The Diagnostic Value of Combined Risk Factor Analysis and Radiological Imaging in Determining Osteoporosis in Post-menopausal Women

Indah Trijoto*, Harry Isbagio**, Bambang Setiyohadi**, Sidartawan Soegondo, Kahar Kusumawidjaja****, Iwan Ariawan********

ABSTRACT

Aim: *to determine the diagnostic value of risk factor analysis (age, duration of menopause, body mass index and physical activities) and radiological imaging (Singh index and cortical index of the femoral neck) in diagnosing osteoporosis in post-menopausal women.*

Methods: *the study was cross sectional on 64 post-menopausal women without secondary risk factor for osteoporosis. They were classified proportionally using the Singh index. Bone density was measured using DEXA (dual x-ray absorptiometry) on the femoral neck and lumbal 2-4 spine areas. The Singh index and cortical index of the femoral neck were evaluated using femoral neck antero-posterior x-ray. Physical activities were measured using a Historical leisure activity questionnaire. Bivariat statistical analysis was conducted using the t-test and chi-square, whereas multivariate analysis was conducted using multinomial logistic regression.*

Results: *there was a significant association ($p < 0.05$) between bone density and age, body weight, height, body mass index, duration of menopause and Singh index. With multinomial logistic regression analysis, it was demonstrated that only Singh index, the duration of menopause and body mass index had the highest sensitivity and specificity. The score system algorithm could be utilized in two steps, the first was to diagnose osteoporosis and the second was to distinguish between osteopenia and normal bone. This score system had a sensitivity of 91.4% and a specificity of 89.6%, a positive prediction value of 91.4% in determining osteoporosis, and a sensitivity of 66.7%, a specificity of 89.1% and a positive prediction value of 70.6% in determining osteopenia, whereas the negative prediction value was 75%.*

Conclusion: *the score system algorithm is the best method for determining osteoporosis in post-menopausal women. If there is osteopenia, evaluation using DEXA is then required. The score system algorithm cannot be used to follow up the therapy.*

Key words: *osteoporosis, osteopenia, dual x-ray absorptiometry (DEXA), post-menopausal women.*

INTRODUCTION

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. Using the World Health Organization definition, an estimated 54% of post-menopausal Caucasian women in the United States have osteopenia and 30% have osteoporosis. Each year in the United States, approximately 500,000 spine fractures, 250,000 hip fractures and 240,000 wrist fractures are attributed to osteoporosis.[1]

Bone densitometry is an accurate and precise method for assessing bone density, and can be used to assess the risk prognosis, to predict the risk of fracture and to diagnose of osteoporosis.[2] Dual x-ray absorptiometry (DEXA) that can determine osteoporosis is not accessible to all areas in Indonesia.[3] Therefore, it is necessary to find an alternative method applicable to the conditions in rural areas to determine early osteoporosis, so that osteoporosis may be treated earlier and osteoporosis-associated fracture may be prevented.

Conventional radiographs provide limited information to bone structure, due to very high

** Department of Internal Medicine, faculty of medicine, University of Indonesia-Dr. Cipto Mangunkusumo National General Hospital, ** Division of Rheumatology, *** Division of Metabolic and Endocrinology, Department of Internal Medicine, Faculty of Medicine, University of Indonesia-Dr. Cipto Mangunkusumo Hospital, **** Department of Radiology, Faculty of Medicine, University of Indonesia-Dr. Cipto Mangunkusumo Hospital, Jakarta, ***** Department of Biostatistic, Faculty of Public Health, University of Indonesia, Depok*

subjectivity. There are also semi-quantitative estimation methods of conventional radiographs to determine bone density, such as the Singh index and cortical index of the femoral neck.[4]

