Bone Mineral Content in a Sample of Indonesian Population

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Abstrak

Telah dilakukan pemeriksaan CT QCT (Quantitative Computed Tomography) pada 223 subjek penelitian yang terdiri dari 164 wanita (rata-rata umur 38,84 tahun) dan 59 pria (rata-rata umur 43 tahun) yang sehat dengan menggunakan pesawat CT-Scan Somatom - CR (Siemens AG, Erlangen Germany). Digunakan fantom kalibrasi dari Siemens yang terdiri atas 2 komponen yaitu air dan 200 mg/ml Hydroxyapatite. Beberapa kesimpulan yang didapat adalah:laju penurunan kandungan mineral tulang menurut umur pada subjek wanita tidak berjalan homogen, yaitu terjadi percepatan penurunan pada masa peri-menopause; laju penurunan kandungan mineral tulang menurut umur pada subjek pria berjalan homogen; nilai kandungan minneral tulang rata-rata pada pria Indonesia pada berbagai kelompok umur tidak jauh berbeda dengan penelitian-penelitian di mancanegara sedangkan pada wanita umur 50 tahun juga tidak jauh berbeda, setelah periode umur tersebut menunjukkan adanya perbedaan; dan nilai rata-rata kandungan mineral tulang menurut umur pada kelompok pria dan wanita berdasarkan model regresi.yang sesuai dapat dipertimbangkan sebagai nilai-nilai acuan di Indonesia.

Abstract

Quantitative Computed Tomography (QCT) was performed on 223 healthy subjects, consisting of 164 females (average age 38.84 years) and 59 males (average age 43 years), using a Somatom - CR CT-Scanner (Siemens AG, Erlangen, Germany). A Siemens calibration phantom, which is composed of 2 components, water and 200 mg/ml hydroxyapatite, was used. The rate of BMC reduction with age in the female subjects was found to be not uniform. There was accelerated reduction during the perimenopausal period. This rate of reduction was found to be uniform in the male subjects. The average BMC of these male Indonesian in the various age groups did not differ greatly from reference values of other countries, as was also found in the female Indonesian subject up to the age of 50. There was a marked disparity from other studies in women over 50. Using the appropriate regression model, these values can be considered as reference values for Indonesians.

Keywords : *Quantitative Computed Tomography, bone mineral content, osteoporosis*

INTRODUCTION

Excessive loss of bone mass, or osteoporosis, leads to an increased risk of fractures from minimal trauma. Osteoporosis will become a major health problem in Indonesia as the number of elderly people in the population increases, the result of a demographic transitional process. In developed countries such as the United States, osteoporosis is considered to be the cause of 1.2 million fractures each year in postmenopausal women.[1] It is estimated that in the United States, 25 % of the women over the age of 60 suffer from one or more vertebral fractures caused by osteoporosis.[2]

There are 2 types of osteoporosis, primary and secondary osteoporosis. Primary osteoporosis is associated with advancing age, and is usually found in postmenopausal women and elderly men. Secondary osteoporosis is related to certain diseases, the use of corticosteroids, or prolonged immobilization.

Osteoporosis usually does not give symptoms until fracture occurs. Although bone biopsy is the most accurate quantitative analysis method of determining the mineral content, it is not routinely performed because it is invasive and difficult. With advanced imaging techniques, such as Quantitative Computed Tomography (QCT), it is possible to diagnose the disease by examining the BMC with high precision and

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accuracy. This technique is also simple, noninvasive, relatively inexpensive, and needs only about 10 - 15 minutes to perform.

QCT is considered to be accurate in the early detection of bone mineral loss.[2-9] Early changes can be detected in the vertebral trabecular bone, which has a turn-over rate of about 8 times than cortical bone.[2] This is because the vertebral bodies is made up of 75 % trabecular bone. QCT can measure the mineral content of trabecular bone selectively, without superposition of the cortical bone or other tissues. By carefully choosing the exact site and directly measuring the bone density with QCT, it is possible to minimize analytical errors caused by cortical bone, osteophytes, sclerosis, and calcification.Bone mineral analysis of the extremities does not reflect the mineral content of the axial skeleton such as the vertebrae.[2]

There has not been many studies on osteoporosis in Indonesia at this time. The average BMC values of Indonesian and the pattern of decline with age in men and women are also not fully known. The results of this study will be of importance to other investigators of osteoporosis, since it is hoped that reference values will be obtained for various age groups of both men and women.

