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Can bone quality be predicted accurately by Singh index in patients with rheumatoid arthritis?

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Abstract The aim of this study was to evaluate Singh index as a simple and inexpensive means of estimation of bone quality in patients with rheumatoid arthritis. Singh index evaluation was made on digital pelvis radiographs in 50 consecutive patients by three observers. Bone mineral density *T* scores of the spine and left proximal femur were assessed using dual energy X-ray absorptiometry. Singh index was correlated with densitometry measurements after grouping the patients as normal, osteopenia and osteoporosis. Intra- and interobserver agreements were evaluated by kappa correlations. Sensitivity, specificity, positive and negative predictive values and likelihood ratio's of Singh index were

calculated. Both intra- and interobserver agreements were 0.71 (range, 0.69 to 0.72) on average. Singh index proved highly sensitive for the diagnosis of osteopenia at the proximal femur (91%) and spine (90%), whereas the specificity of Singh index for identifying of osteoporosis at the femoral neck (93%) and spine (91%) was higher than sensitivity. Predictive values for osteoporosis at the proximal femur and spine were acceptable and positive likelihood ratios of Singh index for osteopenia and osteoporosis at the proximal femur were 2.4 and 10.1, respectively. Singh index can identify osteoporosis with a high specificity in patients with rheumatoid arthritis. However, the patients who are graded as osteopenia by the Singh index should undergo further evaluation with dual energy X-ray absorptiometry.

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Introduction

Osteoporosis occurs more frequently in patients with rheumatoid arthritis (RA) than in healthy individuals [1, 2]. It is an extra-articular complication of RA and associated with disease activity, mobility of the patient and treatment by corticosteroids as well as disease-modifying antirheumatic drugs [3]. The gold standard for the diagnosis of osteoporosis is the measurement of bone mineral density [4, 5]. Despite several non-invasive methods, dual-energy X-ray absorptiometry (DXA) is the most accepted and reference method to diagnose osteoporosis [5–9]. However, its clinical usage is limited because this method is expensive, time consuming and not available in every center [5, 10].

Singh index (SI) is a radiographic evaluation method for the assessment of osteoporosis. It is based on the radiological appearance of the trabecular bone structure in the proximal femur [11]. According to this classification, six grades of trabecular pattern has been determined with grade 1 representing severe osteoporosis and grade 6 describing a normal bone. Although this is a simple and an inexpensive method for the determination of bone quality, several studies have been reported with controversial results about its predictive value [10, 12–19].

Whereas DXA may not be available or economical for routine use and mass screening, plain films can be obtained in most cases during the routine follow-up in outpatient clinics. Therefore, SI may be used as a screening tool to help clinicians in identifying which patients are at increased risk of osteoporosis. To our knowledge, none of the previous studies in the English language medical literature has addressed the clinical value of SI in patients with RA. The aim of the present study was to evaluate the accuracy of SI for the determination of osteopenia and osteoporosis and compare the results to DXA measurements in patients with RA.

Material and methods

We retrospectively evaluated the patients who were selected from rheumatology outpatient clinic between September 2009 and January 2010. Patients who had been diagnosed with rheumatoid arthritis and treated with corticosteroids for at least 1 year were included in the study. The exclusion criteria were history of previous operation of the pelvis due to osteoarthritis or fracture and other associated inflammatory diseases known to affect the skeletal system. Eighteen patients were excluded. The study consisted of 50 (39 women, 11 men) patients with a mean age of 53.3 (range, 27–83) years. All patients signed an informed consent form and the study was approved by the institutional review board.

Digital antero-posterior pelvic radiographs (Axiom Multix M; Siemens AG, Erlangen, Germany) in supine position were obtained for assessment of SI which was evaluated by three observers. These were two orthopaedic surgeons (A and B) and one rheumatologist (C) with 5 to 10 years experience. According to the Singh classification, grade 6 represented normal bone density and grade 1 reflected severe osteoporosis. The evaluation scheme of SI (Fig. 1) was handed out to all

