Validate of Clinical Risk Index for Osteoporosis in Thai Women at Phramongkutklao Hospital

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Background..: *Osteoporosis is a common problem found in elderly people and the cost of treatment with its complications is much higher than the cost of diagnosis and prevention. However, diagnosis of osteoporosis is hindered by an unavailability of dual energy x-ray absorptiometry (DXA). Many clinical risk index-scoring systems were developed to help prediction of osteoporosis such as Khon Kaen Osteoporosis Study (KKOS). The KKOS is one among those scoring systems based on the Thai population database. The objectives of the present study were to validate KKOS for prediction of osteoporosis in Thai women at Gynecologic Clinic of Phramongkutklao Hospital and to study the prevalence of women with osteoporosis diagnosed with KKOS.*

Material and Method: *Four hundred forty six Thai women, aged 40 years or more attending the Gynecologic Clinic of Phramongkutklao Hospital, and had Bone mineral density (BMD) result were enrolled in the present study. The results of BMD were measured at the lumbar spine and femoral neck by DXA and KKOS. The score was evaluated and compared.*

Results: *Sensitivity and specificity of KKOS for prediction of osteoporosis were 48.6% and 68.1%, respectively. Prevalence of osteoporosis using KKOS was 23% while 32% were diagnosed with DXA.*

Conclusion: *KKOS had low sensitivity and specificity for diagnosed osteoporosis in Thai women at Gynecologic Clinic of Phramongkutklao Hospital.*

Keywords: *Osteoporosis, Clinical risk scoring system, KKOS*

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The world population has increased rapidly during this century, especially in the last 30 years and especially in Asia. All countries are beginning to experience the effects of the "Aging Society", including Thailand. Many socioeconomic problems are occurring following these demographic changes[1-3].

Many diseases related to aging people are increasing, including osteoporosis[3-5]. Osteoporosis and its ultimate consequence of low traumatic fracture in postmenopausal women represent one of the major public health problems in Asian countries, due to the rapid ageing of the population. Effort of prevention of osteoporotic fracture by early identification of high-risk subjects is likely the most cost-effective approach in Asia. A previous study has shown a prevalence of 19.8% and 13.6% with lumbar and hip osteoporosis respectively[6]. Bone mineral density (BMD) measured by dual energy x-ray absorptiometry (DXA) is regarded as the standard method for BMD assessment and fracture prediction[7-11].

According to WHO criteria, DXA is the gold standard for osteoporosis diagnosis. T-score of less than -1 and -2.5 defined as osteopenia and osteoporosis, respectively[10].

However, in Thailand, DXA is not widely available and the cost of measurement is high[7,11-15]. It is reasonable to use the clinical risk indices for identifying subjects with low BMD or high-risk fracture individuals[15-17]. Bone mineral density is highly related to age and body weight. Indeed, the two factors collectively account for 40 to 60% variance of BMD in the population[7-12]. Some studies have

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suggested that these two factors were sensitive and specific enough to merit a large-scale identification of low BMD[13,14]. The Osteoporosis Self-Assessment Tools for Asians (OSTA) were developed. Its 91% sensitivity and 45% specificity is largely derived from age and body weight. It has been found to be a good and simple tool for the identification of women with osteoporosis risk[17-19]. OSTA score was calculated by the equation 0.2 x [body weight - age]. If the score is less than -4, will be defined as high-risk for osteoporosis. However, OSTA was developed largely from the Chinese population where lifestyles and behavioral factors are likely different from other developing populations such as Thai.

There is a study about osteoporosis in Thai people. It is based on Thai people, the Khon Kean Osteoporosis Study (KKOS)[12]. In the present model, the relationships between age and weight and osteoporosis were expressed in odds ratio, the KKOS score was derived as the sum of odds ratios, with simple clinical risks, age and body weight, and scoring table. Therefore, the authors could calculate the risk for osteoporosis by combining, age-score, and weight-score together. If the total score was less than -1, then it will define as high-risk for osteoporosis. The KKOS was validated in 2004 and demonstrated 70% sensitivity and 73% specificity. The authors tried to access patients with KKOS and compare the result of osteoporosis risk and DXA.

