SYSTEMATIC REVIEW

Diagnostic Value of Radiographic Singh Index Compared to Dual-Energy X-Ray Absorptiometry Scan in Diagnosing Osteoporosis: A Systematic Review

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Abstract

Objectives: Since various medications can control the rate of fractures and subsequent complications of osteoporosis, the early detection of the disease is crucial. This systematic study aimed to compare the diagnostic accuracy of Singh index (SI) with dual-energy X-ray absorptiometry (DEXA) as a benchmark standard for diagnosing osteoporosis.

Methods: The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) were utilized in the current study. A detailed search was carried out using PubMed and Scopus from inception to 30 May 2022. Examining quality of the studies was performed by the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2).

Results: A total of 22 studies were included. In general, 50% of the studies considered SI a poor screening tool for detecting osteoporosis due to a negligible inter-observer agreement between SI and DEXA or a poor correlation of SI with the bone mineral density (BMD) category or DEXA T-score. A moderate inter-observer agreement was reported for SI in 5 (55.6%) studies. Among the studies assessing the sensitivity and specificity of SI compared to DEXA (n=13), six studies estimated a low sensitivity for SI.

Conclusion: While there is supporting evidence indicating the potential usefulness of SI for predicting femoral neck fractures in individuals with suspected osteoporosis, numerous studies challenge its reliability and diagnostic value as a screening tool for identifying femoral neck osteoporosis. Further primary studies are required to verify the effectiveness of the SI index in identifying populations at risk of osteoporosis.

Level of evidence: V

Keywords: Bone mineral density, DEXA, Dual-energy x-ray, Osteoporosis, Singh index

Introduction

Osteoporosis is known as a severe health problem that decreases the strength of bone and increases the risk of fractures. It has been estimated that more than half of the population over 50 years suffer from this disease.[1, 2] Compared to men, women are more likely to develop this disease.[3] However, the risk of osteoporosis is equal for the two genders in patients with underlying predisposing conditions related to bone demineralization.[4]

Often, osteoporosis is asymptomatic; accordingly, patients do not show any symptoms until the bone breaks. Low bone mineral density (BMD) and decreased bone strength are two main characteristics of this disease. [5-7] Based on the World Health Organization (WHO), a BMD of 2.5 standard deviations ≤ of the mean of BMD in young people is considered osteoporosis.[8] the most important problem related to osteoporosis is its asymptomatic nature; it can progress painlessly until a bone breaks. Due to chronic pain, deformity, and disability as a result of hip and spine fractures, some patients with fractures in these regions never return to their everyday lives. Mortality more

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significant than expected has been reported five years after a fracture in osteoporotic patients with hip or clinical vertebral fractures.[9] These findings highlight the importance of the diagnostic value of BMD testing as the best predictor of fracture risk for detecting patients at high risk of fracture.[10]

Since numerous medication treatments can control the rate of fractures and subsequent complications of osteoporosis, the early detection of the disease is highly important. Radiologic imaging techniques are considered the central part of the early diagnosis of osteoporosis. There are various approaches to measure bone mass and femoral neck trabecular morphology, including radiographic single-energy X-ray absorptiometry, dual-energy X-ray absorptiometry (DEXA), quantitative computed tomography, and quantitative ultrasound, which are used as the main techniques to diagnose osteoporosis. Among these methods, DEXA with a relatively low radiation dose has been introduced as an objective approach for measuring BMD and predicting fracture risk.[11] Two various kilovoltage peaks (i.e., 30-50 and >70 keV) are used in the X-ray approach to evaluate BMD in a definite area of bone, which can provide standard deviations compared to the general population. The main limitation of the DEXA scan is its high cost, which makes it unaffordable, especially in developing countries.[12]

A qualitative evaluation of osteoporosis is possible by plain radiographs, in which reduced bone radiodensity, trabecular loss, and thickening of residual trabeculae can be evaluated. Nevertheless, radiograph indicators are only applicable in cases with advanced bone loss. Availability and inexpensiveness are the main reasons for using these indicators as a screening method and predictor of osteoporosis. The Singh index (SI) is a conventional approach to assess bone density, especially osteoporosis, to describe trabecular patterns in the proximal femur. The SI index is a classical diagnostic classification for estimating the degree of osteoporosis in daily practice. Singh et al. introduced a method for assessing the trabecular bone pattern in the proximal femur for the first time. In this approach, the degree of trabecular bone loss from the proximal femur is described on a scale from grade 1 to 6, indicating osteoporosis severity. In grade 6, all the major trabecular systems are visible, while only the primary compressive trabeculae can be observed in grade 1.[13] the accuracy of the SI has been confirmed by Koot et al. by evaluating the reproducibility of the index and comparing it with the BMD. The results showed that the intra-observer agreement of SI was strong (kappa values between 0.63 and 0.88), while it's inter-observer agreement was unacceptable (kappa values between 0.15 and 0.54). The SI has been used in various ways, and different observers asserted that the intra-observer agreement has been less effective than the inter-observer agreement in assessing the accuracy of SI.[14]

However, some evidence has rejected the role of SI in diagnosing osteoporosis. The SI lacks the required diagnostic accuracy in predicting skeletal bone mass and is remarkably inferior to photon absorptiometry approaches.[14, 15] this systematic study aimed to evaluate the diagnostic accuracy of SI compared to DEXA as a benchmark standard for diagnosing osteoporosis.

Materials and Methods

The Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA) guideline were applied in this systematic review.

Inclusion and exclusion criteria

This study included all published studies comparing the diagnostic accuracy of SI with DEXA in patients with osteoporosis from inception to 30 May 2022. The participants-Intervention-Comparison-Outcome model was used to determine the eligibility criteria.[16] all prospective and retrospective studies with a descriptive nature were entered into this study.

Inclusion criteria were 1) publication in the English language, 2) conduction on human samples, and 3) provision of a clear description of methodological techniques. On the other hand, exclusion criteria were 1) animal or *in vitro* studies, 2) editorial letters, 3) case reports or case series, 4) qualitative narratives, and systematic review studies. Furthermore, comparative studies focusing only on DEXA or SI were removed from the study.