In 1970 Singh et al recognized the basic trabecular patterns of the proximal femur and formulated an x-ray scale called the osteoporosis index. The Singh index describes the changes in trabecular pattern of the upper end of the femur from an x-ray scale formulated in six grades representing increasing degrees of bone loss. Several advantages of this method are that anatomically the upper end of the femur has predominant trabeculae and is composed in a unique trabeculae pattern system, that this region is also the site of the main symptom of osteoporosis and risk of fractures with the highest mortality, and that this method is universally applicable because the grading is independent of age, sex and race. Instead, the trabecular pattern changes as increasing amounts of the original bone are lost.[5]

The trabecular patterns of the femoral neck, cortical thickness of the femoral neck, and the combination of both have been used to measure mineral loss and for the grading of osteopenia.[4,6,7] Evaluation of the cortical thickness in diaphyseal bone on x-ray films has been demonstrated to be a useful tool for the estimation of bone mass.[4,7] Cortical thickness is measured just above the lesser trochanter and corresponds to the thickness of the calcar femorale measured by others.[6] The cortical index of the femoral neck is the ratio between the measured thickness of the medial cortex divided by the width of the femoral neck in its most narrow part.[7,8] The cortical index of the femoral neck does not decrease according to age. However, it decreases in women with fracture, with the value of 0,12. Therefore, it may have some use as an instrument to predict femoral neck fracture.[7] An unpublished research reported that the cortical index of the femoral neck correlated with measured bone mass density in post-menopausal women with spine fracture.[9]

The risk factors for osteoporosis on post-menopausal woman are age, duration of menopause and lowering of estrogen. Whereas the protective factors for osteoporosis are higher estrogen levels, obesity and exercises.[3,10] Women have a higher risk of osteoporosis compared to men because they have a lower peak bone mass, smaller bone measurement and faster bone loss after menopause.[11]

Less physical activity and exercise are risk factors for osteoporosis. In 1892, Wolff, an anatomist from Germany, demonstrated that bone responded to workload and higher physical activity by increasing in thickness or density and thus decreased the incidence rate of bone fracture.[12]

Mizuno et al proved lower body mass index (BMI) as a risk factor for osteoporosis in post-menopausal woman. This condition was due to decreased adrenal androgen conversion to estrone in adiposal cells in woman with lesser body weight.[13]

METHODS

This research was a cross sectional study conducted from January to February 2002 at the outpatient clinic of the Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine of the University of Indonesia/Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia.

There were 64 post menopause women, classified proportionally using the Singh index. Inclusion characteristics were post-menopausal women who were willing to participate in the research. Exclusion characteristics were those suffering from chronic renal diseases, chronic liver diseases, diabetes mellitus, bone malignancy, hyperthyroidism, calcium metabolism disturbance, fracture of both femoral neck, positioning error disturbance during densitometry, anti-resorptive bone treatment, steroid therapy, and history of oovorectomy.

Bone density was measured using DEXA (dual x-ray absorptiometry) of the femoral neck or lumbal 2-4 spine areas. Osteoporosis was defined as bone density of more than 2.5 SD below the mean for young adult women (T score ≤ -2.5 SD). Osteopenia was defined as a T score between 1 SD to 2.5 SD below the mean for young adult women (-1 SD ³ T score > -2.5 SD). Whereas the normal was T score > -1 SD.[2]

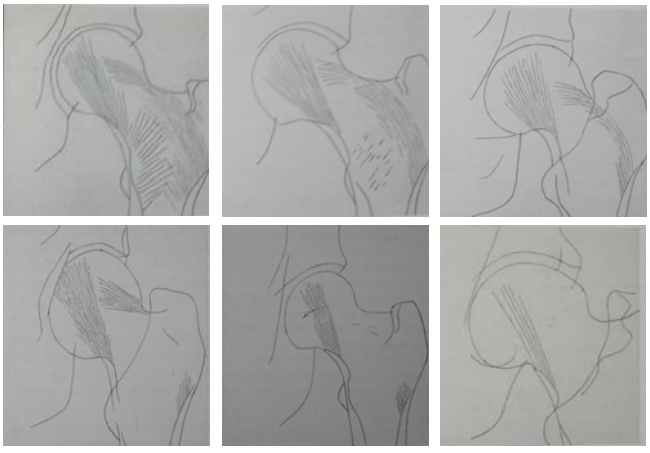
The Singh index and cortical index of the femoral neck were evaluated using femoral neck antero-posterior x-ray. Diagramatic representation of the five normal groups of trabeculae was in the upper end of the femoral neck (figure 1). [5]

