

Performance of the Khon Kaen Osteoporosis Study (KKOS) Score for Identifying Osteoporosis in Men

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Objective: The present study evaluated the diagnostic performance of Khon Kaen Osteoporosis Study (KKOS) score in identifying osteoporosis in men.

Material and Method: This was a cross-sectional investigation in 230 men aged ≥ 50 years. Bone mineral density (BMD) was measured at the femoral neck and lumbar spine by DXA (DPX-IQ densitometer, LUNAR Corporation, Madison, Wisconsin, USA). The KKOS score was calculated for each man using his age and weight. Men with KKOS scores ≤ -1 and > -1 were classified as "high risk" and "low risk", respectively.

Results: The prevalence of osteoporosis in the entire sample was 17% and 7.4% ($n = 39, 17$) by femoral neck BMD and lumbar spine BMD, respectively. Using the KKOS score, 80 (34.8%) men were classified as "high risk" (KKOS score ≤ -1). The proportion of high risk individuals increased with advancing age, ranging from 16.2% in the 50-65 age group to 64.8% in the > 65 age group. Using BMD from DXA as a gold standard, the overall sensitivity and specificity of KKOS in identifying osteoporosis was 72.5% and 73.2%, respectively. However, the sensitivity was higher at the lumbar spine (94.1% vs. 71.8%) than the femoral neck, while the specificity was comparable. The PPV of KKOS was 36%; and was lower at the lumbar spine (20%) compared to the femoral neck (35%). In the present study, men were classified "high risk" from KKOS, the risk (odds ratio; OR) of osteoporosis at the femoral neck and/or lumbar spine was 7.19 (95%CI: 3.34-15.44). However, the risk of osteoporosis was higher in the younger age (50-65 yr) group (OR: 10.29, 95%CI: 3.31-31.94) compared with the older age (> 65 yr) group (OR: 3.65, 95%CI: 1.12-11.91).

Conclusion: KKOS scoring system based on age and body weight, is a simple tool for clinicians to make a decision to further DXA testing for identifying osteoporosis in Thai men. This tool had a high sensitivity and specificity, but modest PPV.

Keywords: Clinical risk index, Epidemiology, Men, Osteoporosis, Thailand

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Osteoporosis is a major health problem through its association with fracture in both men and women^(1,2). Despite its association with disability, death, and increased medical costs, osteoporosis in men has been relatively neglected as a subject of study⁽³⁻⁷⁾. Examining bone mineral density (BMD) is the diagnostic standard

used to detect the disease in men. Unfortunately, diagnostic parameters and screening recommendations for bone mineral density testing have not been firmly established in men⁽⁸⁻¹⁰⁾.

In women, several clinical risk assessment tools have been developed that facilitate the appropriate and more cost-effective use of dual energy x-ray absorptiometry (DXA) and as such help clinicians determine the risk of osteoporosis^(11,12), however the usefulness of these screening tools in men is unknown. The osteoporosis self-assessment screening tool for Asians (OSTA) is a simple and effective clinical risk

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assessment tool for detecting a risk of osteoporosis in both men and women⁽¹³⁻¹⁷⁾. However, the utility of OSTA for predicting osteoporosis in Thai women had some limitations⁽¹⁸⁾.

Khon Kaen Osteoporosis Study score (KKOS), a Thai-specific clinical risk score, has been developed and used for identifying osteoporosis in Thai postmenopausal women⁽¹⁹⁾. This screening tool was more sensitive and specific than OSTA when it was validated in Thai women⁽¹⁹⁾. However, the utility of KKOS in predicting low BMD in Thai men has not been investigated to date. Therefore, the aim of the present study was to evaluate the diagnostic performance of KKOS in identifying Thai men with low BMD.