The aim of this study is to investigate the average BMC and the pattern of change on a sample of Indonesian population of different age and sex. Comparisons will also be made on the Indonesian pattern of change to those reported by other studies.

MATERIALS AND METHODS

Selection of subjects

This is a cross-sectional study and the subjects were selected from a healthy population members of the *Program Jaminan Pemeliharaan Kesehatan* (PJPK), a health insurance program of the St. Carolus Hospital, Jakarta, in a random proportional method. Those selected underwent a medical examination. The exclusion criteria were :

- Prolonged immobilization, of at least 2 weeks for the past few months.
- Receiving steroids, anticonvulsants, anticoagulants, furosemide, or heparin.
- Receiving hormonal therapy, including contraceptives.
- Conditions such as hypogonadism, menstrual irregularities, galactorrhoea, premature menopause, or other hormonal abnormalities.
- Malignancies.
- Malabsorption syndrome.
- Postovariectomy.
- A history of fracture of the femur or vertebra.
- Smokers or heavy drinkers.
- Pregnancy.

There were 223 subjects selected from March to October 1993. They consisted of 164 females and 59 males. The average age of the males was 43 years (SD 13.16), with the youngest 21 and the oldest 73. The females had an average age of 38.84 years (SD 12.92), ranging from 20 to 75.

Table 1. Distribution of age group according to sex

Age group (yr)	Female	Male
20 - 30	48	10
31 - 40	60	20
41 - 50	25	9
51 - 60	16	12
61 -	15	8

The female subjects comprised of Indonesians from various ethnic groups, such as Javanese, Sundanese, Betawis, Bataks, Flores, Balinese, Minangs, Timorese, Palembangs, or of mixed parentage and Chinese. The majority were Javanese (50%), Sundanese (18.9%), and Chinese (8.5%). The male subjects also were Indonesians of various ethnic groups, such as Javanese, Sundanese, Betawis, Bataks, Flores, Balinese, Timorese, Minangs, Palembangs, Dayaks, or mixed parentage and Chinese. The majority of males were Javanese (54.2%), Sundanese (20.3%), and Betawis (11.8%).

CT assessment

The BMC were assessed with a Somatom-CR CT-Scanner (Siemens AG, Erlangen, Germany) at the Radiology Department of the St. Carolus Hospital in Jakarta. A single energy mode of 125 kV was used. An axial section through the center of the L1, L2, and L3 vertebral bodies was made, with a scan time of 7 seconds at 670 mAS. Each section was 4 mm thick. The subject was supine with a calibration phantom composed of water and 200 mg/ml Ca Hydroxyapatite (standard Siemens reference) positioned underneath the lumbar vertebrae. Measurements were made for both trabecular and cortical bones.

Analysis was limited to the BMC of trabecular bone.

Data analysis

The BMC was reported as mean and standard deviation (SD) values in boxplot and line graphs for each male and female age group.

Linear regression analysis was applied to estimate the changes of average bone mineral content with age both in males and females.[13,14]

The estimated values were presented along with a 95 % confidence interval or 2 standard errors in graph and tables. Linear regression assumptions were made and the accuracy of the regression model evaluated with linear, quadratic, cubic, and double-breakpoint models. Data management and analysis used the SPSS computer software for statistics.[15]

Several regression models were evaluated before selecting the right model that precisely describes the pattern of changes in BMC with age, both in the female and male subjects. The BMC was described as y and the age in years as x. The regression models were :

- simple linear regression model : $y = a + bx$
- quadratic linear regression model : $y = a + bx + cx^2$
- cubic linear regression model : $y = a + bx + cx^2 + dx^3$
- double-breakpoint linear regression model :

$$y = a_1 + b_1x \quad \text{for } x < xb_1$$
$$y = a_2 + b_2x \quad \text{for } xb_1 \leq x \leq xb_2$$
$$y = a_3 + b_3x \quad \text{for } x > xb_2$$

The slope and intercept on the simple, quadratic, and cubic models were estimated with the least squares method. The point of intersection is the point where the regression line changes in slope. It was determined by evaluating the change in mean values of 5-year-interval age groups.