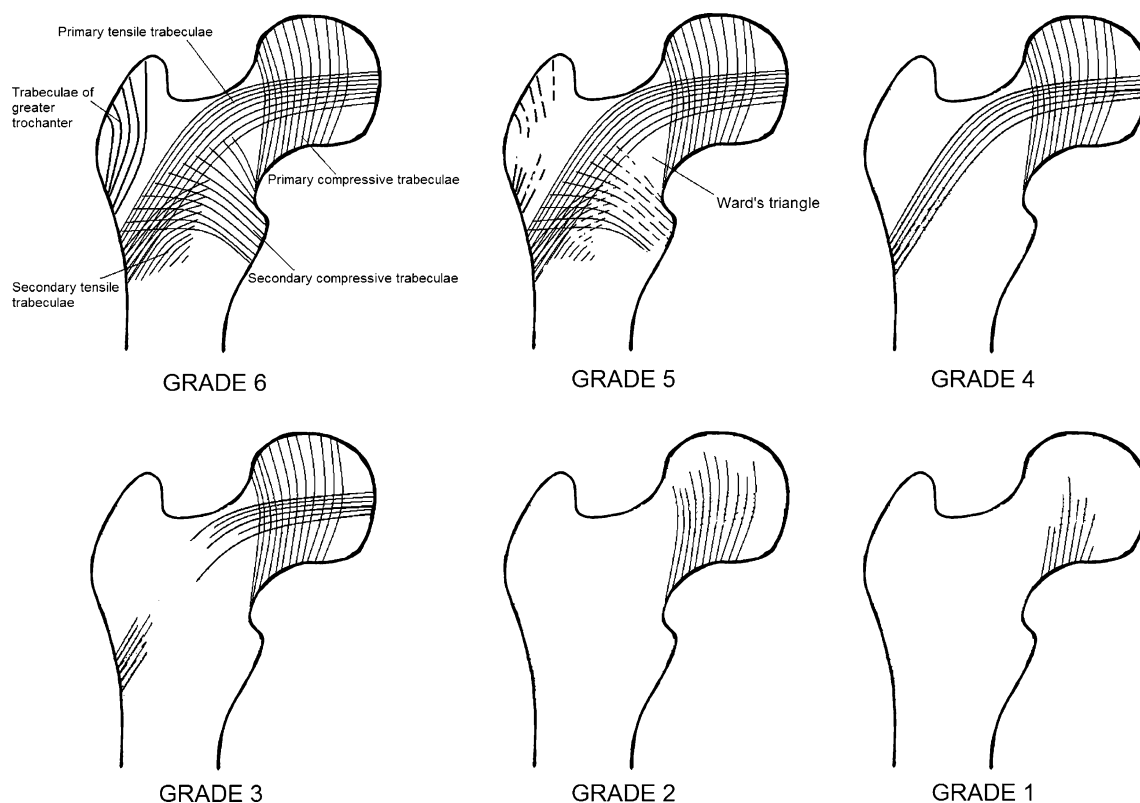


Fig. 1 Cancellous bone of the femur is composed of two distinct systems of trabeculae: compressive and tensile. Five groups of trabeculae have been identified. *Grade 6*: all normal trabecular groups are visible. The proximal femur is completely filled with cancellous bone. *Grade 5*: primary tensile and compressive trabeculae are accentuated. Ward's triangle appears prominent. *Grade 4*: primary

tensile trabeculae are markedly reduced but can still be traced from the lateral cortex to the upper part of the femoral neck. *Grade 3*: continuity of the primary tensile trabeculae is broken opposite the greater trochanter. *Grade 2*: all trabeculae except the primary compressive are nearly reduced. *Grade 1*: even the primary compressive trabeculae are markedly reduced

Table 1 Basic patients characteristics and DXA measurement results (ranges are given in paranthesis)

	Mean	SD
Patients' age (years)	53.3 (27–83)	12.19
Duration of the disease (years)	11.87 (1–38)	9.8
Corticosteroid dosage (mg/day)	5.85 (2–16)	2.79
Duration of corticosteroid treatment (months)	76.8 (12–360)	82.61
DXA <i>T</i> score spine	−1.22 (−5.3 to +2.9)	1.77
DXA <i>T</i> score left femur	−1.18 (−4.4 to +2.2)	1.45

DXA dual-energy X-ray absorptiometry, SD standard deviation

observers prior to evaluation and a short introduction was given to each observer by the corresponding author. Each observer evaluated the series of anonymized radiographs independently and was blinded from the patients' age and bone mineral density measurements. In addition, none of the observers was involved in treatment of the patients recruited. Left proximal femur was assessed in all radiographs. The radiographs were arranged in random order by one author who did not evaluate the radiographs and all observers re-evaluated these radiographs after a period of 2 weeks to determine intraobserver agreement. In the mean time, the observers did not evaluate SI for other radiographs in order to minimize learning effects.