Material and Method

Setting and Subjects

The present study was designed as a cross-sectional study in 230 men living in Muang district, Khon Kaen province, Thailand. All men were of a Thai background and aged ≥ 50 years old. Subjects with pre-existing conditions that affected bone mass, i.e., presence of cancer(s) with known metastasis to bone, hyperthyroidism, chronic renal disease, inflammatory arthropathy, i.e., rheumatoid arthritis, ankylosing spondyloarthropathy, fragility fracture or had a history of taking medications affecting calcium and bone metabolism such as steroids, thyroid hormone, bisphosphonates, parathyroid hormone, strontium ranelate or calcitonin were excluded from the present study. The present study was approved by the Ethics Committee of Khon Kaen University and informed consent was obtained from all subjects. The present study was conducted in accordance with the Helsinki Declaration in 1975 and as revised in 2000 (Edinburgh).

Measurements

Subjects were invited to meet with a trained research nurse, obtain an informed consent form and administered a questionnaire. Body weight (including light indoor clothing without shoes) was measured using an electronic balance scale (accuracy 0.1 kg). BMD (g/cm^2) was measured at the femoral neck and lumbar spine by DXA using a LUNAR DPX-IQ densitometer (LUNAR Corporation, Madison, Wisconsin, USA). BMD was expressed in T-score, the number of standard deviations (SDs) below the young normal mean taken from Thai men⁽²⁰⁾. Each man was classified as having "osteoporosis" if his BMD T-score was equal to or less than -2.5; otherwise the man was classified as "non-osteoporotic".

Statistical analyses

Statistical analyses were performed using SPSS 11.5 (SPSS Inc., Chicago, Illinois). Descriptive results were expressed as the mean, standard deviation (SD) and percent.

Validation of KKOS

The KKOS score was calculated for each man by using his age and weight from Table 1. KKOS score was the summation of age and weight score. Individuals with KKOS scores being less than or equal to -1 were classified as "high-risk", and otherwise, a "low-risk" classification was made⁽¹⁹⁾. The concordance between the KKOS classification and the actual BMD-based classification can be summarized by a 2 x 2 table, from which sensitivity, specificity, and positive predictive value (PPV) and negative predictive value (NPV) were derived. Sensitivity is defined as the proportion of osteoporotic individuals who are identified as "high risk" by the KKOS score. Specificity is the proportion of non-osteoporosis individuals who are identified by the KKOS score as "low-risk". PPV is the probability that an individual with a "high-risk" diagnosis indeed has osteoporosis. NPV is the probability that an individual with a "low risk" by KKOS indeed has non-osteoporosis. The association between osteoporosis defined by DXA (outcome) and KKOS (predictor) was assessed, in which the odds ratio (OR) and 95% confidence interval (CI) were presented.

Table 1. KKOS scoring system

Age (y)	Score	Weight (kg)	Score
< 45	+7.5	< 30	-14
45-49	+6.0	30-34	-12
50-54	+4.5	35-39	-10
55-59	+3.0	40-44	-8
60-64	+1.5	45-49	-6
65-69	0	50-54	-4
70-74	-1.5	55-59	-2
75-79	-3.0	60-64	0
80-84	-4.5	65-69	+2
85-89	-6.0	70-74	+4
> 90	-7.5	75-79	+6
		80-84	+8
		85-89	+10
		> 90	+12

Note; The KKOS score was calculated by the summation of age and weight scores
 KKOS score \leq -1: high risk, KKOS score $>$ -1: low risk

Results

A total of 230 Thai men, aged between 50 and 87 years were included in the present study, of those, 38.3% (n = 88) were aged > 65 years old. The mean \pm SD of age and body weight was 63.4 ± 8.3 years and 62.3 ± 11.4 kg, respectively. Both femoral neck and lumbar spine BMD was normally distributed with a mean 0.85 ± 0.15 g/cm² at the femoral neck and 1.11 ± 0.19 g/cm² at the lumbar spine. The average T-score for femoral neck and lumbar spine BMD was -1.44 ± 1.13 and -0.44 ± 1.46 , respectively. The prevalence of osteoporosis in the entire sample was 17% (n = 39) by femoral neck BMD and 7.4% (n = 17) by lumbar spine BMD. When two BMD measures were considered, the prevalence was 17.4% (n = 40).