RESULTS

Table 2 shows the mean and standard deviation of BMC values in mg/ml for both men and women in various age groups. There was an increased reduction in both males and females over the age of 60, the reduction was more pronounced in females.

Table 2. BMC of male and female in various age groups

	female		male	
Age group	mean	SD	mean	SD
20 - 30	168.03	21.36	183.59	16.29
31 - 40	164.19	25.07	156.76	34.43
41 - 50	156.32	27.62	154.19	35.08
51 - 60	121.45	51.45	122.13	26.85
61 >	78.51	31.61	87.76	8.79
Total	152.11	39.02	144.52	40.28

Figure 1a and 1b shows the distribution of median and mode values for BMC of both males and females of various age groups. There was a marked decrease in median values beginning from the 50 - 60 age group. The decrease was more pronounced in females.

The results of linear regression analysis showed a consistent decline in BMC with age, both in males and females. Theoretically, the rate of decline in the females should accelerate at a certain age, due to changes in the estrogen pattern which affects BMC. A precise regression model needs to be applied which will reflect the true changes.

No improvement in causative information was gained by using the cubic, quadratic, or double-breakpoint regression models in the male group. This meant that, in the male group, the linear regression model was sufficiently accurate in revealing information on BMC change with age.

In the female group, the quadratic regression model (R^2=0.5167) was more exact than the linear regression model (R^2=0.4247) in interpreting BMC changes with age. But compared to the quadratic model, the cubic regression model (R^2=0.5171) was slightly better.

The double-breakpoint linear regression model showed the following result :

Age (years)		mg/ml		
B1	B2	Slope 1	Slope 2	Slope 3
55	60	-0.594	-8.8	-3.95

This model showed a -0.594 mg/ml reduction in BMC each year up to the age of 55. Then an accelerated reduction of -8.8 mg/ml per year until the age of 60. The rate of reduction decreased somewhat after the age of 60. This is clearly shown in figure 2.

DISCUSSION

The average BMC of male and female Indonesians, with ages ranging from 20 to 75, was studied. The subjects were selected from a sample population of *Program Jaminan Pemeliharaan Kesehatan* members, a health plan of the St. Carolus Hospital.

Not all ethnic groups in Indonesia were represented but the majority was well represented.

The population in this study is not a true representation of the entire Indonesian population, since the sample was specified and restricted to members of the health plan. Therefore, the results of this study does not necessarily reflect the true values of the entire population. But if the sample can be considered as reflecting the general, healthy, Indonesian population, then the values can be regarded as reference values of average BMC of male and female Indonesians of various ages.

