ABSTRACT

Background The risk of osteoporosis in patients with psoriatic arthritis (PsA) remains unclear. The aim of this study was to compare bone mineral density (BMD) measured by dual-energy X-ray absorptiometry (DXA) in patients with PsA and controls.

Patients and methods Patients with PsA and controls were recruited from the Nord-Trøndelag Health Study (HUNT) 3.

Results Patients with PsA (n=69) and controls (n=11 703) were comparable in terms of age (56.8 vs 55.3 years, p=0.32), gender distribution (females 65.2% vs 64.3%, p=0.87) and postmenopausal status (75.6% vs 62.8%, p=0.08). Body mass index (BMI) was higher in patients with PsA compared with controls (28.5 vs 27.2 kg/m², p=0.01). After adjusting for potential confounding factors (including BMI), BMD was higher in patients with PsA compared with controls at lumbar spine 1–4 (1.213 vs 1.147 g/cm², p=0.003) and femoral neck (0.960 vs 0.926 g/cm², p=0.02), but not at total hip (1.013 vs 0.982 g/cm², p=0.11). Controls had significantly higher odds of having osteopenia or osteoporosis based on measurements of BMD in both the femoral neck (p=0.001), total hip (p=0.033) and lumbar spine (p=0.033).

Conclusion Our population-based data showed comparable BMD in patients with PsA and controls. This supports that the PsA population is not at increased risk of osteoporosis.

BACKGROUND

Data on systemic bone loss in patients with psoriatic arthritis (PsA) are conflicting, and population-based data are lacking.1–3 It is well documented that patients with rheumatoid arthritis (RA) are at increased risk for osteoporosis, presumably due to factors including systemic and local inflammation, inactivity related to arthritis and treatment with glucocorticoids.4–5 Despite some similar features in clinical presentation and joint damage, substantial differences exist between RA and PsA concerning immunopathogenesis, clinical manifestations and radiographic features. In PsA, activation of both osteoclasts and osteoblasts can be involved, and as a consequence, patients may show signs of both bone destruction (erosions) and bone formation (periostitis, osteophyte formation).6 This in contrast to RA where osteoclast activation is dominating, causing erosions and osteoporosis.7

The aim of this study was to compare bone mineral density (BMD) in patients with PsA and controls.

MATERIALS AND METHODS

Data were retrieved from the Nord-Trøndelag Health Study (HUNT) 3,8 performed between 2006 and 2008. The study population and validation of diagnoses have been described in detail previously.8–9 The study was approved by the Regional Committee for Medical Research Ethics, South-Eastern Norway (REK number 2010/2661).
Inclusion of patients and controls

An experienced rheumatologist reviewed the medical records of persons in HUNT 3 with self-reported PsA, plus self-reported ankylosing spondylitis and psoriasis or self-reported RA and psoriasis to validate PsA. In total, 338 persons in HUNT 3 were found to have PsA according to the Classification of Psoriatic Arthritis criteria. Details on patients with PsA and controls are previously described in detail.9

An invitation to Dual-energy X-ray absorptiometry (DXA) measurement was sent to 14247 persons in the HUNT 3 population born after 1 January 1921 and living in one of the five largest municipalities in the Nord-Trøndelag county. Eleven thousand seven hundred and seventy-two persons participated (82.6%)—7570 women and 4202 men. Of these, 6887 were invited based on a random sample of the total HUNT cohort, and 4885 were invited based on reporting a wide spectrum of lung symptoms (asthma and chronic obstructive pulmonary disease (COPD)), as the DXA study in HUNT 3 was also initially designed as part of a study on patients with pulmonary disease. This sample included 69 patients with PsA (36 invited by random selection and 33 because of self-reported pulmonary symptoms) with age between 20 to 95 years. Controls were all other participants in the HUNT 3 study.