Description of the six different trabecular pattern in Singh index which is representative of increasing degrees of bone loss [5] :

1. Grade six : All the normal groups of trabeculae are visible in the roentgenogram, representing normal bone.
2. Grade five : The principal compressive and tensile trabecular groups become more prominent due to the resorption of many thin trabeculae. The secondary compressive trabeculae are no longer

clearly demarcated. Therefore Ward's triangle looks empty and more prominent. This pattern represents the early stages of bone loss.

3. Grade four : The tensile trabeculae are markedly reduced in number. Resorbtion appears to be proceeding outward from the center of the bone. Therefore the principal tensile trabeculae in the outer of the bone can still be traced in continuity from the lateral cortex to the upper part of the neck of the femur, while the secondary compressive trabeculae are completely resorbed so that Ward's triangle opens up laterally. This picture represents what is considered to be the borderline between osteoporosis and normal skeletons.
4. Grade three : There is a break in the continuity of the principal tensile group of trabeculae opposite the geater trochanter. Therefore, the tensile trabeculae are clearly seen only in the upper part of the femoral neck. This pattern indicates definite osteoporosis.
5. Grade two : The only prominent trabeculae are the principal compressive group. All other groups are more or less completely resorbed. This picture is an index of a moderately advanced osteoporosis.
6. Grade one : The principal compressive trabeculae do not stand out in x-ray and are markedly reduced in number. This pattern shows the most severe degrees of osteoporosis.



F igure 1. The Trabecular Pattern of The Singh Index

Physical activities were measured using a historical leisure activity questionnaire on MET (basal metabolic equivalent).[14] Age and duration of menopause was recorded in year, body mass index in kg/m^2. Bivariate statistical analysis was conducted using t-test and chi-square, whereas multivariate was conducted using multinomial logistic regression with the best subset method.

RESULTS

There was a significant association ($p<0.05$) between bone density and age, body weight, body mass index, duration of menopause and Singh index (table 1).

Correlations between the Singh index and the bone density were as follows: Grade 1 Singh index showed all osteoporosis (100%), grade 2 represented 85.7% osteoporosis and 14.3% non-osteoporosis, grade 3 showed osteoporosis 40% and 60% non-osteoporosis, grade 4 & 5 had the same results for osteoporosis 36.4% and 63.6% non-osteoporosis, grade 6 osteoporosis 42.9% and 57.1% non-osteoporosis (table 2).

Table 1. The Statistical Tests of Risk Factors of Osteoporosis on Post-menopausal Women

No	Independent variable	p
1	Age	< 0,001
2	Duration of menopause	< 0,001
3	Body weight	< 0,001
4	Height	< 0,001
5	Body mass index (BMI)	< 0,001
6	Pregnancy	0,681
7	Physical activities	
	a. 15 - 35 yo	0,16
	b. > 35 yo	0,155
8	Calcium intake	
	a. 15 - 35 yo	0,288
	b. > 35 yo	0,699
9	Cortical index of femoral neck	0,115
10	Singh index	0,003

Table 2. The Singh Index on DEXA

	BMD of femoral neck or vertebrae L2-4 (DEXA)	
Singh index	Osteoporosis (%)	Non-osteoporosis (%)
1	6 (100)	0
2	12 (85,7)	2 (14,3)
3	6 (40)	9 (60)
4	4 (36,4)	7 (63,6)
5	4 (36,4)	7 (63,6)
6	3 (42,9)	4 (57,1)

Singh index was put into four groups because of clinical importance as well as to make statistical analysis easier. Grade 4/5/6 had nearly the same value. Therefore, the results were as follows : grade 1 of Singh index showed osteoporosis 100%, grade 2 85.7% osteoporosis, grade 3 only 40% osteoporosis. Grade 4/5/6 showed 62.1 % osteoporosis. In statistical test, this model had a p value of less than 0.001.