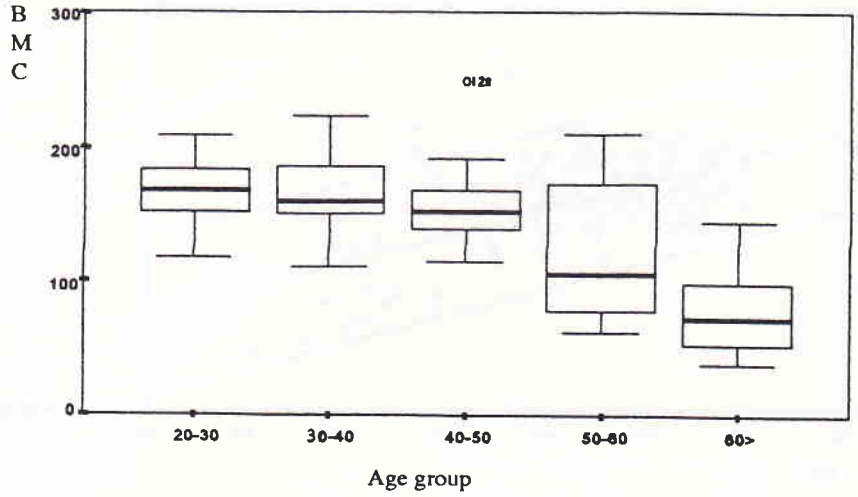

Figure 1a. BMC of females in various age groups

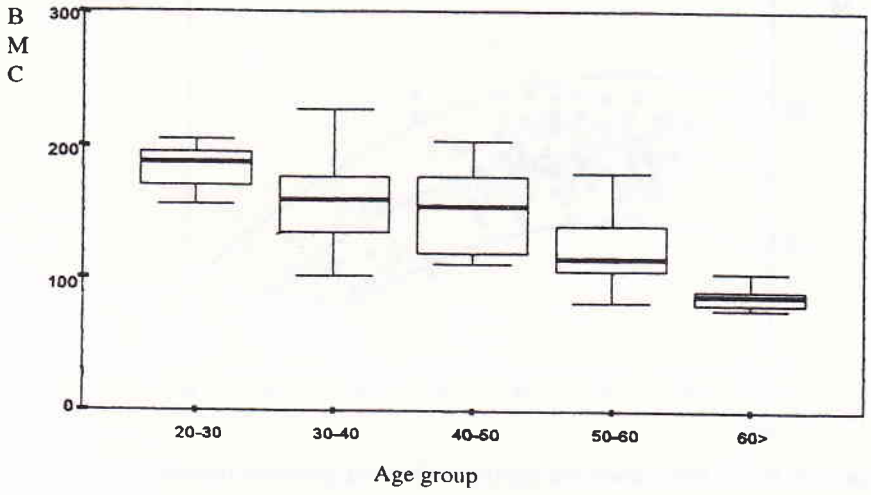

Figure 1b. BMC of males in various age groups

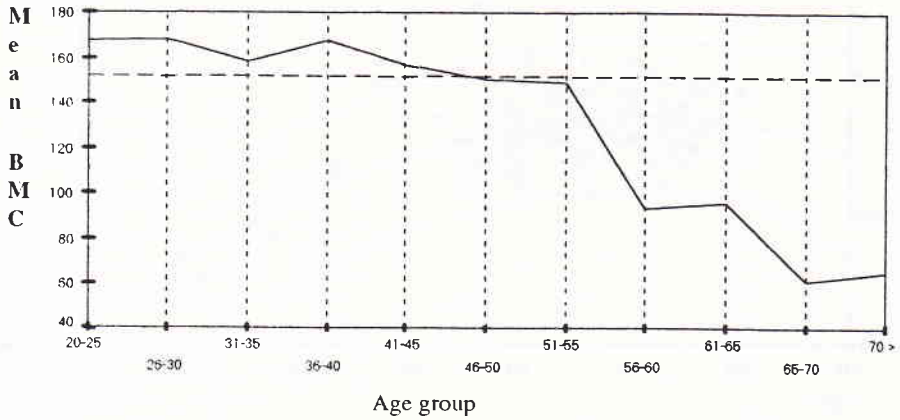

Figure 2. Average BMC in females of various age groups

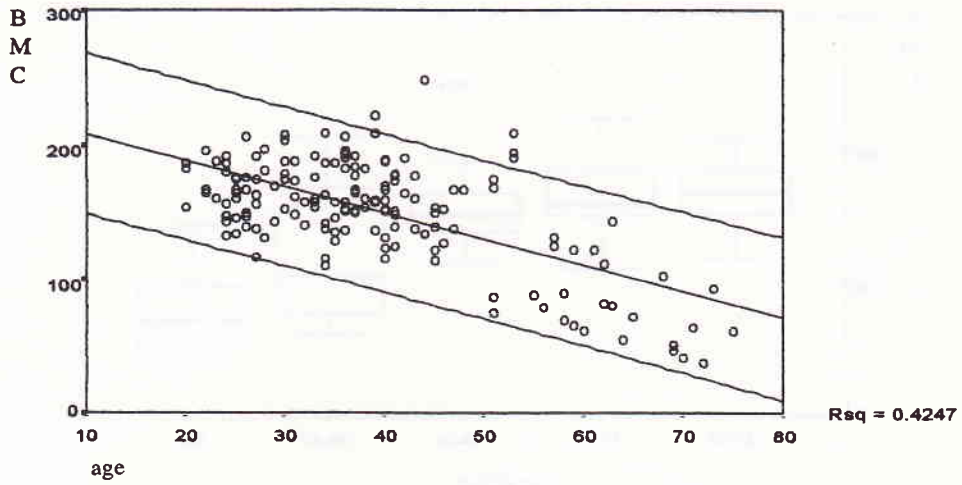

Figure 3a. Plot of BMC values and age in females using linear regression model

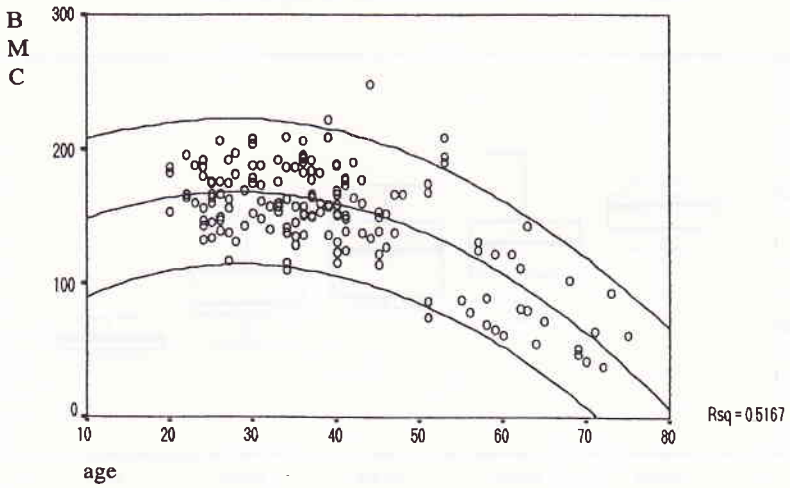

Figure 3b. Plot of BMC values and age in females using quadratic regression model