Measurement of variables

Information about risk factors and disease was collected by self-administered questionnaires, clinical measurements and blood samples. Data on medication use, clinical and disease specific characteristics among the PsA patients were collected from the patient’s hospital journals. Measurements of height and weight were performed with lightweight clothing and no shoes. Females were asked about age at cessation of menstrual cycle.

DXA measurements were performed in the lumbar spine (L1–L4) and hip (femoral neck and total hip) using a Lunar/Prodigy (GE Healthcare) DXA machine. Lumbar spine BMD was calculated as the mean of the BMD score in L1–L4. We preferably used measurements from the left hip. Bone density was expressed as g/cm² and T-score (SD from the mean of a healthy young female population). The data for T-score estimation were stratified on variables have been published previously.10

Using an unpaired two-tailed t-test for normally distributed data. The χ² test, or Fisher exact test when small numbers, was used to examine the associations between categorical variables. A multivariable linear regression model was used to assess the relationship between PsA and BMD, controlling for potential confounders (age, sex, BMI, smoking status, physical activity, asthma/COPD and reason for invitation to DXA measurement). Ordinal logistic regression was used to compare the frequency of osteoporosis in patients with PsA and controls, after assessment of parallel lines.

RESULTS

As shown in table 1, there were no differences between patients with PsA and control subjects concerning age, sex, postmenopausal status, height, smoking, ever use of asthma or COPD medication and C-reactive protein (CRP).

A statistically significant difference between patients with PsA and controls was seen for weight (83.8 kg vs 77.9 kg, p<0.01), BMI (28.5 kg/m² vs 27.2 kg/m², p=0.01) and self-reported asthma (37.7% vs 26.8%, p=0.04) and COPD (14.5% vs 7.1%, p=0.02). Mean disease duration for patients with PsA was 8.3±6.8 years. Among patients with PsA, 14 (20.3%) had axial involvement in addition to peripheral joint disease. We excluded 60 persons in the control group with bilateral hip prostheses or invalid measurements from further analyses of BMD of the hip. BMD values and T-scores for patients with PsA and controls are presented in table 2.

When adjusting for potential confounding factors listed in table 2, BMD was significantly higher in patients with PsA compared with controls in spine L1–L4 (1.213 vs 1.147 g/cm², p=0.003) and femoral neck (0.960 vs 0.926 g/cm², p=0.02) but not in total hip (1.013 vs 0.982 g/cm², p=0.11). In females, the PsA group had significantly higher BMD in the lumbar spine (mean difference 0.056, 95% CI 0.003 to 1.109, p=0.04) but not in the hip. Postmenopausal patients with PsA (n=34) had significantly higher BMD than controls at femoral neck (mean difference 0.071, 95% CI 0.025 to 0.117, p=0.043) and spine (mean difference 0.106, 95% CI 0.045 to 0.166, p=0.009) when controlling for potential confounding factors (data not shown).

Neither univariable nor multivariable linear regression models (controlling for age, sex, BMI, smoke and asthma diagnosis) showed an association between disease duration and BMD (adjusted p values for femoral neck BMD 0.93, total hip BMD 0.98, spine L1–L4 0.09).

As shown in table 3, the odds of being classified as having osteopenia or osteoporosis was greater for the control subjects than the patients with PsA (ordinal logistic regression).

DISCUSSION

This population-based cohort study found a higher BMD in the lumbar spine and femoral neck in individuals with PsA compared with individuals without PsA. Our findings are in line with other publications that report comparable BMD in
Table 1  Demographic and clinical characteristics in patients with psoriatic arthritis and controls with bone density measurement in the HUNT 3 study. Results are mean (±SD) for continuous variables or absolute values (percentages) for categorical variables

