Original article

Validity and role of vertebral fracture assessment in detecting prevalent vertebral fracture in patients with rheumatoid arthritis

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ABSTRACT

Objectives: We aimed to identify the validity and the role of vertebral fracture assessment (VFA) for the diagnosis of prevalent vertebral fracture (VF) in rheumatoid arthritis (RA) patients.
Methods: Total of 100 women with RA who were 50 years or older were enrolled. All participants underwent lateral imaging of the thoraco-lumbar spine by radiography and VFA. All radiographs were analyzed by two radiologists. Discrepancies between radiologists for spine radiography were resolved by consensus and these results were defined as the reference standard. VFA interpretation was done independently by two nuclear medicine physicians. Fracture defined by VFA measure was done only when two physicians both independently reported fracture. The inter-rater agreement for the detection of VF on VFA was evaluated by kappa statistics. We calculated percent values for the diagnostic validity of VFA in detecting VF in the 100 women as a whole and according to the presence of previous fracture or back pain.
Results: The prevalence of VF identified by spine radiography was 47%. Inter-rater agreement of VFA per vertebra by two VFA readers showed moderate agreement (kappa = 0.60). The sensitivity, PPV, specificity and NPV of VFA compared to spine radiography were 57.3%, 30.9%, 89.1% and 96.1% for total vertebrae. All patients with history of previous VF ($n = 13$) were visualized with VFA with 100% sensitivity but it has 64.7% sensitivity and 79.3% specificity in patients without previous VF ($n = 87$).
Conclusion: VFA is most useful to identify patients without VF because of its high specificity and NPV in all spine level.

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1. Introduction

Rheumatoid arthritis (RA), one of the most common multisystem inflammatory disorders, is characterized by chronic and progressive inflammation and destruction of synovial joints [1,2]. Estimates of the prevalence of RA range between 0.5% and 1% and increase with age, reaching a peak in the sixth decade of life [1,3,4]. Several major comorbidities, including cardiovascular disease, infection, lymphoproliferative malignancy, and peptic ulcer disease are known to be independent risk factors for premature death in RA [5]. In addition, osteoporosis and related fractures are recognized as the main extra-articular complication of RA and can influence the outcome of RA patients [6].

The risk factors for vertebral fracture (VF) in RA patients are age, disability, low body mass index, previous non-VF in general, long-standing disease duration, and glucocorticoids use [6–8]. Prevalent vertebral fractures have only been shown to predict incident vertebral fractures with a relative risk as high as 4.4. Whereas, the relative risk of subsequent hip fractures in those with compared to those without prior VF is much less, 2.3 [9]. VFs are also linked to higher mortality rates at 5 years [10]. Therefore, it is important to detect VF in high-risk groups, especially older RA patients [11]. Nevertheless, VF might be ignored in RA patients because screening for VF is not typically performed for all patients, rather it is performed only for patients complaining of back pain. Moreover, severe joint pain and the consequent use of painkillers lead to delay in diagnosis and increased morbidity of VF in RA patients [12].

The standard method to screen for VF is spine radiography of the thoraco-lumbar spine, but this technique cannot be used routinely because of its inconvenience and concerns about radiation [13]. The detection of vertebral fractures using dual-energy X-ray absorptiometry (DXA), also known as vertebral fracture assessment (VFA),

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is a convenient method to assess vertebral deformities because VFA offers point-of-service convenience for the patient when it is done at the same visit as for bone mineral density (BMD) measurement by DXA, with far less radiation than standard radiography (3 μSv compared to 600 μSv in spine radiography), and lower cost than spine radiography [14]. The method has been validated in the general population through several studies, but reports on the use of VFA in RA patients have been limited [15,16].

Thus, we aimed to identify the validity of vertebral fracture (VF) and its role for the diagnosis of prevalent vertebral fracture (VF) in RA patients.

2. Methods

2.1. Study participants

We enrolled 100 women (1300 vertebrae from T4 to L4) with RA who visited our university hospital for periodic examination between April 2011 and August 2011. Patients aged 50 years or older and who fulfilled the American College of Rheumatology (ACR) 1987 revised classification criteria for RA were included. Among the candidates who visited during above period (n = 169), patients who were recently checked for BMD or not consented were excluded (n = 69). All patients provided informed consent under an institutional review board (IRB)-approved protocol.

