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RELATIONSHIP BETWEEN SERUM TESTOSTERONE AND OSTEOPOROSIS IN OLDER MEN: A CROSS-SECTIONAL STUDY

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Abstract

Introduction: Low testosterone levels in older men cause a decrease in bone mass density. Osteoporosis is divided into primary and secondary types: the former occurs without known risk factors, whereas risk factors have been identified for the latter. The causes of secondary osteoporosis in older men include hypogonadism (i.e., decreased levels of the hormone testosterone). The Singh index is an affordable and straightforward method of determining bone mass density at a fracture site. The current study investigated the relationship between serum testosterone levels and the severity of osteoporosis (according to the Singh index) in older men.

Materials and Methods: This cross-sectional study was conducted at Wahidin Sudirohusodo hospital, Makassar, Indonesia. with participants comprised of men aged greater than 50 years. The Singh index is divided into six grades ranging from 1 (severe osteoporosis) to 6 (normal bone density). Anteroposterior pelvic X-ray was conducted to determine bone density. Testosterone serum levels were examined by an ELISA method (enzyme-linked immunosorbent assay).

Results: The average testosterone level was 117.88 ± 110.22 ng/dL. The highest osteoporosis score was Singh index grade 3 (definitive osteoporosis), which was recorded for 14 patients (26%; $p < 0.001$). There was a significant correlation between serum testosterone levels and the severity of osteoporosis according to Singh index grade among older men (p-value < 0.001).

Conclusions: Decreased serum testosterone levels in elderly men were significantly related to the severity of osteoporosis according to the Singh index grade. The Singh index could therefore be a useful screening method for the assessment of osteoporosis.

Keywords: cross-sectional study; osteoporosis; Singh index; testosterone.

Introduction

Osteoporosis is a major public-health issue worldwide [*Sozen et al., 2017*]. While traditionally viewed primarily as a disease of postmenopausal women, osteoporosis in men represents a growing, yet frequently underdiagnosed and undertreated, clinical challenge. Both men and women may begin to experience bone loss around the age of 50

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years, and one in eight men aged >50 years will experience a fracture due to osteoporosis [*Kaufman et al., 2013*]. One-third of all hip fractures occur in older males, and these fractures are associated with higher morbidity and mortality rates compared to women, making this a severe clinical health problem. The risk of osteoporotic fracture among Caucasian men aged ≥60 years has been estimated as 21% in England and Wales, and as 15% in Australia for those aged ≥75 years [*Sozen et al., 2017; Kaufman et al., 2013*]. Despite these alarming statistics, male osteoporosis remains inadequately screened.

Osteoporosis is broadly divided into primary and secondary types [*Foroutan, 2024*]. Primary osteoporosis occurs without known secondary risk factors and is generally associated with age-related bone loss. In contrast, specific medical conditions or treatments cause secondary osteoporosis. The causes of secondary osteoporosis in older men are diverse and include hypogonadism (decreased testosterone levels), prolonged use of glucocorticoids, immunosuppressant drugs, anticonvulsants, excessive alcohol intake, smoking, hypocalcemia, hyperthyroidism, and hyperparathyroidism [*Fink H. et al., 2006; Golds et al., 2017; Aggarwal W et al., 2023*]. Among these, age-related decline in sex steroids is a critical but often overlooked factor.

Serum total testosterone reference ranges were based on harmonized values reported by Bhasin et al. and recommendations from the Endocrine Society, with normal adult male levels ranging from 9.2 to 31.8 nmol/L and age-related decline observed in elderly men (Table 1) [*Bhasin* et al., 2017].

Osteoporosis has been shown to be more prevalent among elderly men with severe testosterone deficiency. Conversely, deficiency of total testosterone or estradiol is more frequently detected in elderly men with osteoporosis [*Fink H., 2006*].

It has been reported that osteoporosis was noted in 39.3% of elderly men aged >60 years attending the outpatient department. Decreased serum testosterone levels were significantly associated with male osteoporosis, as measured by Bone Mineral Density (BMD). The association between testosterone levels and osteoporosis was statistically significant, with a p-value of 0.019 (Table 2) [*Aggarwal V., 2023*].

The reported prevalence of male osteoporosis was high; therefore, it is important to develop a screening protocol for elderly men to diagnose osteoporosis early and prevent osteoporotic fractures where possible (Table 3) [*Kanis et al., 2012; Watts, 2012; Bhasin, 2018; Camacho et al., 2020; Aggarwal et al., 2023*].