Literature search

To find the related studies, a detailed search was carried out on the electronic databases, including PubMed and Scopus. In addition, manual research was conducted to find the studies that might not have been found in these databases.

The authors also searched grey literature, such as conference papers, technical reports, theses, and dissertations in databases. The search process was performed using the following terms: "Radiographic Singh index", "Radiographic methods", "Dual-energy X-ray", and "DEXA" in combination with "Osteoporosis" and "Bone mineral density". Two trained researchers performed all search processes.

Data extraction and study design

Two researchers performed the search process independently regarding the predetermined keywords. The titles and abstracts of all studies were reviewed during the search process, and the unrelated studies were excluded based on the eligibility criteria. The final screening was performed in the next step by reviewing the remained studies.

Data included were extracted by two researchers who were continuously in contact. Finally, the obtained results, including the type of study, demographic information, fracture, number of observers, sensitivity, specificity, Kappa coefficient between observers, and outcome were recorded in a researcher-made checklist.

Quality assessment

Two reviewers independently evaluated the quality of all included studies utilizing the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2). Any discrepancy in the evaluation was resolved by the third author.

Four domains were reported for the original QUADAS-2 as follows: patient selection, index test(s), reference standard, and flow and timing.

Results

Results of the Literature Search

In the first search of the databases, 1,096 records were found, of which 794 studies were screened for title and abstracts after the removal of duplicates. Of the remaining 48 studies, we removed articles published in other languages, except for English (n=5), irrelevant articles (n=3), books (n=5), editorial letters or short communications (n=6), qualitative and narrative articles, or systematic reviews (n=7). Finally, 22 studies remained and were entered into this review [Figure 1].

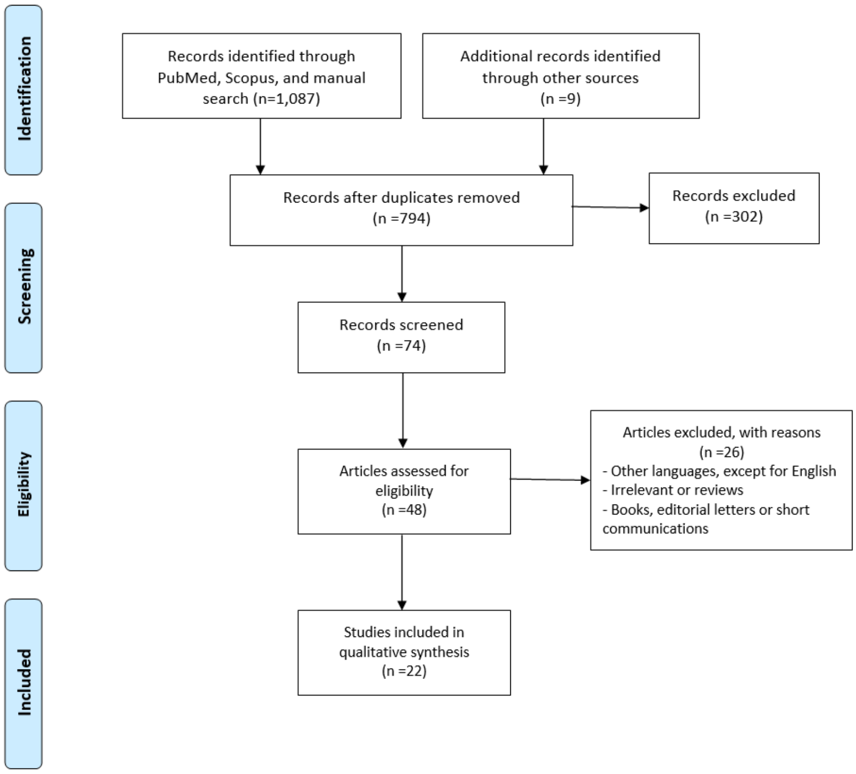

Figure 1. Study flow diagram of literature search

General characteristics of the included studies

In general, 86.3% (n=19) and 13.6% (n=3) of the entered studies were retrospective and prospective, respectively. [15, 17, 18] Characteristics of the included studies are presented in [Table 1]. The majority of studies were conducted in Asia (54.5%), among which 4 (18%) studies were performed in India, 3 (13.6%) in the Middle East (Turkey=1, Iran=1, Pakistan=1), 2 (9%) in the Far East (South Korea=1, China=1), and 2 (9%) in Southeast Asian (Thailand=1, Indonesian=1). Furthermore, 8 (36.3%) studies were performed in Europa (Germany=2, Austria=1, UK=1, Sweden=1, Netherlands=1, Israel=1, Romania=1) and 2 (9%) in the USA.

The entered studies were performed on 2,556 cases. Five (22.7%) studies were conducted on patients older than 55 years. In the other studies, the mean age was between 52.8 and 78 years ranging between 20 and 84.

The female: male ratio was 9:1; however, it was not specified in three studies. [14, 19, 20] Ten (45.4%) studies were conducted only on women. [15, 21-29]

Diagnostic accuracy of SI compared to DEXA

In general, 11 (50%) studies considered SI as a poor screening tool for detecting osteoporosis due to a negligible inter-observer agreement between SI and DEXA [18, 23, 30] or poor correlation between SI and BMD category or DEXA T-score.[14, 15, 17, 19, 21, 22, 27, 31] On the other hand, 6 (27.2%) studies showed a relatively good correlation between SI and BMD/DXA.[20, 24, 25, 29, 32, 33] The other studies presented inconclusive results on the prognostic value of SI .[26, 28, 34-36] Of 22 entered studies, intra-observer reproducibility or inter-observer reproducibility of SI had been assessed in 9 (40.9%) studies. Among them, a relatively good inter-observer agreement for SI was reported by 5 (55.6%) studies; [17, 19, 31, 32, 36] while 3 (33%) studies showed a low inter-observer agreement.[18, 30, 35] Additionally, a relatively good intra-observer agreement was observed in 4 (44.4%) studies ,[14, 32, 34, 35] whereas 2 (22.2%) studies showed a low inter-observer agreement.[14, 30]

Among studies assessing the sensitivity and specificity of SI compared to DEXA (n=13), six studies estimated a low sensitivity for SI, while seven studies indicated a high sensitivity for the index. The specificity was identified as low, moderate, and high in four, one, and eight studies, respectively. Among six studies assessing positive prediction values, three, one, and two showed low, moderate, and high positive prediction values, respectively. Negative prediction values were low, moderate, and high in one, two, and three studies, respectively. The sensitivity and specificity of SI were assessed in 13 (59%) studies. Among them, the sensitivity and specificity of SI were in the ranges of 29-96% and 2-97%, respectively. Positive prediction values of SI ranged from 25% to 88%, and its prediction values ranged from 50%-94%.