With multinomial logistic regression analysis, only Singh index, duration of menopause and body mass

index had higher sensitivity and specificity. The Singh index had the highest predictive value between them.

Table 3 shows the results of multinomial logistic regression analysis. There are two steps to determine bone density status. The first step is to determine the score of osteoporosis and non-osteoporosis, if the score equals to or is more than 0, it is concordant with osteoporosis and a score less than 0 represents non-osteoporosis (osteopenia or normal). We then continue to the second step to determine the scores for osteopenia and normal. Score [3] is concordant osteopenia and score < 0 is normal.

Table 3. The Multinomial Logistic Regression Analysis

		koefisien	standar error koef	p
Osteoporosis	Konstante	11,46	8,21	0,16
	Menopause	0,32	0.16	0,04
	BMI	-0,56	0,32	0,08
	Singh 1	17,15	0	< 0,001
	Singh 2	22,03	16164,57	0,99
	Singh 3	-0,64	2,06	0,75
	Singh 4,5,6	0	-	-
Osteopenia	Konstante	0,81	6,52	0,90
	Menopause	0,15	0,14	0,90
	BMI	-0,06	0,25	0,29
	Singh 1	-2,04	0	0,80
	Singh 2	18,52	16164,57	< 0,001
	Singh 3	0,93	1,46	0,99
	Singh 4,5,6	0	-	-

The First Step: Osteoporosis Score

Grade 1 & 2 in Singh index with this formula always showed score 0.[3] Thus, in this step only the following formula is needed :

Singh 1 and 2 : Osteoporosis

Singh 3 :

Score = 11.46 – 0.64 + 0.32 MP – 0.56 BMI
= 10.82 + 0.32 MP – 0.56 BMI
~ 10.8 + 0.3 MP – 0.6 BMI

Singh 4/5/6 :

Score = 11.46 + 0.32 MP – 0.56 BMI
~ 11,5 + 0.3 MP – 0.6 BMI

Scores 0 indicated osteoporosis
< 0 indicated osteopenia or normal bone, and continued to the second step.[3]

The Second Step: Osteopenia Score

Singh 3 :

Score = 0.81 + 0.93 + 0.15 MP – 0.06 BMI
= 1.74 + 0.15 MP – 0.06 IMT
~ 1.8 + 0.2 MP – 0.1 IMT

Singh 4/5/6 :

Score = 0.81 + 0.15 MP – 0.06 IMT
~ 0.8 + 0.2 MP – 0.1 IMT

Scores 0 indicated osteopenia
< 0 indicated normal bone.[3]

Sensitivity :
Osteoporosis : 32/35 = 91.4% (CI 95%: 75.8 – 97.8%)
Osteopenia : 12/18 = 66.7% (CI 95% : 41.2 – 85.6%)

Positive predictive value :
Osteoporosis : 32/35 = 91.4% (CI 95% : 75.8 – 97.8%)
Osteopenia : 12/17 = 70.6% (CI 95% : 44.0 – 88.6%)

Negative predictive value : 9/12 = 75%
(CI 95%: 42.8 – 93.3%)

Table 2x2 analysis brought about the model having :

Specificity
Osteoporosis : 26/29 = 89.6% (CI 95% : 67.9 - 100%)
Osteopenia : 9/11 = 81.8% (CI 95% : 47.8 – 96.8%)

Accuracy value of the model :

$$\frac{32 + 12 + 9}{64} = \frac{53}{64} = 82.8\ \%$$

DISCUSSION

In this study, the mean of menopause age was 48.1 years old. Kriska et al (1988) reported the mean of age of menopause in American women was 49.1 years old.[15] Riphagen (1985) reported 48 years old in Indonesian women and 50 years old in American women, he stated that the age of menopause in developing nations was lower than in developed nations.[16]