Objective

The aim of the present study was to validate KKOS for prediction of osteoporosis in Gynecologic Outpatient Department, Phramongkutklao Hospital, Bangkok, Thailand and to evaluate prevalence of women with osteoporosis diagnosed with KKOS.

The 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

Material and Method

The present study was performed in the Gynecologic Outpatient Department, Phramongkutklao Hospital. The present study was approved by the Institutional Review Board, Royal Thai Army, Medical Department.

Subjects were invited to meet with a trained research nurse who completed a questionnaire and an informed consent form. Body weight (including light indoor clothing) was measured using an electronic balance scale (accuracy 0.1 kg) and standing height (without shoes) with a standiometer (nearest 0.1 cm).

In all, 446 patients aged 40 years or older with result of bone mineral densitometry using a LUNAR DPX-IQ densitometer (LUNAR Corporation, Madison, WI, USA) were recruited in the present study. Written informed consent was obtained after explaining the research protocol to the patients. Demographic data, including risk factors of osteoporosis and BMD result were recorded, age, and body weight were computed for KKOS, then categorized into high or low risk for osteoporosis.

The results were compared with gold standard and codified, then the sensitivity, specificity, positive predictive and negative predictive values were analyzed. Multiple regression analysis was employed to calculate the correlation between clinical risk factor and KKOS score. Statistical significant was set for $p < 0.05$. Statistical analysis was performed with SPSS® statistical package version 15.0 (Chicago, IL). Descriptive statistics were used for demographic and baseline data and summarized as mean $\pm$ standard deviation (SD) or percent. The sensitivity, specificity, positive predictive and negative predictive values with 95% confidence interval (95% IC) were also computed.

Results

Four hundred forty six patients were included in the present study with and age range between 40 to 79 years old. Most patients were 51 to 60 years old. The average age was 57.31 $\pm$ 7.19 years old.

Average height was 155.33 $\pm$ 5.31 cm, average weight and time of menarche were 57.22 $\pm$ 8.53 kg and 14.62 $\pm$ 1.96 years respectively as show in Table 1.

Most patients were menopausal women, 96.64%, with a history of regular menstruation. The top contraception in this group was oral contraceptive

pill, 63.51%. Eighty six percent of the patients had received some calcium supplement. Only 2.98% of patients were vegetarian. However, 61.17% of patients consumed caffeine. In addition, 78.25% of patients did some exercise.

Forty-four patients had underlying disease. Most were diabetic mellitus (61.36%) and hyperthyroidism (11.36%). Others were rheumatoid arthritis and SLE, which non-active disease. No patient in the present study was currently use steroid.

Concerning osteoporosis, the present study showed 32% of patients had osteoporosis in at least one point of the examined bone. Compared with KKOS, high risk for osteoporosis was 23%.

Table 1. Baseline characteristics

Characteristic factors (n = 446)	n (%)
Age (yr) (mean ± SD)	57.31 ± 7.19
40-50	77 (17.2)
51-60	237 (53.1)
61-70	107 (23.9)
≥ 71	25 (5.6)
Height (cm) (mean ± SD)	155.33 ± 5.31
BW (kg) (mean ± SD)	57.22 ± 8.53
Menarche (yr) (mean ± SD)	14.62 ± 1.96
History of regular menstruation	400 (89.69)
Menopause	431 (96.64)
History of contraception	209 (46.86)
Risk factors of osteoporosis	
Calcium supplement	387 (86.77)
Vegetarian	13 (2.98)
Caffeine consumption	271 (61.17)
Exercise	349 (78.25)
History of fracture	53 (11.8)
Family history of osteoporosis	61 (14.02)

Table 2. Performance of KKOS for diagnoses osteoporosis women

KKOS		95% CI	
		Lower	Upper
Sensitivity	48.6%	44.01	53.29
Specificity	68.1%	63.73	72.39
PPV	33.5%	29.16	37.92
NPV	80%	76.29	83.71

KKOS = Khon Kaen osteoporosis study; PPV = positive predictive value; NPV = negative predictive value

When calculating the performance of KKOS, 48.6% sensitivity, 68.1% specificity, 33.5% positive predictive and 80% negative predictive value was found (Table 2).

Calculating the risk factors affecting the prediction of osteoporosis, it was found that age group, menopausal state and caffeine consumption were statistically significant (Table 3). Using multiple logistic regression model to analyze this data, only age and caffeine consumption demonstrated statistical significance (Table 4).