Based on recommendations defining biochemical thresholds for testosterone deficiency in older men (200–300 *ng/dL)* [*APTRM, 2001*], participants were categorized as testosterone deficient (<200 *ng/dL* [6.9 *nmol/L*]), possibly testosterone deficient (200–400 *ng/dL* [6.9–13.9 *nmol/L*]), or normal (≥400 *ng/dL* [≥13.9 *nmol/L*]). Secondary analyses further stratified participants into subgroups: <200 *ng/dL*, 200–<300 *ng/dL*, 300–<400 *ng/dL*, 400–<500 *ng/dL*, and ≥500 *ng/dL* [*Fink et al., 2006*].

Low testosterone levels in older men can cause a significant decrease in bone mineral density. Sex steroid hormones play an essential role in regulating bone formation and bone mass in both men and women [*Aggarwal et al., 2023*]. Testosterone promotes bone health both directly, by binding to androgen receptors on osteoblasts and osteocytes to stimulate bone formation, and indirectly, through aromatization into estrogen, which inhibits bone resorption. A study in the United States found that decreased testosterone levels were associated with a 2.5-fold increase in the risk of non-vertebral fractures [*Binkley et al., 2014; Golds et al., 2017*]. Consequently, early identification of hypogonad-

TABLE 1.

Reference ranges of serum total testosterone in adult and elderly men

Age (years)	Testosterone (nmol/L)
20–39	9.2 – 31.8
40–49	8.6 – 29.0
50–59	7.6 – 27.0
60–69	6.7 – 25.7
≥70	5.4 – 24.6

TABLE 2.

Association between serum testosterone levels and osteoporosis in elderly men aged >60 years [Aggarwal, V 2023].

Testosterone levels	Osteoporeses present	absent	Total	p-value
> 300 ng/dL	50	51	101	0.019
< 300 ng/dL	111	196	307	
Total	161	247	408	

Table 3.

Serum Total Testosterone Levels in Elderly Men According to the Degree of Osteoporosis and Singh Index Grades .

Osteoporosis Grade		Bone Tissue Characteristics	Testosterone (nmol/L), Mean ± SD	Singh Index Grade	Testosterone (nmol/L), Mean ± SD
Normal	No osteoporosis	Normal bone density	18.5 ± 4.2	VI	19.0 ± 4.1
				V	16.3 ± 3.9
Osteopenia	Pre-osteoporosis	Moderate decrease in bone density	14.2 ± 3.8	IV	13.8 ± 3.6
Grade I osteoporosis	Early osteoporosis	Initial significant decrease	11.6 ± 3.5	III	11.2 ± 3.1
Grade II osteoporosis	Moderate osteoporosis	Marked decrease in bone density	9.8 ± 2.9	II	9.1 ± 2.8
Grade III osteoporosis	Severe osteoporosis	Pronounced morphological and structural changes	7.9 ± 2.6	I	7.5 ± 2.4

ism is essential for preventing osteoporotic fractures in aging men.

Accurate diagnosis and screening of osteoporosis are essential for timely intervention. The current gold standard for measuring bone mineral density is dual-energy X-ray absorptiometry (DXA). However, DXA is expensive, requires specialized equipment, and is often unavailable in resource-limited or rural healthcare settings. This necessitates alternative, cost-effective screening methods. The proximal femur contains trabecular bone arranged in intersecting arches, which are closely related to its weight-bearing function, as mechanical load is transmitted from the femoral head to the shaft through this trabecular architecture [*Osterhoff et al., 2016*].

In 1970, Singh and colleagues introduced a morphological classification of trabecular patterns at the proximal femur as a radiographic index of osteoporosis. The Singh Index is an affordable, accessible, and straightforward method for assessing bone density at fracture-prone sites using standard pelvic radiographs. By evaluating the disappearance of specific trabecular groups, clinicians can estimate the degree of bone loss. However, this method has been criticized due to inter-observer variability, and the boundaries between categories may sometimes be subjective [*Kanakaris & Lasanianos, 2015; Liu et al., 2017*]. Despite these limitations, in settings where advanced densitometry is unavailable, the Singh Index remains a clinically useful triage tool.

Given the critical role of androgens in male bone health and the practical utility of radiographic indices in routine clinical practice, further investigation is warranted. The present study aimed to investigate the relationship between serum testosterone levels and the severity of osteoporosis assessed by the Singh Index in older men.