The mean of physical activity in the period of 15-35 years old was 182.96 MET (52.92 – 293.43 MET) and 172.972 MET (70.14 – 286.23 MET) in the period of >35 years old. There was no significant association between physical activities for both periods with bone mass density. Several prospective and case control studies reported that weight bearing physical activity increased bone density compared to control.[17-22] Thus it is protective factor to osteoporosis. Kriska M et al (1988) demonstrated a significant association between past physical activity (using Paffenbarger survey and the large scale integrated motor activity monitor) and bone density 223 post-menopausal women, although the correlation was weaker than the correlation between age and body mass index, especially in >58 years old.[15] The difference between this study and that may be due to a difference in methods. This research was a proportional cross sectional study using Singh index, with a dominant sample of older women (59.4% >60 years old) with a mean BMI of 22.97 kg/m^2.

The association between cortical index of the femoral neck and bone density in post-menopausal women was not significant. Fredensborg and friends (1977) reported a significant correlation in post-menopausal women with femoral neck fracture.[7,8] Gutteridge (2000) also reported that it had a significant correlation in post-menopausal women with spine fracture.[9] Both of them demonstrated that cortical index of the femoral neck did not decrease with age.[7,9] A different result was obtained by Fredensborg and Gutteridge, because this result was not due to fracture, but it was concordant with Hartoko R (2001), who demonstrated that cortical index of the femoral neck had no correlation with bone density (DEXA) of femoral neck.[23]

The Singh index has a significant correlation with bone density in DEXA. This result is concordant with a report by Singh (1970) that Singh index has a correlation with the grading of iliac biopsy histology to estimate bone density.[5] Hartoko R (2001) also reported a correlation between Singh index and DEXA of femoral neck.[23]

Body habits influence osteoporosis. Body weight has a strong and positive association with bone mass density, [24] thin body mass poses increase risk of osteoporosis.[25] In this study, there was a significant association between body weight, height and BMI with bone mass but on logistic regression analysis, BMI was found to have a better predictive value than body weight and height.

Age and bone density have a significant association in post-menopausal women. This is concordant with subsequent studies reporting that bone density decreases in people over 40-50 years old. Older people have decreased intestinal calcium absorption, increased parathyroid hormone, decreased calcitonin products and older multicellular bone units. These are predisposition factors for bone mass decrease.[24]

Bone mass loss will increase 1%/year after menopause due to the decrease in estrogen and progestin. It will be further decreased in 60-65 years old.[24] This is in concordant with the results of this study, where the duration of menopause demonstrates an influence on bone density.

Statistically tested, the method had a 91.4% sensitivity in measuring bone density to diagnose osteoporosis, with DEXA as a gold standard. This means that when DEXA was used to diagnose osteoporosis, 91.4% of cases could be diagnosed using the algorithm score system method. The positive predictive value was 91.4%, which means that when the model of algorithm score system indicates osteoporosis, the probability of bone density proving osteoporosis is as much as 91.4%, the remainder 8.6% being osteopenia and 0% normal. The specificity test results using 2 x 2 table to differentiate between osteoporosis and non-osteoporosis (osteopenia and normal) demonstrated an 89.6% specificity of that method, which means that if DEXA indicates no osteoporosis, that method will show bone density being non-osteoporosis (osteopenia and normal) as much as 89.6%.

The sensitivity of method for diagnosis of osteopenia was 66.7%, which means that if DEXA shows osteopenia, 66.7% of those cases can be diagnosed using the algorithm score system. The positive predictive value was 70.6%, which means that if the model of algorithm score system shows osteopenia, the probability of bone density proving osteopenia is as much as 70.6%, 17.6% of which should be osteoporosis, 11.8% normal. The specificity test using 2 x 2 table to differentiate between osteopenia and non-osteopenia (normal) resulted in a specificity of 81.8%. This means that if DEXA shows no osteopenia, as much as 81.8% will show a bone density of non-osteopenia (normal).