Discussion

KKOS score was one clinical risk index that demonstrated the correlation with diagnosis of osteoporosis, even though weak correlation and difference from the previous study. The previous study was performed with the women aged not less than 45 years, which is older than in the present study. This increases the chance to meet the osteoporosis women and increase the sensitivity of the KKOS from a previous study[12]. The present study collected data from patients that came to the gynecologic department for gynecologic conditions and from some healthy women who asked for a health-screening program. Probably the life styles of people who live in Bangkok (such as daily meal, official working) may be different from the people in Khon Kean province and might be the causes of a different result.

Few women in the present study had underlying disease, 21 from 446 were diabetics. Eleven women were diagnosed of thyrotoxicosis, but completed treatment for more than five years, just one from 11 thyrotoxicosis women currently on PTU 50 mg per day with euthyroid state. Another five patients with a history of rheumatoid arthritis completed treatment and quit steroid use (latest steroid use in the year 2002). Only one woman with a history of SLE, which was diagnosed for 20 years ago, was in remission for 13 years. The data from those women was also included in the present study, and the authors found one from the thyrotoxicosis group and another two women from the diabetics group had osteoporosis, which was probably age related. Those three women were more than 60 years old.

One amazing result from the present study was the women who consumed caffeine were less likely to have osteoporosis, explained by the fact that most of caffeine consumers were younger than the other non-caffeine consumers, so younger patients were more active and at lower risk for osteoporosis.

Table 3. Univariated analysis of each clinical factor and osteoporosis (n = 446)

	n	%	p-value	Odds ratio	95% CI	
					Lower	Upper
Age group						
≤ 60 yr	314	70.40	<0.001	4.878	3.160	7.532
> 60 yr	132	29.60				
History of contraception						
None	235	52.69		1.00		
Hormonal	170	38.12	0.487	0.849	0.535	1.347
Non-hormonal	41	9.19	0.907	1.045	0.494	2.213
Menopausal status	431	96.64	0.016	8.266	1.077	63.450
History of regular menstruation	400	89.69	0.400	0.753	0.389	1.457
History of breast feeding	312	70.11	0.648	0.906	0.592	1.385
Risk factors of osteoporosis						
Smoking	33	7.40	0.276	0.644	0.292	1.421
Alcohol consume	7	1.57	0.255	0.291	0.035	2.436
Calcium supplement	387	86.77	0.126	0.621	0.338	1.143
Vegetarian	13	2.98	0.852	0.897	0.288	2.792
Caffeine consume	271	60.70	0.002	0.532	0.358	0.791
Exercise	349	78.25	0.152	0.701	0.431	1.139
Family history of osteoporosis	61	14.02	0.154	0.671	0.388	1.161
Underlying disease	44	9.87	0.154	1.490	0.861	2.579

Table 4. Multivariate analysis of each clinical factor and osteoporosis (n = 446)

	n	%	p-value	Adjusted odds ratio	95% CI	
					Lower	Upper
Age group						
≤ 60 yr	314	70.40	<0.001	4.923	3.144	7.709
> 60 yr	132	29.60				
Menopausal status						
Yes	431	96.64	0.130	4.892	0.627	38.196
No	15	3.36				
Caffeine consume						
Yes	271	61.17	0.001	0.467	0.304	0.718
No	172	38.83				

That much difference from the knowledge base the authors have, however some studies that reported about the caffeine effect with osteoporosis that is still controversial[21,22]. Cooper C et al[22] found that caffeine consumption tended to be associated with higher bone mineral at younger ages. However, among those aged 60 years old and above, there was a small negative relationship between bone mineral and caffeine intake. In the present study, this is not the objective, so the authors cannot conclude that it is a protective factor for osteoporosis.

The osteoporosis screening by KKOS at Phramongkutklao Hospital, still cannot be used as a screening tool due to its low sensitivity and specificity. However, if the authors would create a new cut point for diagnosis of high-risk for osteoporosis, it may be useful.

Because DXA machines are not available and the KKOS is not sensitive enough, using a clinical risk index in clinical practice may encourage women to take preventative measures to preserve their skeletal status. This could ultimately reduce fracture incidence.

Increase the osteoporosis preventive idea could reduce osteoporosis fracture and osteoporosis complications.