Table 1. Data extracted from each included article in this review

Author (years) Reference & Country	Type of study	Sample Size	Age mean (year)	Female/ male ratio	Assessed area	Fracture	Approach	Sensitivity	Specificity	Positive prediction values	Negative prediction values	Kappa coefficient between observers	Outcome
Hübsch (1992) [1] Austria	Prospective comparative study	156 (116 patients and 12 cadaver specimens)	58.5	118/38	Right and left proximal femur (Femoral neck, Ward's triangle, and the trochanteric region)	No fracture	Data were examined by two observers	--	--	--	--	Good agreement between two observers in SI	The applicability of the SI was rejected to predict the BMD Of the proximal femur.
Masud et al. (1995) [2] UK	Retrospective	659	52.8 45-70	659/0	Trochanteric and Intertrochanteric regions, femoral neck, Ward's region, Lumbar spine, and total hip	No fracture	Data were examined by two observers	35.1%	90%	--	--	Intra-observer reproducibility: 0.64 Inter-observer reproducibility 0.61	A correlation was reported between SI with lumbar spine BMD and the femoral neck BMD.
Karlsson et al. (1996) [3] Sweden	Retrospective	125	78	92/33	Hip-axis length, width of collum femoris, and femoral shaft and neck-shaft angle	Consecutive hip fracture	Single observer	--	--	--	--	--	A good correlation was found between SI and BMD/DEXA.
Koot et al. (1996) [4] Netherland	Retrospective	72	>55	Unspecified	The femoral neck or trochanteric	Fractures of the femoral neck or trochanteric region	Radiographs were examined by six observers	--	--	--	--	Inter-observer: 0.15 to 0.54 Intra-observer: 0.63 to 0.88	No correlation was reported between SI and BMD.
Chung et al. (1999) [5] South Korea	Retrospective	60	--	--	Proximal femur	No fracture	Data were examined by six observers	--	--	--	--	Inter-observer agreement: 0.45 (moderate)	A low clinical value was reported for SI.
Anburajan et al. (2001) [6] India	Retrospective	45	>65	45/0	Femoral neck, trochanter, and Ward's triangle	No fracture	--	82%	94%	88%	91%	--	A good correlation was reported between SI and DXA results, while the correlation of SI with trochanteric BMD and T-scores was low.
Soontrapa et al (2005) [7] Thailand	Prospective	130	72.5	130/0	Left hip joint	No fracture	--	SI≤4: 58% SI≤3:29%	SI≤4: 55% SI≤3: 92%	SI≤4: 29% SI≤3:43 %	SI≤4: 81% SI≤3:78%	--	It was reported that SI was a poor screening tool for detecting femoral neck osteoporosis.
Trijoto et al. (2006) [8] Indonesian	Retrospective	64 post-menopausal women	--	64/0	Femoral neck and lumbal	No fracture	--	Osteoporosis: 91.4% Osteopenia:66.7%	Osteoporosis: 89.6 % Osteopenia:89.1%	Osteoporosis: 91.4% Osteopenia:70.6%	75%	--	Due to the high sensitivity and moderate specificity of the DEXA test, determining osteoporosis by SI needs to be confirmed by this test.
Sah et al. (2007) [9] USA	Retrospective	32 postmenopausal Caucasian osteoarthritic women	67 (47 to 90)	32/0	Femoral neck, spine, and greater trochanter	Hip arthroplasty	--	85%	79%	--	--	--	No correlation was reported between SI and the DEXA scan.