Conversely, if the algorithm score system used to measure bone density shows normal density, the probability of bone density being normal is as much as 75%. (negative predictive value), the remainder 25% being osteopenia and 0% osteoporosis.

Based on these statistical tests, the algorithm score system is the best alternative method to detect the bone mineral density, especially to establish the diagnosis of osteoporosis in post-menopausal women, in places where DEXA or other equipment is absent. But when this method shows osteopenia, we should confirm the diagnosis using DEXA equipment. The osteoporosis state is the moment for women to begin to receive anti-resorptive therapy.

To measure bone mineral density, we performed measurement of bone density based on the WHO recommendation in this study, in which examination was conducting using DEXA densitometry, with the lowest value of bone density taken from at least 2 locations (especially column femur and vertebrae). Therefore, if the algorithm score system shows osteoporosis, treatment can be started.

Radiographic appearance of osteoporosis bone in plain film is more radiolucent than normal bone, but it is generally well accepted that osteoporosis state in plain film can be recognized if bone mass decreases to about 30%.[26,27] Using a combination of radiographic appearance of the column femur and risk factors

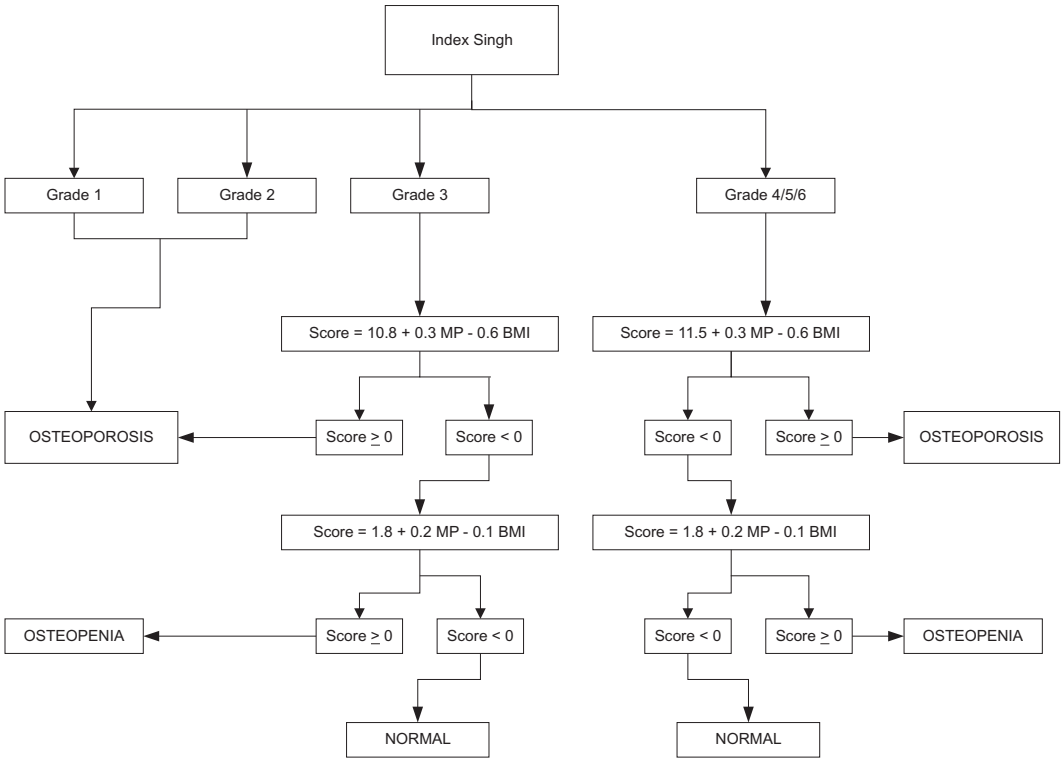


Figure 2. The Algorithm Score System

(menopause interval and bone mass index), osteoporosis state can be detected earlier in areas in which bone densitometry (DEXA or another) equipment is absent.