The patients also were evaluated by DXA system (Lunar DPX-L; GE Medical Systems, Madison, WI), which measured the bone mineral density of the left proximal femur and the spine. The mean value of the femoral neck was evaluated for the proximal femur and the data were reported as the *T* score. The patients were classified according to World Health Organization (WHO) [7] guidelines as normal (*T* score above −1 standard deviation), osteopenic (*T* score between −1 and −2.5 standard deviation) or osteoporotic (*T* score less than −2.5 standard deviation).

The statistical analyses were performed using the NCSS 2007 program (NCSS Statistical Software, Kaysville, UT, USA). Descriptive statistics (mean and standard deviation) were computed. Intra- and interobserver agreements of SI were evaluated by weighted Cohen's kappa statistics. Kappa values were classified using the rating scale introduced by Landis and Koch [20]. According to this rating scale, values between 0 and 0.20 were accepted as

slight; values between 0.21 and 0.40 were accepted as fair; values between 0.41 and 0.60 were accepted as moderate; values between 0.61 and 0.80 were accepted as substantial and values between 0.81 and 1.0 were accepted as perfect agreements. We also compared the DXA results to the results of the Singh classification, using the results of the observer with the highest intraobserver agreement. To determine the sensitivity and specificity of SI, we rearranged the results of SI into three grades as following: grades 6 and 5 as normal, grades 4 and 3 as osteopenia and grades 2 and 1 as osteoporosis. Then, we compared these results to both spine and femoral neck *T* scores separately. In addition, the positive and negative predictive values (the proportion of patients with positive and negative test results who are correctly diagnosed) and positive and negative likelihood ratios (which describe how much the odds of the disease increase or decrease when a test is positive or negative) of SI measurements were determined.

Results

The baseline characteristics of the patients are shown in Table 1. The mean *T* scores of the proximal femur and spine measured by DXA were −1.18 and −1.22, respectively. The average of the first and second measurements of SI for each observer were 3.7 (A), 3.8 (B) and 3.8 (C) (Table 2). Nine (18%) of the 50 patients were classified identically by all observers for both measurements. After grouping the six grades of SI into three as normal, osteopenia and osteoporosis, the number of identically classified patients was 25 (50%).

Table 2 The average SI measurements for each observer and kappa values for intra- and interobserver agreements of SI

Observers	Average SI measurements		Kappa value	
	First	Second	Intraobserver	Interobserver
A	3.8	3.5	0.71	
B	3.9	3.6	0.70	
C	3.9	3.7	0.72	
AB				0.72
AC				0.72
BC				0.69

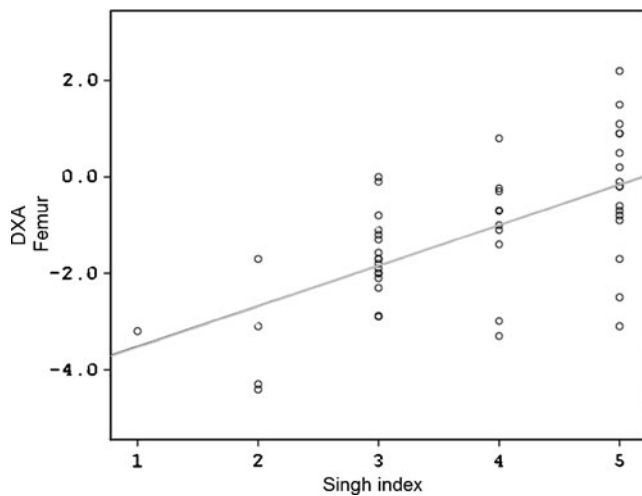


Fig. 2 Scatter diagram shows the relationship between SI and *T* scores at the proximal femur measured by DXA. The grey line gives the expected relationship

The kappa values for intra- and interobserver agreement of SI ranged from 0.70 to 0.72 (mean 0.71) and 0.69 to 0.72 (mean 0.71), respectively (Table 2). Both results showed substantial agreement.

We found acceptable correlation between the SI and DXA measurements (Fig. 2). SI had high sensitivity for the diagnosis of osteopenia at the proximal femur (91%) and spine (90%), whereas the specificity of SI for identifying osteoporosis at the femoral neck (93%) and spine (91%) was higher than sensitivity. Predictive values for osteoporosis at the proximal femur and spine were acceptable. Positive likelihood ratios of SI for osteopenia and osteoporosis at the proximal femur were 2.43 and 10.12, respectively (Table 3). According to these results, SI could successfully determine the patients with osteoporosis.