TABLE 1. Continued

Memon et al. (2007) [10] USA	Retrospective	98 Post-menopausal females r	59	98/0	Femur/pelvis	No fracture	--	SI≤4: 44% SI≤3:55%	SI≤4: 97% SI≤3: 84%	--	--	--	SI had low sensitivity and high specificity.
Hauschild et al. (2009) [11] Germany	Retrospective	100	69.43	79/21	Femoral neck and trochanteric region	Previous fracture of left femur in 7 cases	Data were examined five independent observers	83.3%	24.2 %	--	--	Intra-observer agreement: 0.43 Inter-observer agreement: 0.199	There were moderate intra-observer agreements and poor inter-observer agreements.
Karabulut et al. (2010) [12] Turkey	Retrospective	47	63.21	47/0	Without previous hip fractures	Previous hip fractures or hip surgery	Data were assessed by five observer radiologist, physical therapist, and anatomists	--	--	--	--	--	A correlation was observed between SI and BMD.
Salamat et al. (2010) [13] Iran	Prospective	72	>50	68/4	Femoral neck and trochanteric	Fracture of the femoral neck or trochanteric	Three separate sessions by three experienced orthopedists,	96%	2%	38%	50%	Inter- observer agreement 1 and 2: 0.01 1 and 3: 0.07 2 and 3: 0.09	A negligible inter-observer agreement was reported.
Shankar et al. (2011) [14] India	Retrospective	50 Post-menopausal:39	20-84	50/0	Trabecular microarchitecture of the proximal femur	No fracture	An experienced radiologist	--	--	--	--	--	A correlation was found between SI grade and BMD.
Bes Cemal et al. (2012) [15] Turkey	Retrospective	50	53.3(27–83)	39/11	T scores of the spine and left proximal femur	Operation of the pelvis due to osteoarthritis or fracture	Three observers	Proximal femur (91%) Femoral neck (90%)	Proximal femur (93%) Femoral neck (91%)	50%-80%	89%-94%	Inter-observer agreements were 0.71 (range, 0.69 to 0.72)	A high specificity was reported for SI in predicting osteoporosis. The results of SI were not the same as those obtained with DEXA.
Kapishnikov et al (2013) [16] Israel	Retrospective	42	57.4	--	Right femur	No fracture	Three experienced radiologists	--	--	--	--	--	A correlation was found between SI and BMD.
Klatte et al. (2015) [17] Germany	Retrospective	128 human cadaveric femora of 64 patients	66.7 (24–89)	35/29	Trochanteric region, femoral neck, Ward's region, and total region of each femur	No fracture	Three independent observers	45.2 %	92.3 %	--	--	Inter-rater reliability : 0.629 CI: 0.439- 0.763	A poor correlation was reported between SI and DXA-BMD.
Qadir et al. (2016) [18] Pakistan	Prospective	120 post-menopausal women	62.91	120/0	Proximal femur	Prior fracture after age 50	--	--	--	--	--	--	A slight agreement was reported between SI and DEXA.
Alexa et al. (2017) [19] Romania	Retrospective	129	<65: 31 >65: 98	70/59	Antero-posterior plain radiographies of proximal femurs	No fracture	Four observers (orthopedists) three months reexamined	--	--	--	--	Inter-observer: 0.15. Intra- observer: 0.19.	There was a slight inter-observer agreement.
Liu et al (2017) [20] China	Retrospective	261	74	261/0	Hip joint with full length femur in anterior posterior and Lateral views	Hip fracture in 87 cases	Single observer	42.5%	88.2 %	--	--	--	A combination of OSTA with SI could be used to screen hip fracture risk in osteoporosis.
Mir et al. (2021) [21] India	Retrospective	100	>50	100/0	Right or left hip joint of proximal femur	No fracture	Radiographs were assessed by an experienced observer	Not adequate	Not adequate	--	--	--	SI grade showed no correlation with BMD category and DEXA T-score.
Burli et al. (2021) [22] India	Retrospective	80	>50	53/27	Lumbar spine followed by Bilateral hip joint	No fracture	Single observer	100%	>74 %	58%	100%	Intra-observer reliability: (0.59)	A moderate level of agreement was reported between SI and the DEXA scan.

Quality assessment of the studies

Index scores based on the QUADAS-2 are illustrated in [Table 2]. As indicated, risk of bias and applicability concerns were assessed as follows: low risk/concern ("+" signs in green color), high risk/concern ("-" signs in red color), and unknown risk/concern ("?" signs in yellow color).

It should be noted that studies with inadequate data were not considered for quality assessment. As shown by the results, two articles were assessed as low within all domains of risk of bias and applicability concerns. Moreover, a high risk of bias and especially high applicability concerns were found in the domain of patient selection among the included studies. Only one study gained a high risk of bias in the flow and timing domain.

In total, the majority of the studies (n=13) had an unclear risk of bias in the domain of reference standards. Applicability concerns were most predominant in the patient selection domain, including eight studies with unclear and four studies with high applicability concerns, implicating the use of constrained populations (e.g., only included women or post-menopausal women). Applicability concerns were recognized as low across the studies for the reference standard except for one study that was unclear [Table 2 and Figure 2].

Table 2. Study quality assessment

First author, year	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Alexa, 2017	+	+	?	+	+	+	+
Bes, 2011	+	+	+	+	?	+	+
Burli, 2020	+	+	?	+	+	+	+
Hauschild, 2019	+	+	+	+	-	+	+
HÜBSCH, 1992	-	?	?	+	?	+	+
Karabulut, 2010	+	+	?	+	?	+	+
Klatte, 2015	+	+	+	+	+	+	+
Koot, 1996	+	+	?	-	-	+	?
Liu, 2017	-	?	?	+	?	+	+
Masud, 1996	+	+	+	+	+	+	+
Mir, 2021	+	-	?	+	+	?	+
Qadir, 2016	+	?	?	+	?	+	+
Sah, 2007	+	+	?	+	?	+	+
Salamat, 2010	+	?	?	+	-	+	+
Shankar, 2011	+	?	?	+	?	+	+
Soontrapa, 2005	+	+	?	+	?	+	+
Trijoto, 2005	+	?	?	+	-	+	+