Validation of KKOS

Using the KKOS scoring system, 80 (34.8%) men were classified as "high-risk" (KKOS score \leq -1). The proportion of high risk individuals increased with advancing age, ranging from 16.2% in the 50-65 age group to 64.8% in the > 65 age group. The overall sensitivity and specificity of KKOS was 72.5% and 73.2%, respectively. However, there was a significant variation in the diagnostic measures with sites. For instance, at the femoral neck, the sensitivity and speci-

ficity was 71.8 and 72.8%, respectively, while the sensitivity was higher at the lumbar spine (94.1%) with comparable specificity (70.0%). The PPV of KKOS was 36%; however, it was lower at the lumbar spine (20%) compared to the femoral neck (35%). Moreover, there was a significant variation in the diagnostic measures with age. For instance, in the younger group (50-65 years), the sensitivity was 56.3%, but the specificity was higher (88.9%); on the other hand, among those aged > 65 years old, the specificity was 41.5% compared with the sensitivity of 82.6%. The PPV of KKOS was comparable in the younger age group (39.1%) and older group (35.1%), (Table 2).

In the present study, subjects were classified "high-risk" from KKOS, the risk (odds ratio; OR) of osteoporosis at the femoral neck and/or lumbar spine was 7.19 (95%CI: 3.34-15.44). However, men were classified "high-risk" from KKOS, the risk of osteoporosis was higher in the younger age group (OR: 10.29, 95%CI: 3.31-31.94) compared to the older age group (OR: 3.65, 95% CI: 1.12-11.91), (Table 2).

Discussion

Indeed, osteoporosis is a silent disorder in both men and women until fracture occurs. Yet, screening for osteoporosis is particularly important in men

Table 2. Diagnostic performance of KKOS for identifying osteoporosis in Thai men

Patients's characteristics	Based on either FN or LS BMD	Based on FNBMD	Based on LSBMD
All age groups (n = 230)	(%)	(%)	(%)
Sensitivity	72.5	71.8	94.1
Specificity	73.2	72.8	70.0
Positive predictive value	36.3	35.0	20.0
Negative predictive value	92.7	92.7	99.3
Area under curve	0.78 (0.70-0.86)	0.77 (0.69-0.85)	0.85 (0.75-0.95)
Odds ratio (95%CI)	7.19 (3.34-15.44)	6.80 (3.16-14.65)	37.25 (4.84-286.88)
Age group: 50-65 (n = 142)			
Sensitivity	56.3	56.3	80.0
Specificity	88.9	88.9	86.1
Positive predictive value	39.1	39.1	17.4
Negative predictive value	94.1	94.1	99.2
Area under curve	0.78 (0.65-0.92)	0.78 (0.65-0.92)	0.78 (0.51-0.99)
Odds ratio (95%CI)	10.29 (3.31-31.94)	10.29 (3.31-31.94)	24.84 (2.63-234.34)
Age group: 65+ (n = 88)			
Sensitivity	83.3	82.6	100.0
Specificity	42.2	41.5	40.8
Positive predictive value	35.1	33.3	21.1
Negative predictive value	87.1	87.1	100.0
Area under curve	0.72 (0.59-0.85)	0.70 (0.67-0.92)	0.82 (0.71-0.92)
Odds ratio (95%CI)	3.65 (1.12-11.91)	3.38 (1.03-11.05)	1.27 (1.11-1.45)

because fragility fractures are more likely to lead to fatal consequences than in women⁽²⁻⁸⁾. Without a diagnosis of osteoporosis, treatment interventions that can prevent fractures in men are not initiated⁽⁸⁻¹⁰⁾. Advancement of better health outcomes for men at risk for osteoporosis begins with a greater awareness of the need for osteoporosis screening and treatment whenever appropriate. Notwithstanding, little evidence exists that any screening for osteoporosis is done in men who have not had a fracture.