Discussion

The clinical usage of SI has been limited because there are many controversial results in the literature about its objectivity. Some studies reported that this method might not be as reliable or accurate as originally proposed for

assessing osteoporosis [12, 17–19, 21]. Koot et al. [12] found kappa values of 0.15 to 0.54 and 0.63 to 0.88 for inter- and intraobserver agreement in a study consisted of conventional radiographs of 80 patients. Hauschild et al. [19] found kappa values of 0.02 to 0.75 (mean 0.19) and 0.20 to 0.89 (mean 0.43) for inter- and intraobserver agreement in a study consisted of digital pelvic radiographs of 100 patients. Both studies showed reasonable intra-observer agreement, whereas the interobserver agreement was poor. Therefore, it was concluded in these studies that the SI had no value in assessing the grade of osteoporosis.

On the contrary, other studies showed that SI provided a reliable estimate of osteoporosis and mechanical bone quality of the proximal femur [10, 15, 16, 22]. Cooper et al. [16] performed a study in which the weight and volume of excised femoral heads were compared to radiographic indices of bone quality. They reported that SI of the proximal femur and calcar width were correlated with bone mineral density of the femur. In addition, SI was proposed as a valuable and reliable indicator which might reflect structural integrity in trabecular bone [10, 22]. Masud et al. [18] reported a low sensitivity but a relatively high specificity of SI in a population study consisted of 659 patients. They found the kappa value of SI as 0.61 and concluded that the SI was a reproducible tool which might detect differences in bone mass between populations or subgroups within populations.

Our study showed substantial reliability level of kappa values for both intraobserver (mean 0.71) and interobserver (mean 0.71) agreements with a high sensitivity for the diagnosis of osteopenia and high specificity for the diagnosis of osteoporosis. According to these results, we conclude that SI can be used as a screening tool to help clinicians for identifying which patients are at increased risk of osteoporosis.

Generally, radiographs have been considered less valuable in the assessment of bone mineral density because it is believed that 30–50% bone loss must be present to be detected on plain radiographs [8]. Therefore, it is difficult to conclude that the predictive value of SI for osteoporosis is equal to that obtained with DXA. On the other hand, whereas DXA may not be available or economical for routine use, plain radiographs can be obtained in most cases during the routine

Table 3 Sensitivity, specificity, positive and negative predictive values and likelihood ratio of SI for the diagnosis of osteopenia and osteoporosis detected by DXA

		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR(+) (%)	LR(–) (%)
Osteopenia	Femur	91	62	62	91	2.43	0.14
	Spine	90	61	50	94	2.32	0.16
Osteoporosis	Femur	71	93	80	89	10.12	0.32
	Spine	74	91	78	89	8.11	0.29

PPV positive predictive value, NPV negative predictive value, LR(+) positive likelihood ratio, LR(–) negative likelihood ratio)

follow-up in outpatient clinics. In addition, DXA requires skilled and well-trained technical staff in order to acquire reliable and valid measurements. Moreover, physicians need experience in the interpretation of measurement results to avoid potential pitfalls [23].

Practical, rapid, simple and low-cost measurement methods of bone mineral density are needed for clinical decision making. SI can be used as an alternative method for the evaluation of mechanical quality of cancellous bone if densitometry is not available. SI can identify osteoporosis with high specificity in patients with rheumatoid arthritis. However, the patients who are graded as osteopenia by SI should undergo further evaluation with DXA. If DXA measurements at spine and femur differ, the lower value should be used as suggested by most national guidelines on the treatment of osteoporosis. In this situation, Singh classification should be referred to femoral measurements.

There are several limitations to this study. The first limitation is retrospective character of the study. However, we believe that it has few effects on the results. The second limitation is relatively small number of patients, which could effect the spread of the data. In addition, the number of patients who was rated as osteoporotic according to WHO criteria (10 for femur and 15 for spine) was also low. Although SI evaluation seems to be sufficiently reliable to predict osteoporosis in RA patients, additional studies with a large number of patients are needed to validate the value of SI in this patient population.

Conclusion

SI is a practical and reproducible method for the evaluation of osteoporosis and can help clinicians to identify which patient with rheumatoid arthritis is at increased risk for osteoporosis.

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Disclosures None.

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