- High Risk of Bias ? Unclear Risk of Bias + Low Risk of Bias

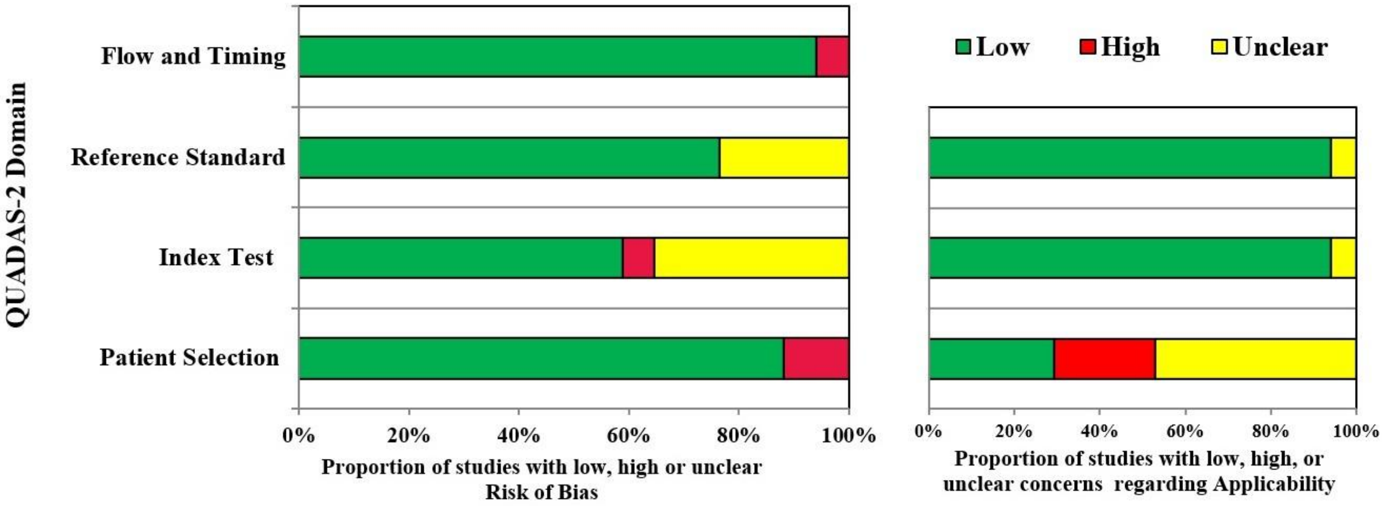

Figure 2. Quality assessment of the study

Discussion

This systematic review compared the diagnostic accuracy of SI with the gold standard of BMD assessment (DEXA) in patients with osteoporosis. Overall, 50% of the studies considered SI a poor screening tool for detecting osteoporosis due to a negligible inter-observer agreement between SI and DEXA or a poor correlation of SI with the BMD category or DEXA T-score. Although SI has been confirmed as an appropriate approach for diagnosing osteoporosis, previous evidence has shown that the SI index has poor reliability and diagnostic value in screening femoral neck osteoporosis. [14,15] The main problems attributed to the employment of the SI in diagnosing osteoporosis are the inability to clearly show the trabeculae by radiographs because of the soft tissue shadow in overweight patients and poor quality of radiographs due to technical problems, including poor positioning of the issues and insufficient image resolution.[15] Evidence has shown that the sensitivity of plain radiographs is very low; accordingly, about 30-40% of demineralization occurs before the appearance of changes on a plain radiograph.[32]

Correlation of SI with DEXA

In general, half of the included studies considered SI a poor screening tool for detecting osteoporosis,[14,15,17-19,21-23,27,30,31] while 27.2% indicated a good correlation between SI and DEXA findings.[30,24,25,29,32,33] This discrepancy between studies may be due to primary differentiation, including sample characteristics. For example, the human cadaveric femora were also assessed in some studies. Several studies were conducted only on women older than 55. Hip fractures were reported in some studies, whereas others were carried out on subjects without fractures. Moreover, the same areas were not evaluated in different studies.

There were some challenges regarding the reliability of the predictive value of SI in establishing osteoporosis. Some evidence has shown an excellent diagnostic value of SI in predicting hip fractures in the femoral neck area, trochanteric region width, and thickness of the femoral cortex.[37, 38] The reliability of SI and cortical thickness index (CTI) were compared with DEXA to diagnose osteoporosis in a study by Burli et al., which indicated a strong correlation between CTI and DEXA scan T-score.[34] A good correlation was also found between SI and BMD/DEXA in a study by Karlsson et al.[33] In addition, Masud et al. reported a correlation between SI and DEXA in the BMD of the femoral neck, areas of the proximal femur, and the lumbar spine.[32] A correlation was reported between total hip BMD and SI in another study conducted by Anburajan et al. in India.[29] Shankar et al. showed that the percentage decrease of femur neck BMD was statistically similar with both DEXA and SI in women with osteoporosis.[24] However, inconsistent results in similar studies could be attributed to the geographical distinctions and different characteristics of patients, including mean age or having hip fractures.[27, 39]

The applicability of SI to predict the BMD of the proximal femur has been rejected by Hübsch et al.[17] Mir et al. found that SI grade did not correlate with BMD category, absolute DEXA BMD value, and DEXA T-score.[21] Based on a study by Sah et al., no correlation was found between SI and DEXA scan,[27] while James et al. introduced SI as a reliable tool for screening osteoporosis.[40] Meanwhile, in a study by Gupta et al., SI was significantly correlated with the DEXA scan.[41] However, these two recent studies were not included in this review, since the SI results were not compared with that of DEXA findings in terms of reliability. The differences in the results of various studies might be due to the various types of radiography. In some studies, clearer X-ray films were used, whereas, in conventional radiographs, fat overlap might musk the trabecular pattern. Furthermore, we should observe the possibility of observer bias due to a single observer in the studies, as mentioned earlier.

Although the predicted value of SI has been confirmed in the diagnosis of fractured neck femur in subjects suspected of osteoporosis,[13] there are multiple evidence rejecting the reliability and diagnostic value of SI in screening femoral neck osteoporosis.[14, 15, 42, 43] To a large extent, the Singh categories' accuracy depends on the physician's experience or the radiologist. Moreover, the index classification is complicated because of the minimal differences between its classes. Due to the subjectivity of SI, which can include a large number of categories, this approach could not be used as a valuable tool for the prognosis of osteoporosis except in combination with other methods of screening.[22, 44] Some evidence has suggested the employment of digital radiography to decrease the subjectivity of the index.[35] In a study by Liu et al., a better diagnostic value was reported for SI combined with the Osteoporosis Self-Assessment Tool for Asians (OSTA) and BMD of the lumbar spine for screening hip fracture risk compared to SI alone. These results were valid for OSTA alone.[22] these study results are valuable since both SI and OSTA are simple, quick, and inexpensive tools. Therefore, physicians can use the combination of these tools in countries and regions where DEXA is highly expensive and unavailable.

Inter-observer and intra-observer agreement in SI

Most studies assessing inter- and intra-observer agreement generally showed an acceptable inter-and intra-observer agreement for SI. Salamat et al. compared SI and BMD measurements using DEXA. A total of 72 subjects who were suspected of having osteoporosis were examined, and the evaluations were performed by three orthopedists. The study found a negligible inter-observer agreement, indicating a lack of consensus. They concluded that SI should not be used for osteoporosis diagnosis due to no correlation between the SI index and bone densitometry. The study also highlighted two primary deficiencies of SI, which included similar SIs in individuals with different BMDs and no inter- and intra-observer agreements.[18]