Conclusion

KKOS was validated in Phramongkutklao Hospital. It showed low sensitivity and specificity, which much different from a previous study of KKOS at another location.

Each clinical risk index scoring systems is appropriate to its specific population, but when adopting any scoring system to use as a screening tool, validation is necessary with careful interpretations.

Osteoporosis will continue be an increasing health problem. Not only early diagnosis, but also primary preventions such as advocating calcium supplements and encouraging weight barring exercise should be done.

Potential conflicts of interest

None.

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ความแม่นยำของดัชนีชี้วัดความเสี่ยงทางคลินิกในการวินิจฉัยโรคกระดูกพรุนในหญิงไทย กองสูตินรีเวชกรรม โรงพยาบาลพระมงกุฎเกล้า

เอกชัย ลีอังกูรเสถียร, ปองรัก บุญญานุรักษ์, ฉัตรเลิศ พงษ์ไชยกุล, สุธี พานิชกุล

ภูมิหลัง: *โรคกระดูกพรุนมีความสำคัญและมีการวินิจฉัยได้หลายวิธี วิธีการใช้ดัชนีความเสี่ยงทางคลินิก (clinical risk index) เช่น Osteoporosis self-assessment tool for Asian (OSTA) หรือ Khon Kaen Osteoporosis Study (KKOS) เพื่อเป็นการคัดกรองเบื้องต้นหาผู้ที่มีความเสี่ยง หรือ การทำนายโอกาสต่อการเป็นโรคกระดูกพรุน เป็นการลดค่าใช้จ่ายและเกิดความคุ้มค่าในการตรวจและรักษา การศึกษานี้มีวัตถุประสงค์เพื่อศึกษาความแม่นยำของดัชนีความเสี่ยงทางคลินิกโดยใช้ Khon Kaen Osteoporosis Study ในการช่วยวินิจฉัยในผู้ป่วยหญิงไทย ซึ่งรับการตรวจรักษาในห้องตรวจผู้ป่วยนอก กองสูตินรีเวชกรรม โรงพยาบาลพระมงกุฎเกล้า และเพื่อศึกษาถึงความชุกของภาวะกระดูกพรุนในผู้ป่วยที่มาตรวจที่โรงพยาบาลพระมงกุฎเกล้า โดยใช้ดัชนีความเสี่ยงทางคลินิกโดยใช้ Khon Kaen Osteoporosis Study*

วัสดุและวิธีการ: *ผู้ป่วยที่มารับการรักษาที่ห้องตรวจผู้ป่วยนอก กองสูตินรีเวชกรรม โรงพยาบาลพระมงกุฎเกล้า ที่มีอายุตั้งแต่ 40 ปี ขึ้นไป และมีผลตรวจความหนาแน่นมวลกระดูก (DXA) แยกผู้ป่วยที่มีโรค หรือ อยู่ระหว่างการได้รับยาที่มีผลต่อความหนาแน่นมวลกระดูก โดยหลังจากผู้ป่วยให้ความยินยอมในการเข้าร่วมการศึกษาจะได้รับการสอบถามข้อมูลต่าง ๆ เกี่ยวกับโรคกระดูกพรุน และบันทึกผลลงในแบบบันทึกข้อมูล หลังจากนั้นจึงรวบรวมข้อมูลและนำไปวิเคราะห์หาความสัมพันธ์*

ผลการศึกษา: *พบว่า KKOS ให้ผลความไวในการวินิจฉัยโรคกระดูกพรุน 48% ความจำเพาะ 68% โดยมีค่า positive predictive value 33.5% และ negative predictive value 80% พบว่าเมื่อใช้ KKOS ในการวินิจฉัยภาวะกระดูกพรุนในกลุ่มผู้ป่วยดังกล่าว มีความชุกของโรคกระดูกพรุน 23% เมื่อเปรียบเทียบกับวิธีมาตรฐานที่ตรวจพบความชุก 32%*

สรุป: *KKOS ให้ผลลัพธ์ในการทำนายภาวะกระดูกพรุนได้ตามวิธีการตรวจมาตรฐาน แต่มีความไวและความจำเพาะต่ำเมื่อนำมาใช้ที่โรงพยาบาลพระมงกุฎเกล้า*