BMD measured by DXA is regarded as the standard method for BMD assessment and fracture prediction in both men and women⁽¹⁾. However, in some developing countries including Thailand, DXA is not widely available and the cost of measurement is high. It is reasonable to use the clinical risk indices for identifying subjects with low BMD or high risk fracture individuals. BMD is highly related to age and body weight. Indeed, the two factors collectively account for 40 to 60 percent variance of BMD in the population⁽²¹⁻²⁴⁾. Some studies have suggested that these two factors were sensitive and specific enough to merit a large-scale identification of low BMD in men^(15,25). In a previous study of Thai men, the authors noted that age and weight contributed significantly to the variance in BMD⁽²⁶⁾. Therefore, using these factors as the predictors, are reasonable to examine the association with low BMD in men as well as in women.

An assessment tool (KKOS) was originally developed from a study in postmenopausal Thai women aimed at assessing clinical risk factors (age and weight) associated with osteoporosis⁽¹⁹⁾. KKOS has been validated in Thai women⁽¹⁹⁾ and has been applied with success. In the present study, using KKOS in Thai men, it yielded a sensitivity of 72.5% and a specificity of 73.2% with an AUC of 0.78 in the presented population. Additionally, using the older age group (> 65 years), the sensitivity increased while the specificity decreased. In the present study, the sensitivity of KKOS was higher at the lumbar spine compared with the femoral neck BMD while the specificity was similar.

The foremost purpose of a risk assessment tool for osteoporosis is to identify individuals at high risk for osteoporosis for whom BMD measurement will be of the clinical relevance in not only the definite diagnosis and fracture risk prediction, but also when obtaining this information will ultimately influence the treatment decision. This present study demonstrated that individuals with high risk from KKOS, the risk of osteoporosis were increased 7-fold. Nevertheless, the

authors suggested that all men with age at ≥ 50 years should be measured and evaluated the BMD by DXA before starting treatment. Moreover, the authors also found that the PPV of KKOS was modest; suggesting its use for an individual is not warranted because of the high false positive rate. The present study finding is limited to apply in a large population with low prevalence of osteoporosis.

The present study has some strength. The authors investigated the prevalence of low BMD in a broad age range of Thai men according to the International Society for Clinical Densitometry (ISCD) recommendation, which is considered a low risk for osteoporosis⁽²⁷⁾. DXA measurements were calculated using a Thai male normative database at the hip and lumbar spine. It very possibly resulted in an accuracy of the prevalence of osteoporosis in the presented population. However, the findings should be interpreted within the context of several limitations: the study subjects were Thai, among whom, body size, lifestyles, and environmental factors are different from other populations. Thus, care should be taken when extrapolating these results to other populations. Indeed, the association among age, body weight, and BMD in men was different from women. Therefore, the scoring system that was developed from women, might have limitations when used in men. The measurement error of BMD could result in misclassification of osteoporosis^(28,29). Body weight was measured at a single time point and may not reflect a true long-term weight of a subject. These two sources of measurement errors albeit inevitable, could have affected the result. However, such a limitation is present in any study of this type. Furthermore, the KKOS as well as other instruments were designed to identify low BMD individuals. However, not all fractures result from low BMD^(30,31). Therefore, the sensitivity and specificity of this instrument in the prediction of fracture cases are expected to be low⁽³²⁾.

In conclusion, KKOS scoring system based on age and body weight, is a simple tool for clinicians to make a decision to further DXA testing for identifying osteoporosis in Thai men. The score is sensitive and specific, but had modest positive predictive value. Its use in the population is not warranted at present due to the high false positive rate; however, its utility may help reduce the costs of investigation and intervention among Thai men.