Material and Methods

This cross-sectional study was conducted at Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia, from December 2023 to November 2024. The study population comprised men aged >50 years. The institutional ethics committee approved the protocol (No: UH21090579). The inclusion criteria were men aged >50 years. The exclusion criteria included a history of chronic diseases affecting bone metabolism, prior pelvic fracture due to trauma, and treatment with glucocorticoids or anticonvulsant drugs for >6 months.

Singh Index grades: The Singh Index is divided into six grades ranging from 1 (severe osteoporosis) to 6 (normal bone density) [*Kanakaris & Lasanianos, 2015; Liu et al., 2017*].

Anteroposterior pelvic X-ray: Plain radiographs of the anteroposterior pelvis were obtained using a Multix Select DR system (Siemens Healthineers, Germany). Imaging was performed in the supine position with both legs extended and 15° internal rotation. The central beam was focused on the pubic symphysis with a voltage of 60–70 *kVp*, exposure time of 1 s, and source-to-image distance of 1 *m.* Images were evaluated for quality, and the proximal femoral trabecular pattern was assessed according to the Singh Index [*Julka et al., 2012; Liu et al., 2017*].

Measurement of serum testosterone levels: Serum testosterone levels were measured using an enzyme-linked immunosorbent assay (ELISA) kit (VIDAS

reagent; bioMérieux SA, Marcy-l'Étoile, France; catalog No. 1007817140). Men were classified as testosterone deficient if levels were <12 *nmol/L*, while normal or borderline levels ranged from 12–40 nmol/L (~>200 *ng/dL*) [*Watts et al., 2012*].

Statistical analysis: Data were analyzed using SPSS version 20. Descriptive statistics were presented as frequencies and percentages. The Spearman correlation test was used to assess the relationship between serum testosterone levels (continuous/ordinal) and Singh Index grades (ordinal). A p-value ≤0.05 was considered statistically significant.

RESULTS

This study aimed to determine serum testosterone levels in elderly men, assess osteoporosis grading using the Singh Index, and evaluate the association between testosterone levels and osteoporosis severity. This cross-sectional study was conducted at Wahidin Sudirohusodo hospital, Makassar, Indonesia, from December 2023 to November 2024 onwards.

Table 4 presents the demographic and clinical distribution of serum testosterone levels and osteoporosis severity according to the Singh Index.

The mean testosterone level in the study population was 117.88 ± 110.22 *ng/dL*. As shown in Table 4, testosterone levels >200 *ng/dL* were observed in 17 participants (31.5%), while ≤200 *ng/dL* was observed in 37 participants (68.5%).

The results of osteoporosis classification in elderly men according to different grades of the Singh index are presented in Table 5.

The data shown in Table 5 indicate that, in the classification of osteoporosis in elderly men, the most common finding was Grade 3 according to the Singh index (i.e., confirmed osteoporosis), which was identified in 14 patients (26%).

TABLE 4.
Association of low and borderline testosterone levels with Singh Index grades among elderly men in Indonesia

Variable	Number (%)
Testosterone level (ng/dl)	
> 200	17 (31.5%)
≤ 200	37 (68.5%)
Osteoporosis Singh Index grade	
Heavy	4 (7%)
Moderate	11 (20%)
Definitive	14 (26%)

TABLE 5.
Distribution of patients with osteoporosis in Indonesia according to Singh Index grades

Singh Index score	Distribution according to Singh Index grades			P-value
	Osteoporosis grading	n	%	
I	Severe	4	7	2.43 ± 1.62
II	Moderately advanced	11	20	
III	Definitive	14	26	
IV	Transition between normal bone and osteoporosis	7	13	
V	Early stage	7	13	
VI	Normal	11	20	

The mean serum testosterone level was 117.88 ± 110.22 ng/dL. The most common osteoporosis grade was Singh Index Grade 3 (26%). A statistically significant correlation was observed between serum testosterone levels and Singh Index grade ($p < 0.001$). The Spearman correlation analysis demonstrated a strong positive association between testosterone levels and Singh Index grade ($r = 0.942$, $p < 0.001$) in 54 elderly men [*Alam A., 2022*] .

DISCUSSION

In the present study, among older men, the highest prevalence was observed for Singh Index grade 3 (definitive osteoporosis), recorded in 14 patients (26%), whereas the lowest prevalence was observed for Singh Index grade 1 (severe osteoporosis), recorded in four patients (7%). Singh Index grade 2 (moderately advanced osteoporosis) was observed in 11 patients (20%), grade 4 (transition between normal bone and osteoporosis) in seven patients (13%), grade 5 (early-stage osteoporosis) in seven patients (13%), and grade 6 (normal bone) in 11 patients (20%). The Singh Index is an affordable and straightforward method for assessing trabecular bone density at the proximal femur.