| Demographic variables | Psoriatic arthritis n=69 | Controls n=11703 | p Value* |
|-----------------------|--------------------------|-----------------|----------|
| Female                | 45 (65.2)                | 7525 (64.3)     | 0.87     |
| Postmenopausal females| 34 (75.6)                | 4722 (62.8)     | 0.08     |
| Age, years            | 56.8 (12.5)              | 55.3 (16.5)     | 0.32     |
| Weight, kg            | 83.8 (16.3)              | 77.9 (15.4)     | <0.01    |
| Height, m             | 1.70 (0.09)              | 1.69 (0.09)     | 0.09     |
| BMI, kg/m²             | 28.5 (4.3)               | 27.2 (4.5)      | 0.01     |
| Daily smoking         | 18 (26.1)                | 2814 (24.0)     | 0.69     |
| Physical activity ≥2 times per week | 40 (58)                | 6848 (58.5)     | 0.93     |
| Asthma ever           | 26 (37.7)                | 3138 (26.8)     | 0.04     |
| COPD/emphysema ever   | 10 (14.5)                | 830 (7.1)       | 0.02     |
| Ever use of asthma/ COPD medication last 5 years | 23 (33.3)                | 2800 (23.9)     | 0.07     |
| C-reactive protein, mg/L | 3.9 (4.9)                | 2.9 (5.8)       | 0.17     |
| Self-reported fractures |                        |                 |          |
| Forearm (PsA n=65)    | 11 (16.9)                | 1938 (17.3)     | 0.93     |
| Hip (PsA n=65)        | 1 (1.5)                  | 187 (1.7)       | 1.00†    |
| Spine (PsA n=63)      | 3 (4.8)                  | 649 (6.0)       | 1.00†    |
| Self-reported osteoporosis (PsA n=64) | 6 (9.4)                | 538 (4.8)       | 0.08     |
| Ever use of hormone replacement therapy among females | 16/30 (53.3%)            | 1541/3766 (40.9) | 0.17     |
| Disease duration, years | 8.3 (6.8)                | NA              |          |
| Peripheral joint involvement | 69 (100)                | NA              |          |
| Joint involvement     |                         |                 |          |
| Isolated DIP joint    | 1 (1.4)                  | NA              |          |
| Monoarthritis         | 1 (1.4)                  | NA              |          |
| Oligoarthritis        | 44 (63.8)                | NA              |          |
| Polyarthritis         | 23 (33.3)                | NA              |          |
| Axial involvement     | 14 (20.3)                | NA              |          |
| Enteritis             | 43 (62.3)                | NA              |          |
| Ever use of peroral steroids |                 |                 |          |
| Previous              | 25 (36.2)                | NA              |          |
| Current               | 4 (5.8)                  | NA              |          |
| Ever users of anti-TNF therapy |                 |                 |          |

Continued

Table 1 Continued

| Demographic variables | Psoriatic arthritis | Controls | p Value* |
|-----------------------|---------------------|----------|----------|
| Ever use of methotrexate |                    |          |          |
| Previous              | 11 (15.9)           | NA       |          |
| Current               | 18 (26.1)           | NA       |          |
| Ever use of synthetic DMARDs other than methotrexate |                 |          |          |
| Leflunomide           | 15 (21.7)           | NA       |          |
| Salazopyrin           | 7 (10.1)            | NA       |          |
| Ever use of NSAIDs    |                     |          |          |
| previous              | 14 (20.3)           | NA       |          |
| current               | 44 (63.8)           | NA       |          |

*χ² test for counts and independent samples t-test for continuous variables.
†Fisher’s exact test due to small numbers.

Psoriatic arthritis

patients with PsA and the general population.3 11–14 However, comparing results across studies is difficult, as outcomes and comparison groups differ.2 A rather low proportion of patients with PsA in this study were currently using tumour necrosis factor (TNF)-inhibitors. This may be explained by the inclusion being performed between 2006 and 2008 when use of TNF-inhibitors was still low in PsA patients in Norway. As the patients with PsA in our study were identified from a population survey and had similar CRP as the control group, we also suspect a relatively low disease activity. The patients with PsA had higher BMI, which is associated with greater BMD in the general population.15 However, controlling for BMI in a multivariable linear regression model did not influence the results on BMD in our study. Further, the spine may be affected by new bone formation in PsA, which should be taken into account when evaluating BMD data from the lumbar spine.9