The reliability of the Singh classification was assessed by Koot et al., who reported an unacceptable inter-observer agreement between SI and DEXA (0.15 to 0.54); however, a remarkable strength was observed in intra-observer agreement (0.63 to 0.88). On the other hand, because each observer used the SI differently, the inter-observer agreement was more important than the intra-observer agreement. Even when the authors rearranged the SI into three grades,[14] the mentioned results should be assessed with caution since only patients with underlying osteoporosis were admitted due to the femoral neck fracture or trochanteric region. Furthermore, the study exclusively included participants aged 55 years or older and concluded that SI is not a reliable tool for identifying osteoporosis due to the low intra-class correlation (r=0.629) between SI and DXA-BMD. They observed a weak correlation between these tools, especially in the neck and trochanteric regions. The maximum correlation between DXA and SI was 0.582, and the correlation of inter-rater reliability was poor for SI.[31]

Another study was conducted by Hauschild et al. on 100 cases in the absence of the DEXA findings. Among five observers, only one was able to reach a significant level. They indicated that the correlation between SI and DEXA findings was not notable, even with the more visibility of trabeculae of the bone by digital radiography.[35] A higher intra-observer agreement was reported in a study by Koot et al., which might be explained by its different study design. In a study by Hauschild et al., all observers re-evaluated the radiographs. Moreover, they reported a poor inter-observer agreement, which was strong among the radiologists and trauma surgeons.[35] In this regard, it is important to recognize the significance of comparable clinical backgrounds when evaluating SI, as well as the subjective nature inherent in this approach.

Singh index's sensitivity, specificity, and prediction values compared to DEXA scan

In the current review, conflicting results were found with regard to the sensitivity, specificity, positive prediction values, and negative predictive values of SI compared to DEXA. These contradictory findings hindered us from favoring one perspective over another and thus prevented us from making a definitive conclusion.

The broad overlap of bone densities between the grades of SI was the most critical limitation of this approach. Masud et al. reported a high specificity (90%) and low sensitivity (35.1%) for SI to diagnose osteoporosis with a criteria osteoporosis of ≤ SI grade 4. An increase in the SI grade led to a decrease in the ratio of cases under the fracture threshold from 100% (SI grade 2) to 16.8% (SI grade 6). They claimed that although the sensitivity of the SI technique would be decreased (11.3%) by changing osteoporosis criteria to ≤ SI grade 3, its specificity would be increased (97.2%).[32] Histologically, SI grade 4 has been determined as the borderline between normal and osteoporotic individuals.[45] Similarly, Masud et al. showed that 62.9% of the patients had a bone density below the fracture threshold in ≤ SI grade 3, 23.6% in SI grades 5 and 6.[32] Likewise, Memon et al. reported high specificity (44% for ≤SI grade 4 and 55% for ≤SI grade 3) and low sensitivity (97% for ≤SI grade 4 and 84% for ≤SI grade 3) for SI in diagnosing osteoporosis.[26]

In some studies, the high sensitivity, specificity, and positive and negative predictive values for SI have introduced SI as an inexpensive instrument for detecting post-menopausal osteoporosis.[27, 29] similarly, the results of a study by Trijoto et al. showed high sensitivity and specificity for SI in diagnosing osteoporosis. Moreover, they found a high positive predictive value for the SI, which means only 8.6% of the cases diagnosed with osteoporosis by SI would be expected by DEXA. However, the sensitivity and specificity of SI in diagnosing osteopenia were moderate, which seems that SI results need to be confirmed by a DEXA test.[28] Nevertheless, in a study by Soontrapa et al., poor sensitivity and positive predictive value were reported for an SI of < 4 or 3. The area under the curve was less than 50%. The angle was nearly perfect diagonal, which indicated that the SI had a low value for the diagnosis of osteoporosis, especially for the femoral neck.[15]

Based on the findings of the study by Salamat et al., a high sensitivity (96%) and poor specificity (25%) in screening were reported for SI. Positive and negative prediction values were estimated at 38% and 50%, respectively. In the mentioned study, grade 3 and lower indicated increasing degrees of osteoporosis.[18]

In a study by Hauschild et al., a poor correlation was reported between BMD and SI (r=0.22), and moderate sensitivity (82.3%) and low specificity (24.2%) were observed for SI in detecting osteoporosis.[35] However, Masud et al. found low sensitivity and high specificity.[32] As a limitation, it should be noted that in a study by Masud et al., the DXA T-score of < -1.0 was considered a pathological BMD. In another study conducted by Klatte et al., a T-score of < -2.5 was selected for the definition of osteoporosis; however, they reported lower values for sensitivity and specificity.[31] The cut-off value should be considered a definition of osteoporosis to assess the sensitivity and specificity of the SI. Nonetheless, the results of the study by Klatte et al. might have been affected by lowering the cut-off level considering osteoporotic in SI 1 and 2, osteopenia in SI 3 and 4, and normal bone in SI 5 and 6.[31]

Bes et al. indicated relatively high sensitivity and specificity for SI in diagnosing osteopenia and osteoporosis. However, these findings were not consistent with DXA results.[36] although they found a high diagnostic value for SI in the diagnosis of osteoporosis, they still needed the subjects diagnosed with osteopenia to undergo further evaluation with DXA. These results were confirmed by Trijoto et al.,[28] however, the retrospective nature of the studies and the low sample size might have affected the spread of the data.

In a study by Liu et al., the Youden index was used; they considered the balance between sensitivity and specificity [area under the curve of >0.75). They showed low sensitivity and reasonable specificity for SI in diagnosing hip fracture; however, it could not be used as an excellent predictive tool, mainly if used alone. Similar results were observed for OSTA. On the other hand, the tool demonstrated a correlation with the mechanical parameters of the trabecular bone in the proximal femur.[22]

Mir et al. showed that the sensitivity and specificity of SI were not adequate indicators for diagnosing osteoporotic patients.[21] In a separate study, Burli et al. compared the reliability of SI and CTI with DEXA for diagnosis of osteoporosis. The cut-off value of CTI anteroposterior and lateral was calculated at 0.43 with a sensitivity of 100% and specificity of > 74%. Moreover, positive and negative predictive values of CTI anteroposterior and lateral were higher than 58% and 100%, respectively. A strong correlation and moderate level of agreement were reported between CTI and DEXA scan T-score.[34]

There have been reports suggesting that the distance between the subject and the X-ray tube, as well as the type of radiograph films, could potentially impact the quality and resolution of images in SI. The SI has no diagnostic value except for high sensitivity for screening. Furthermore, it is recommended to compare the SI with other diagnostic techniques in screening osteoporosis, including quantitative computed tomography and quantitative ultrasonography.