The Singh Index has been widely applied for osteoporosis screening and assessment in the literature; however, its diagnostic performance remains controversial. For instance, Shankar et al. reported no significant agreement in Singh Index grading when assessed using kappa statistics, sug-

gesting limited reliability in determining osteoporosis severity [*Shankar, 2013*]. In contrast, Julka et al. demonstrated significantly lower Singh Index scores in patients with femoral neck fractures compared to age-matched controls ($p < 0.05$), supporting its potential clinical utility [*Julka et al., 2012; Liu et al., 2017*].

Another study involving 72 patients reported no significant correlation between Singh Index grading and hip bone mineral density ($p = 0.14$). Although the Singh Index demonstrated high sensitivity (96%), its specificity was very low (2%). Compared with dual-energy X-ray absorptiometry (DXA), it showed a positive predictive value of 38% and a negative predictive value of 50%. However, a significant inverse relationship was observed between bone mineral density and age, indicating progressive bone loss with aging [*Salamat et al., 2010*].

In the present study, 17 patients (31.5%) had serum testosterone levels >200 *ng/dL*, while 37 patients (68.5%) had levels ≤200 *ng/dL*. Testosterone deficiency is generally defined as serum levels <12 *nmol/L* (~<350 *ng/dL* depending on assay calibration). Testosterone replacement therapy is recommended in selected hypogonadal men at high risk of fracture, according to endocrine society guidelines [*Watts et al., 2012*].

The analysis demonstrated a statistically significant association ($p < 0.05$) between serum testosterone levels and osteoporosis severity according to the Singh Index. Similarly, Julka et al. reported significant differences in Singh Index scores between fracture patients and controls, supporting its potential role in fracture risk assessment [*Julka et al., 2012*]. Additionally, Singh Index grades below 4 have been associated with increased risk of femoral neck fractures, particularly grades 1 and 2. The index has also been proposed as a tool for identifying patients who may benefit from prophylactic hip interventions in high-risk populations [*Patel & Murphy, 2006*].

Karabulut et al. demonstrated a significant positive correlation between Singh Index grades and bone mineral density in postmenopausal women without prior hip fractures, indicating that higher Singh Index grades reflect better bone quality [*Karabulut et al., 2010*].

Large cohort studies have shown inconsistent associations between testosterone levels and fracture risk. The Concord Health and Ageing in Men Project (958 men aged >70 years) found no association between testosterone levels and fracture risk but identified a significant relationship with hip bone mineral density [*Hsu et al., 2016; Shigehara et al., 2021*]. Similarly, the Longitudinal Aging Study Amsterdam (623 men aged >55 years) reported a significant association between testosterone levels and hip bone mineral density over follow-up [*Kuchuk et al., 2007*]. In contrast, larger population-based studies such as the Osteoporotic Fractures in Men Study (USA, n = 1,436) and Hong Kong Osteoporotic Fractures in Men Study (n = 1,498) found no significant association between testosterone levels and hip bone mineral density [*Golds et al., 2017*].

Liu et al. evaluated the combination of the Singh Index and the Osteoporosis Assessment Tool for Asians in patients with type 2 diabetes mellitus and reported significant differences in bone mineral density across anatomical sites between fracture and non-fracture groups. They recommended this combined approach as an alternative screening method in resource-limited settings [*Liu et al., 2017*].

Testosterone exerts both anabolic and androgenic effects on bone metabolism, promoting bone formation through androgen receptor activation in osteoblasts and indirectly via aromatization to estrogen, which inhibits bone resorption [*Mohamad et al., 2016; Chen et al., 2019; Zhang et al., 2022*]. Therefore, radiographic tools such as the Singh Index may provide a cost-effective alternative for osteoporosis screening in settings where DXA is not available [*Liu et al., 2017*].

In the present study, a statistically significant relationship ($p < 0.05$) was observed between serum testosterone levels and osteoporosis severity according to Singh Index grading in older men. These findings suggest that testosterone assessment may have potential value in identifying individuals at risk of osteoporosis.

Conclusions

The present study demonstrated that higher Singh Index grades were associated with lower

prevalence of severe osteoporosis, with Grade 3 being the most frequently observed category among older men. This suggests that the Singh Index may be a useful preliminary screening tool for assessing osteoporosis severity.

A significant association was also observed between decreased serum testosterone levels and higher severity of osteoporosis according to Singh Index grading. These findings support the potential role of combined hormonal and radiographic assessment in osteoporosis screening among elderly men.

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