Higher BMD in PsA compared with RA has been reported.16 17 Further, it is well documented that patients with RA are at increased risk for osteoporosis and fracture.5 18 The pathophysiological mechanisms that affect bone appear to be different in PsA and RA. In RA, the inflammatory process causes an increased stimulation of the osteoclasts, together with a downregulation of the osteoblasts, whereas in PsA both osteoclasts and osteoblasts are stimulated.19 Autoantibodies such as anticyclic citrullinated peptide antibodies are known to represent a higher risk of developing bone erosions by directly stimulating the differentiation of
### Table 2  Bone mineral density in patients with psoriatic arthritis and controls in the HUNT 3 study

| DXA Females and males | PsA n=69 | Controls n=11703 | Mean difference (95% CI) (PsA vs controls) | p Value* | p Value† |
|-----------------------|----------|------------------|-----------------------------------------------|----------|----------|
| **Left femoral neck**  |          |                  |                                               |          |          |
| BMD                   | 0.960 (0.134) | 0.926 (0.157)  | 0.034 (-0.003 to 0.071)                       | 0.07     | 0.02     |
| T-score               | -0.42 (0.99)  | -0.70 (1.24)    | 0.30 (0.04 to 0.52)                           | 0.02     | 0.02     |
| **Left total hip**    |          |                  |                                               |          |          |
| BMD                   | 1.013 (0.141) | 0.982 (0.158)  | 0.030 (-0.007 to 0.067)                       | 0.11     | 0.11     |
| T-score               | -0.15 (1.04)  | -0.41 (1.22)    | 0.26 (-0.03 to 0.54)                          | 0.09     | 0.11     |
| **Spine L1–L4**       |          |                  |                                               |          |          |
| BMD                   | 1.213 (0.177) | 1.147 (0.183)  | 0.065 (0.021 to 0.108)                        | 0.003    | 0.003    |
| T-score               | 0.15 (1.43)   | -0.39 (1.50)    | 0.55 (0.19 to 0.91)                           | 0.003    | 0.003    |
| Females PsA n=45      |          |                  |                                               |          |          |
| BMD                   | 0.921 (0.106) | 0.897 (0.155)  | 0.024 (-0.008 to 0.056)                       | 0.14     | 0.19     |
| T-score               | -0.487 (0.88) | -0.69 (1.29)    | 0.20 (-0.06 to 0.47)                          | 0.14     | 0.19     |
| **Left total hip**    |          |                  |                                               |          |          |
| BMD                   | 0.973 (0.115) | 0.946 (0.153)  | 0.026 (-0.007 to 0.061)                       | 0.13     | 0.30     |
| T-score               | -0.22 (0.96)  | -0.45 (1.28)    | 0.22 (-0.065 to 0.51)                         | 0.13     | 0.30     |
| **Spine L1–L4**       |          |                  |                                               |          |          |
| BMD                   | 1.174 (0.148) | 1.118 (0.181)  | 0.056 (0.003 to 0.109)                        | 0.04     | 0.04     |
| T-score               | -0.05 (1.23)  | -0.52 (1.51)    | 0.46 (0.02 to 0.91)                           | 0.04     | 0.04     |

Mean (±SD).
*Independent samples t-test,
†Linear regression analysis with adjustments made for age, sex, BMI, physical activity, smoking, asthma/COPD and reason for invitation to DXA, ‡Linear regression analysis with adjustments made for age, BMI, physical activity, smoking, asthma/COPD and reason for invitation to DXA, BMD, bone mineral density; BMI, body mass index; DXA, dual-energy X-ray absorptiometry; COPD, chronic obstructive pulmonary disease; HUNT, Nord-Trøndelag Health Study; PsA, psoriatic arthritis.