Even though this method is useful to make the first diagnosis, it cannot be used to evaluate follow up therapy, because appearance of trabeculae structure on plain film does not change after therapy.

If we want to use this algorithm score system method to evaluate bone density, we will need to prepare situations to reduce the limitation of this method, such as through standardization of filming conditions, and introduction of the Singh index to radiologists and clinicians.

Suggestions to post-menopausal women to prevent osteoporosis are to decrease risk factors of osteoporosis, by increasing calcium intake and increasing body weight so that bone mass index will increase.

Example :

Grade 3 Singh index :

5 years menopause (MP) and BMI 25,7 kg/m^2

BMD by DEXA test : Femoral neck = -2.34

Spine lumbal 2-4 = -2.05 ~ Osteopenia

Using algorithm the score system:

1st step : Score = 10.8 + 0.3 MP – 0.6 BMI

= 10.8 + 0.3 (5) – 0.6 (25.7)

= 10.8 + 1.5 – 15.42

= -3.12 ~ Osteopenia/normal

2nd step : Score = 1.8 + 0.2 MP – 0.1 BMI

= 1.8 + 0.2 (5) – 0.1 (25,7)

= 1.8 + 1 – 2.57

= 0.23 ~ Osteopenia

CONCLUSION

The diagnosis of osteoporosis, osteopenia and normal in post-menopausal woman without risk factors of secondary osteoporosis, can be established using the score system of algorithm from Singh index, duration of menopause and BMI in the areas without the DEXA test.

The score system of algorithm has a sensitivity of 91.4%, a specificity of 89.6% and a positive predictive value of 91.4% in determining osteoporosis. It has a sensitivity of 66.7%, a spesificity of 81.8% and a positive predictive value of 70.6% in determining osteopenia. The negative predictive value is 75%.

The score system of algorithm is better in determining osteoporosis in post-menopausal women but if it shows osteopenia, there will be further necessity to confirm with DEXA test.

The score system algorithm can be used to make the first diagnosis of osteoporosis, but cannot be used to

do follow up therapy.

There is a positive trend between calcium intake and bone density, especially in the period of <35 years old.

Standardization of film conditions for evaluation using the Singh index and training to read the Singh index should decrease variation of measurement.

Osteoporosis in post-menopausal women can be prevented by increasing body weight and calcium intake.

Additional study is needed to learn the role of Singh index and risk factor analysis in evaluating treatment respond.