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ความแม่นยำของดัชนีความเสี่ยงทางคลินิก Khon Kaen Osteoporosis Study (KKOS) ในการช่วยวินิจฉัยโรคกระดูกพรุนสำหรับผู้ชายไทย

ฉัตรเลิศ พงษ์ไชยกุล, เอกลักษณ์ วโนทยาโรจน์

วัตถุประสงค์: เพื่อประเมินการนำดัชนีความเสี่ยงทางคลินิก Khon Kaen Osteoporosis Study (KKOS) ในการค้นหาโรคกระดูกพรุนในผู้ชายไทย

วัสดุและวิธีการ: เป็นการศึกษาแบบตัดขวางในผู้ชายจำนวน 230 คนที่มีอายุตั้งแต่ 50 ปีขึ้นไป ทำการวัดความหนาแน่นของกระดูกที่ตำแหน่งกระดูกสะโพกและกระดูกสันหลังด้วยเครื่องวัดความหนาแน่นของกระดูกยี่ห้อ DPX-IQ บริษัท Lunar ประเทศสหรัฐอเมริกา ค่าความหนาแน่น KKOS จากอายุและน้ำหนัก ผู้ที่คะแนน ≤ -1 และ > -1 จัดเป็นผู้ที่มีความเสี่ยงสูงและต่ำในการเกิดโรคกระดูกพรุนตามลำดับ

ผลการศึกษา: พบความชุกของโรคกระดูกพรุนร้อยละ 17 และ 7.4 ที่ตำแหน่งกระดูกสะโพกและกระดูกสันหลังตามลำดับ มีจำนวน 80 คน (คิดเป็นร้อยละ 34.8) ที่จัดอยู่ในกลุ่มผู้ที่มีความเสี่ยงสูง (คะแนน KKOS ≤ -1) และพบมีความสัมพันธ์กับอายุที่เพิ่มขึ้นโดยพบร้อยละ 16.2 ในกลุ่มอายุ 50-65 ปีและเพิ่มเป็นร้อยละ 64.8 ในกลุ่มอายุ > 65 ปี เมื่อใช้ความหนาแน่นของกระดูกจากเครื่องวัดความหนาแน่นกระดูกเป็นเกณฑ์มาตรฐาน พบว่า sensitivity และ specificity ของ KKOS ในการวินิจฉัยโรคกระดูกพรุนคิดเป็นร้อยละ 72.5 และ 73.2 ตามลำดับ โดยพบ sensitivity ที่ตำแหน่งกระดูกสันหลังสูงกว่าที่ตำแหน่งกระดูกสะโพก (ร้อยละ 94.1 เทียบกับร้อยละ 71.8) ในขณะที่ specificity ใกล้เคียงกัน พบว่า PPV ของ KKOS เท่ากับร้อยละ 36 โดยมีค่า PPV ในการทำนายกระดูกพรุนที่กระดูกสันหลังต่ำกว่าที่กระดูกสะโพก (ร้อยละ 20 เทียบกับร้อยละ 35) การศึกษานี้พบว่าผู้ที่จัดอยู่ในกลุ่มที่มีความเสี่ยงสูงจาก KKOS จะมีความเสี่ยงในการเกิดโรคกระดูกพรุนที่กระดูกสะโพกและ/หรือกระดูกสันหลัง 7.19 เท่า (ค่าความเชื่อมั่น: 3.34-15.44) อย่างไรก็ตามพบว่าความเสี่ยงของการเกิดโรคกระดูกพรุนในกลุ่ม 50-65 ปี เท่ากับ 10.29, ค่าความเชื่อมั่น: 3.31-31.94) ซึ่งสูงกว่าความเสี่ยงของการเกิดโรคกระดูกพรุนในกลุ่มอายุ > 65 ปี (เท่ากับ 3.65, ค่าความเชื่อมั่น: 1.12-11.91)

สรุป: ดัชนีความเสี่ยงทางคลินิกในการทำนายโรคกระดูกพรุน KKOS ซึ่งคำนวณจากอายุและน้ำหนักเป็นเครื่องมือที่ง่ายสำหรับแพทย์ในการประเมินเพื่อตัดสินใจทำการส่งตรวจวัดความหนาแน่นของกระดูกเพื่อหาโรคกระดูกพรุนในผู้ชายไทย เครื่องมือนี้มี sensitivity และ specificity ที่สูงแต่มี PPV ต่ำ