Osteoclasts and promoting bone resorption. In PsA, there is an absence of recognised autoantibodies. The clinical implications of these pathophysiological differences are that osteoporosis and joint erosions are more prominent in RA, whereas PsA is also characterised by new bone formation. This may explain the higher BMD seen in patients with PsA compared with patients without PsA in our population cohort, particularly in the spine where syndesmophytes are common in PsA. In our PsA cohort, 14 patients (20.3%) had axial involvement based on clinical and radiological

### Table 3  Osteoporosis, osteopenia and normal bone mineral density (BMD) among patients with psoriatic arthritis and controls in the HUNT 3 study: Ordinal regression shows higher odds of being classified as having osteopenia or osteoporosis for the control group

| Based on T-score femoral neck | PsA Psoriatic Arthritis | Controls | Overall p - Value* | Overall p - Value †† |
|--------------------------------|------------------------|----------|-------------------|---------------------|
| Osteoporosis                   | 1 (1.4)                | 739 (6.4) | 0.002             | 0.001               |
| Osteopenia                     | 15 (21.7)              | 4065 (35.4)|                 |                     |
| Normal BMD                     | 53 (76.8)              | 6690 (58.2)|                 |                     |

**Based on T-score total hip**

|                          | PsA Psoriatic Arthritis | Controls | Overall p - Value* | Overall p - Value †† |
|--------------------------|------------------------|----------|-------------------|---------------------|
| Osteoporosis             | 1 (1.4)                | 474 (4.1) | 0.024             | 0.033               |
| Osteopenia               | 12 (17.4)              | 3143 (27.5)|                 |                     |
| Normal BMD               | 56 (81.2)              | 7824 (68.4)|                 |                     |

**Based on T-score spine L1–L4**

|                          | PsA Psoriatic Arthritis | Controls | Overall p - Value* | Overall p - Value †† |
|--------------------------|------------------------|----------|-------------------|---------------------|
| Osteoporosis             | 3 (4.4)                | 903 (7.8) | 0.021             | 0.033               |
| Osteopenia               | 11 (16.2)              | 3065 (26.4)|                 |                     |
| Normal BMD               | 54 (79.4)              | 7629 (65.8)|                 |                     |

Frequency (percentage).
*Ordinal regression with no adjustments made,
†Ordinal regression with adjustments made for age (continuous), BMI, physical activity, smoking, asthma/COPD and reason for invitation to DXA (randomly or based on self-reported pulmonary symptoms).
BMD, bone mineral density; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DXA, dual-energy X-ray absorptiometry; HUNT, Nord-Trøndelag Health Study; PsA, psoriatic arthritis.
findings, but we were unable to obtain X-ray of the spine for all patients with PsA to control for syndesmophytes or degeneration of the spine. New bone formation may also form at the hip, and may therefore in theory also affect the BMD value of both femoral neck and total hip.21 High correlation between BMD measurements and bone strength in hip and spine has been demonstrated in in vitro studies, and a strong association between BMD and risk of fracture exists.22 However, besides BMD, there are several other risk factors for fracture. One study found higher cortical porosity and lower cortical bone density of the distal radius on high-resolution CT in patients with PsA despite a normal BMD.23 This may affect the cortical bone quality and predispose the bone to fractures. Other studies have reported higher frequency of fractures in PsA despite comparable BMD.13 14

The strengths of this study include the population-based study design and the use of objective criteria for the PsA diagnoses. A limitation is the relatively small number of PsA cases. We did not have access to clinical data on disease activity of the patients with PsA, but CRP was similar in the two groups. Unfortunately, we had limited information about steroid use in the control group and could therefore not include this variable in our regression models. In addition, we did not examine radiological images of the patients with PsA to control for syndesmophytes in the spine or new bone formation of the hip area, or calcifications of the aorta, which may influence the BMD values at these sites.

CONCLUSION
Our population-based data showed similar BMD in patients with PsA and controls. Slightly higher BMD values at femoral neck and lumbar spine were observed in patients with PsA. A higher proportion of the PsA population had a normal BMD. Thus our findings support that patients with PsA do not seem to have a significantly increased risk of osteoporosis compared with the background population.

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