REFERENCES

1. Lenchik L, Sartoris DJ. Current concepts in osteoporosis. AJR 1997;168:905-11.
2. Setiyohadi B. Pendekatan klinis osteoporosis. The 1st Indonesian course on osteoporosis. Sukabumi: Aryaduta, Lido; 2000.
3. Isbagio H, Kasjmir YI, Setiyohadi B. Osteoporosis in Asean: the Indonesian experience. The 1st Indonesian course on osteoporosis. Sukabumi: Aryaduta, Lido; 2000.
4. Cooper C, Barker DJP, Hall AJ. Evaluation of the Singh index and femoral calcar width as epidemiological methods for measuring bone mass in the femoral neck. Clin Radiol 1986;37: 123-5.
5. Singh M, Nagrath AR, Maini PS, et al. Changes in trabecular pattern of the upper end of the femur as an index of osteoporosis. J Bone Joint Surg 1970;52-A:457-67.
6. Griffiths HJ, Virtama P. Cortical thickness and trabecular pattern of the femoral neck as a measure of osteopenia. Invest Radiol 1990;25:1116-9.
7. Fredensborg N, Nilsson BE. Cortical index of the femoral neck. Acta Radiol Diag 1977;18:492-6.
8. Fredensborg N, Nilsson BE. The bone mineral content and cortical thickness in young women with femoral neck fracture. Clin Radiol Related Res 1977;124:161-4.
9. Guterridge (unpublish)
10. Rachman IA. Osteoporosis: on overview. The 1st Indonesian course on osteoporosis. Sukabumi: Aryaduta, Lido; 2000.
11. Biben A. Penatalaksanaan osteoporosis pada wanita pasca menopause. The 1st Indonesian course on osteoporosis. Sukabumi: Aryaduta, Lido; 2000.
12. Twomey L. Physical activity and aging bones. J Paed Obstet Gyn 1992: 23-31.
13. Mizuno K, Suzuki A Asada Y, Kikhawa F, et al. Post menopausal bone loss in Japanese women. Int Fedr Gyn Obst 1995;50: 33-9.
14. Pereira MA, Fitzgerald SJ, Gregg EW, Joswiak ML, Ryan WJ, Suminski RR, et al. A collection of physical activity questionnaires for health-related research. Med Sci Sport Exerc 1997;29(suppl 6):S1-S205.
15. Kriska AM, Sandler RB, Cauley JA, Laporte RE, Hom DL, Pambianco G. Assessment of historical physical activity and its relation to adult bone parameters. Am J Epidemiol 1988;127:1053-63.
16. Samil RS, Affandi B. Menopause di Indonesia : Globalisasi dan bangsa yang mandiri. Dalam : Hestiantoro A, Baziad A, Sungkar A, Samil RS, eds. Makalah seminar menopause. Kongres Obstetri & Ginekologi XI ; 2000 Juli 1 ; Bali, Indonesia. Jakarta : Panitia KOGI XI; 2000.p. 1-10.
17. Dalsky GP, Stocke KS, Ehsani AA, Slatopolsky E, Lee WC, Birge SJ. Weight-bearing exercise training and lumbar bone mineral content in postmenopausal women. Ann Int Med 1988;108:824-8.
18. Nguyen TV, Kelly PJ, Sambrook PN, Gilbert C, Pocock NA, Eismen JA. Lifestyle factors and bone density in the elderly: Implications for osteoporosis prevention. J Bone Mineral Res 1994;9:1339-46.
19. Cooper C, Barker DJP. Risk factors for hip fracture. N Engl J Med 1995;332:814-5.
20. Jaglal SB, Kreiger N, Darlington G. Past and recent physical activity and risk of hip fracture.Am J Epidemiol 1993;138:107-18.
21. Rahayu RR. Faktor-faktor risiko terjadinya osteoporosis pada wanita pasca menopause. Tesis. Jakarta: Bagian Ilmu Penyakit Dalam FKUI, 1997.
22. Gregg EW, Cauley JA, Seeley DG, Ensrud KE, Bauer DC. Physical activity and osteoporotic fracture risk in older women. Ann Int Med 1988;129:81-8.
23. Hartoko R. Menilai korelasi indeks Singh dan indeks kortek leher femur dengan Dual X-Ray Absorptiometry (DEXA) leher femur. Tesis. Jakarta: Bagian Radiologi FKUI, 2001.
24. Morgan SL, Saag KG, Julian BA , Blair H. Osteopenic bone diseases. Arthritis and allied condition, 14th ed. Philadelpia: Lippincott Williams & Wilkins;2001. p. 2449-513.
25. Hahn BH. Osteopenic bone diseases. Arthritis and allied condition, 13th ed. Baltimore: William & Wilkins;1997. p. 2203-31.
26. Resnick P. Osteoporosis: radiographic – pathologic correlation. In: Genant HK, ed. Osteoporosis update 1987. California: University of California printing services;1987. p. 31-9.
27. Ahmed AIH, Ilic D, Blake GM, Rymer JM, Fogelmen I. Musculosceletal imaging. Review of 3,530 referrals for bone density measurement of spine and femur: evidence that radiographic osteopeni predicts low bone mass. Radiology 1998; 207:619-24.