Study limitations

Due to the retrospective nature of most studies, we should cautiously generalize the results. Our study's main limitation was differentiation between studies in terms of sample characteristics and evaluated areas. Therefore, diversity in populations, methodologies, and study designs were sources of heterogeneity between different studies, resulting in the infeasibility of conducting meta-analysis and considerably constraining data pooling.

Conclusion

While there is evidence to suggest that SI can be useful in predicting fractures of the femoral neck in individuals suspected of having osteoporosis, numerous studies contradict its reliability and diagnostic value as a screening tool for femoral neck osteoporosis. Therefore, conducting additional primary studies that address the limitations of previous research could be beneficial in validating the use of the SI index for identifying populations at risk of osteoporosis.

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References

1. Wright N, Saag K, Dawson-Hughes B, Khosla S, Siris E. The impact of the new National Bone Health Alliance (NBHA) diagnostic criteria on the prevalence of osteoporosis in the USA. Osteop Int. 2017; 28(4):1225-32. doi: 10.1007/s00198-016-3865-3.
2. Sarafrazi N, Wambogo EA, Shepherd JA. Osteoporosis or low

bone mass in older adults: United States; 2021.
3. Tu KN, Lie JD, Wan CK, et al. Osteoporosis: a review of treatment options. Pharm Therap. 2018; 43(2):92.
4. Akkawi I, Zmerly H. Osteoporosis: current concepts. Joints. 2018; 6(2):122-7. doi: 10.1055/s-0038-1660790
5. Pouresmaeili F, Kamalidehghan B, Kamarehei M, Goh YM. A comprehensive overview on osteoporosis and its risk factors. Therapeutics and clinical risk management. 2018; 14:2029. doi: 10.2147/TCRM.S138000
6. Bover J, Ureña-Torres P, Torregrosa JV, et al. Osteoporosis, bone mineral density and CKD–MBD complex (I): Diagnostic considerations. Nefrología (English Edition). 2018; 38(5):476-90. doi: 10.1016/j.nefro.2017.12.006
7. Bover J, Ureña-Torres P, Laiz Alonso AM, et al. Osteoporosis, bone mineral density and CKD-MBD (II): therapeutic implications. Nefrología (English Edition). 2019; 39(3):227-42. doi: 10.1016/j.nefro.2018.10.009
8. de Wit M, Cooper C, Tugwell P, et al. Practical guidance for engaging patients in health research, treatment guidelines and regulatory processes: results of an expert group meeting organized by the World Health Organization (WHO) and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). Aging Clin Exp Res. 2019; 31(7):905-15. doi: 10.1007/s40520-019-01193-8.
9. Marques A, Lourenço Ó, Da Silva J. The burden of osteoporotic hip fractures in Portugal: costs, health related quality of life and mortality. Osteoporos Int. 2015; 26(11):2623-30. doi: 10.1007/s00198-015-3171-5
10. Salamat M, Rostampour N, Shanehsazzadeh S, Tavakoli M, Siavash M, Almasi T. Assessment of bone mineral density with dual energy X-ray absorptiometry in pre-and post-menopausal women. Iran J Radiat Res. 2008; 6(2):103-7.
11. Punda M, Grazio S. Bone densitometry–the gold standard for diagnosis of osteoporosis. Reumatizam. 2014; 61(2):70-4.
12. Messina C, Monaco CG, Ulivieri FM, Sardanelli F, Sconfienza LM. Dual-energy X-ray absorptiometry body composition in patients with secondary osteoporosis. Eur J Radiol. 2016; 85(8):1493-8. doi: 10.1016/j.ejrad.2016.03.018
13. Julka A, Shrivastava S, Pandey R, Bhargav P, Ajmera A. To evaluate the utility of Singh index as an indicator of osteoporosis and a predictor of fracture neck femur. J Anatom Soc India. 2012; 61(2):192-8. doi: 10.1016/S0003-2778(12)80031-1
14. Koot V, Kesselaer S, Clevers GJ, De Hooge P, Weits T, van der Werken C. Evaluation of the Singh index for measuring osteoporosis. J Bone Joint Surg Br. 1996; 78(5):831-4. PMID: 8836082
15. Soontrapa S, Soontrapa S, Srinakarin J, Chowchuen P. Singh index screening for femoral neck osteoporosis. J Med Assoc Thailand. 2005; 88:S13. PMID: 16869101
16. Cumpston M, Li T, Page MJ, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst Rev. 2019; 10:ED000142. doi: 10.1002/14651858.ED000142
17. Hübsch P, Kocanda H, Youssefzadeh S, et al. Comparison of dual energy X-ray absorptiometry of the proximal femur with morphologic data. Acta Radiologica. 1992; 33(5):477-81.
18. Salamat M, Rostampour N, Zoufaghari SJ, Hosseinipanah H, Javdan M. Comparison of Singh index accuracy and dual energy X-ray absorptiometry bone mineral density measurement for evaluating osteoporosis. Iran J Radiat Res. 2010; 8(2):123-8.
19. Chung CY, Son YC, Bae JB, Park BJ. Evaluation of the Singh index for measurement of osteoporosis. J Korean Orthop Assoc. 1999; 34(5):871-5. PMID: 8836082
20. Kapishnikov A, Pervushkin S, Gaidel A, Alekhin E. Efficient textural features selection for computer-aided diagnosis (CAD) of osteoporosis by plain hip radiography. European Congress of Radiology-ECR 2013; 2013: C-1358. doi: 10.1594/ecr2013/C-1358
21. Mir FR, Nazir I, Naseed M. Comparison of radiographic singh index with dual-energy x-ray absorptiometry scan in diagnosing osteoporosis. Matrix Science Medica. 2021; 5(1):17. doi: 10.4103/MTSM.MTSM_41_20
22. Liu Z, Gao H, Bai X, Zhao L, Li Y, Wang B. Evaluation of Singh Index and Osteoporosis Self-Assessment Tool for Asians as risk assessment tools of hip fracture in patients with type 2 diabetes mellitus. J Orthop Surgery Res. 2017; 12(1):1-7.
23. Qadir RI, Bukhari SI. Singh's index accuracy with DEXA scan for evaluation of osteoporosis. J Med Sci. 2016; 24(1):12-5.
24. Shankar N, Vijay A, Ligesh AS, Kumar A, Anburajan M. Comparison of Singh's index with Dual energy x-ray absorptiometry (DXA) in evaluating post-menopausal osteoporosis. IEEE. 2011; 1:361-4. doi: 10.1109/ICECTECH.2011.5941772
25. Karabulut Ö, Tuncer M, Karabulut Z, Hatipoğlu E, Nazaroğlu H, Akkuş Z. Evaluation of the Singh index and femur geometry in osteoporotic women. Open Med. 2010; 5(5):601-10. doi: 10.2478/s11536-009-0136-0
26. Memon MA, Sohail S, Ahmed A. Radiographic morphometry of the osteoporotic femur: Comparison with densitometry. J Surg Pak. 2007; 12(4):144.
27. Sah AP, Thornhill TS, LeBoff MS, Glowacki J. Correlation of plain radiographic indices of the hip with quantitative bone mineral density. Osteop Int. 2007; 18(8):1119-26. doi: 10.1007/s00198-007-0348-6
28. Trijoto I, Isbagio H, Setiyohadi B, Soegondo S, Kusumawidjaja K, Ariawan I. The diagnostic value of combined risk factor analysis and radiological imaging in determining osteoporosis in post-menopausal women. Acta Med Indones. 2005; 37(1):26-32. PMID: 15879634
29. Anburajan M. Evaluation of osteoporosis using conventional radiographic methods and dual energy x-ray absorptiometry. Med Physics. 2001; 28(6):1142-2. doi: 10.1118/1.1376643
30. Alexa O, Puha B, Alexa ID, Gheorghevici TS, Filip A, Veliceasa B. Is the Singh Index useful for evaluating osteoporosis? IEEE. 2017; 1:205-8. doi: 10.1109/EHB.2017.7995397
31. Klatte T, Vettorazzi E, Beckmann J, Pueschel K, Amling M, Gebauer M. The Singh Index does not correlate with bone mineral density (BMD) measured with dual energy X-ray absorptiometry (DXA) or peripheral quantitative computed tomography (pQCT). Arch Orthop Trauma Surg. 2015; 135(5):645-50. doi: 10.1007/s00402-015-2187-9
32. Masud T, Jawed S, Doyle D, Spector T. A population study of the screening potential of assessment of trabecular pattern of