2.2. Demographic and clinical findings

Participants completed questionnaires via interviews about demographics (sex, age, race, height and weight), medical history (use of glucocorticoids) and menopausal status. Risk factors for osteoporosis and fractures were assessed by structured questionnaires. Disease duration was defined as the time elapsed between onset, or first disease-related symptoms, and enrollment. The clinical and laboratory data were collected at the DXA time points. This included 28 tender joint counts (TJCs) and swollen joint counts (SJCs), visual analog scale (VAS) scores for pain and patient's assessment of disease activity, HAQ score, Rheumatoid factor (RF), and erythrocyte sedimentation rate (ESR). The disease activity score (DAS) was calculated. BMD measurements by DXA of the hip (femoral neck) and lumbar spine L1–4 in anteroposterior view were carried out by trained technician.

2.3. Fracture assessment

All participants underwent lateral imaging of the thoracolumbar spine by radiography and VFA on either the same day or within seven days of each other. Acquisition of VFA was performed according to the manufacturer's recommendations.

2.3.1. Spine radiography

All radiographs were analyzed by two experienced radiologists. Discrepancies between radiologists in the presence of fracture, fracture type and grade were resolved by consensus and these results were defined as the reference standard. By two radiologists, qualitative fracture evaluation was performed to decide whether the vertebral fracture was present or not and semiquantitative method was used to classify the severity of vertebral deformity as mild (grade 1), moderate (grade 2), or severe (grade 3) [17]. Vertebral levels that could not be adequately visualized were classified as "unreadable".

For morphometric radiography, vertebral heights were manually measured by one of the two radiologists. Six points (anterior, mid, posterior on upper and lower end plate) were marked with electronic calipers on each of the 13 vertebral bodies from T4 to L4 using PACS workstation software. Radiologists did not use a graduated magnification glass. From that, Ha (anterior height), Hm (middle height), Hp (posterior height), the two ratios Ha/Hp (wedge compression ratio), Hm/Hp (biconcavity ratio), and Hp-1/Hp (crush ratio) were calculated.

2.3.2. Vertebral fracture assessment (VFA)

Lateral spine images from T4 to L4 were taken for all patients (1,300 vertebrae) using the VFA software of the DXA device. VFA examination was performed using a bone densitometer (Discovery W, Hologic Inc., Bedford, MA, USA) with the patient in lateral decubitus position. For assessment of VFs, two experienced nuclear medicine physicians used qualitative and the semiquantitative methods of Genant [17]. Six parameters were calculated automatically by the DXA device. VFA interpretation was done independently by two nuclear medicine physicians. We considered a vertebra as fractured only when the two VFA readers interpreted it as fractured. However, consensus reading between two readers was not done for different interpretations.

2.4. Statistical analysis

Demographic characteristics are presented as means ± SD (range) and categorical variables are expressed as frequencies. The prevalence of VF was analyzed descriptively per person (n = 100) basis. We calculated percent values for the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of VFA detecting VFs according to level of spine. The inter-rater reproducibility between the two readers for VFA was calculated using standard kappa statistics. In addition, we calculated the prevalence-adjusted and bias-adjusted kappa (PABAK) to assess the effect of the imbalance in observations [18]. The vertebral heights and height ratios calculated by MRX and VFA were compared using estimates of the intraclass correlation coefficient (ICC) [19]. The sensitivity and specificity of VFA compared with spine radiography were evaluated in clinical practice such as history of previous VFs and back pain. All analyses were performed via SPSS 19.0 (SPSS, Chicago, IL, USA).

3. Results

3.1. Participants

We selected 169 women with RA who were 50 years of age or older between April 2011 and August 2011. Among them, 100 patients were consecutively enrolled, excluding 69 patients who were recently checked for BMD or did not agree to participate in the study. The clinical characteristics of participants are presented in Table 1. At baseline, they had a mean age of 61.2 years with a median (range) disease duration of 6.5 years (0.2–22.4). Ninety-seven patients (97%) had reached menopause and 57 patients (57%) were taking glucocorticoids at enrollment.

A diagnosis of osteoporosis or osteopenia was made using calculations according to World Health Organization (WHO) T-score criteria (T-score ≤ −2.5 or −2.5 < T-score < −1); 37 (37%) of the patients were classified as having osteoporosis and 51 (51%) as having osteopenia.

3.2. Reliability of VFA

The reliability of vertebral fracture assessment (VFA) for detecting VFs is given in Table 2. We considered a vertebra as fracture only when the two VFA readers interpreted it as fractured. The sensitivity, PPV, specificity and NPV of VFA compared to spine radiography were 57.3, 30.9%, 89.1 and 96.1% for total vertebrae.