The femoral neck (Singh index): the Chingford Study. Br J Radiol. 1995; 68(808):389-93. doi: 10.1259/0007-1285-68-808-389

33. Karlsson KM, Sernbo I, Obrant KJ, Redlund-Johnell I, Johnell O. Femoral neck geometry and radiographic signs of osteoporosis as predictors of hip fracture. Bone. 1996; 18(4):327-30. doi: 10.1016/8756-3282(96)00004-x
34. Burli U, Patil KS, Chamakeri PH, Mittal AR. Reliability of radiological indices in comparison with dual energy x-ray absorptiometry in diagnosis of osteoporosis: A cross-sectional study. Int J Orthop. 2020; 6(3):643-6. doi: 10.22271/ortho.2020.v6.i3j.2265
35. Hauschild O, Ghanem N, Oberst M, et al. Evaluation of Singh index for assessment of osteoporosis using digital radiography. Eur J Radiol. 2009; 71(1):152-8. doi: 10.1016/j.ejrad.2008.03.019
36. Bes C, Güven M, Akman B, Atay EF, Ceviz E, Soy M. Can bone quality be predicted accurately by Singh index in patients with rheumatoid arthritis? Clin Rheumatol. 2012; 31(1):85-9. doi: 10.1007/s10067-011-1786-2
37. Kanis JA. Diagnosis of osteoporosis and assessment of fracture risk. Lancet. 2002; 359(9321):1929-36. doi: 10.1016/S0140-6736(02)08761-5
38. Glüer CC, Cummings SR, Pressman A, et al. Prediction of hip fractures from pelvic radiographs: the study of osteoporotic fractures. J Bone Mineral Res. 1994; 9(5):671-7. doi: 10.1002/jbmr.5650090512
39. Yeo AK, Ahrberg AB, Theopold JD, et al. Are radiographic indices reliable indicators for quantitative bone mineral density and vitamin D status after femoral neck fractures? A retrospective study in 112 elderly patients. Patient Safety Surg. 2015; 9(1):1-7. doi: 10.1186/s13037-015-0085-2
40. James D, Williams S. Determining prevalence of osteoporosis in health-seeking population of rural central India using singh's index: A resource optimization model to fight a silent epidemic. CHRISMED J Health Res. 2018; 5(3):173. doi: 10.4103/cjhr.cjhr_35_18
41. Gupta G, Rani S, Umar S, Singh S, Haider S, Kumar M. Correlate of radiological indexes for osteoporosis with histological status of osteoid of bone. JDMS. 2016; 15(04):20-8.
42. Lems WF. Fracture risk estimation may facilitate the treatment gap in osteoporosis.

Ann Rheum Dis. 2015; 74(11):1943-5. doi: 10.1136/annrheumdis-2015-208245

43. Epanov VV, Palshin GA, Epanova AA, et al. X-ray densitometry and frax model in predicting the risk of osteoporosis and low-energy fractures in postmenopausal women. Wiad Lek. 2015; 68(4):526-8.
44. Natu N, Yadav S, Kosta S, Dave A, Kumar R. Detection of osteoporosis in postmenopausal women by singh's index. J South Asian Feder Menopause Soc. 2016; 4(1):8-10. doi: 10.18314/jbo.v1i1.29
45. Singh M, Nagrath AR, Maini P. Changes in trabecular pattern of the upper end of the femur as an index of osteoporosis. JBJS. 1970; 52(3):457-67.