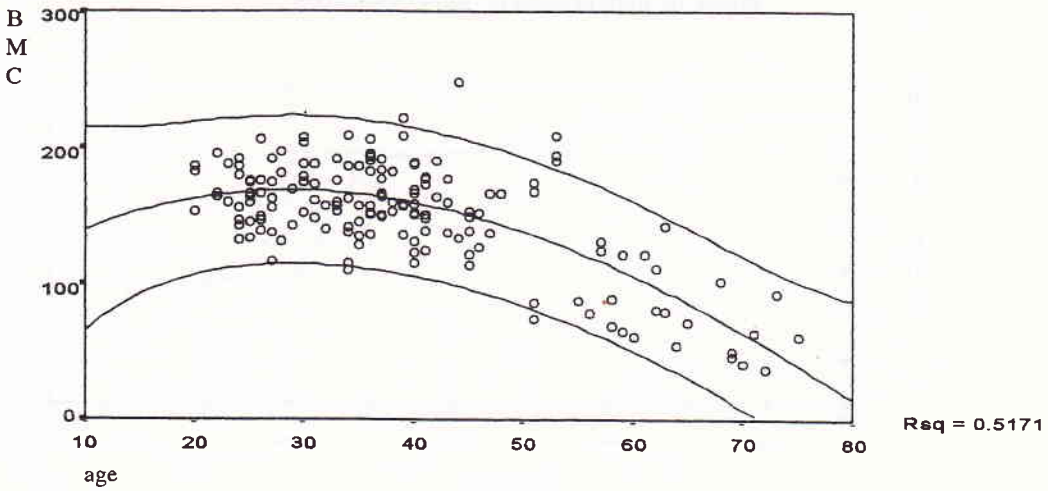

Figure 3c. Plot of BMC values and age in females using cubic regression model

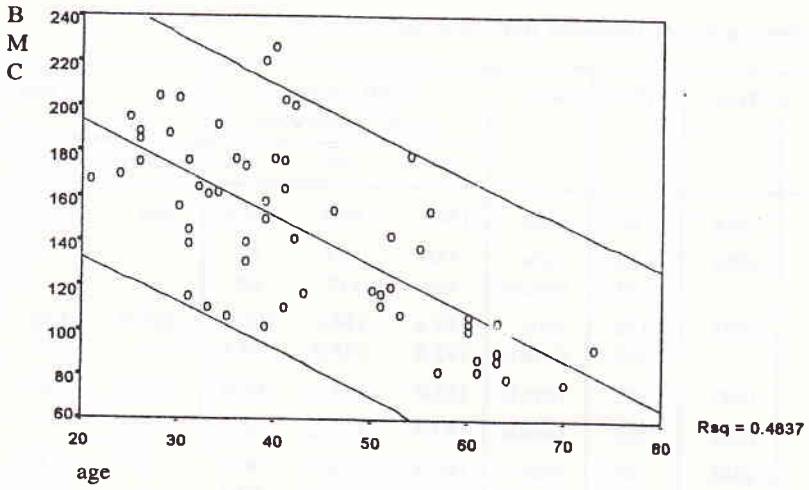

Figure 4a. Plot of BMC values and age in males using linear regression model

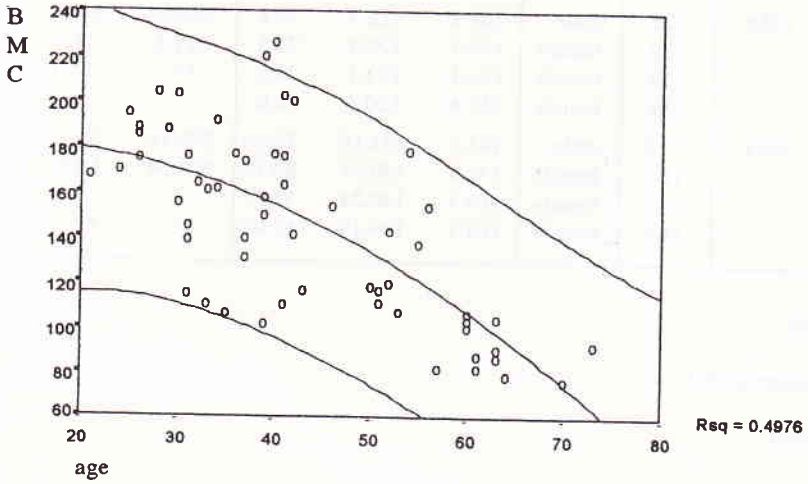

Figure 4b. Plot of BMC values and age in males using quadratic regression model

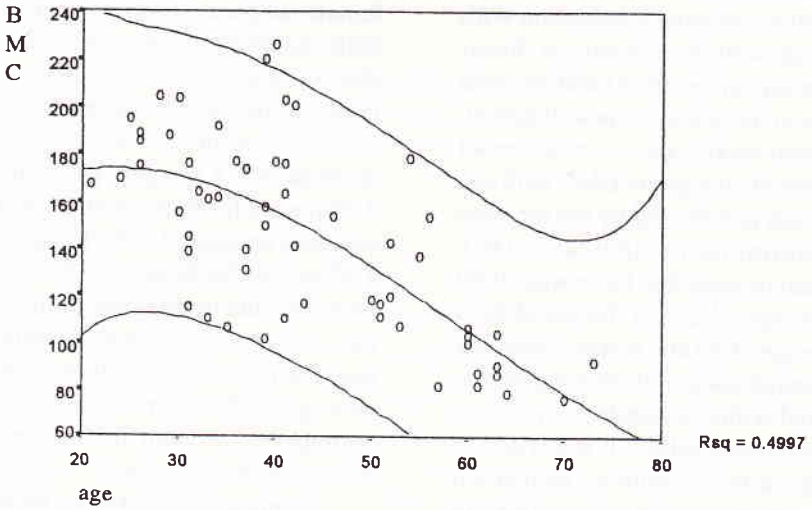

Figure 4c. Plot of BMC values and age in males using cubic regression model.

Table 3. Comparison of reference data on trabecular BMC from various studies

Authors	Year	(N)	Sex	BMC (mg/ml) at age parameters			Regression			
				25	50	75	intercept	Slope	SE	r
Meier et al	1984	62	male	154.6	92.3	65.6	199.1	-1.78	-	-0.72
Laval-Jeantet et al	1984	98	male	146	113	69	-	-	-	-
		143	female	159	117	65	-	-	-	-
Cann et al	1985	120	male	184.4	144.1	103.9	224.6	-1.61	27.7	-0.69
		203	female	172.0	138.0	76.4	**	**	30.8	
Pacitici et al	1987	153	female	168.4	117.1	65.9	219.6	-2.05	25.0	-0.67
Montag et al	1988	203	female	147.5	115.1	60.0	**	**	20	-
Compston et al	1988	66	male	161.5	126.0	90.5	197	-1.42	-	-0.62
		63	female	163.8	116.5	69.3	211	-1.89-	-	-0.81
Block et al	1988	538	female	181.5	131.0	80.5	232.0	-2.02	26.5	-0.67
		538	female	165.0	130.5	74.0	**	**	26.0	-0.69
Kalender et al	1988	135	male	164.8	122.3	79.8	207.3	-1.70	26.3	-0.73
		139	female	166.3	120.8	75.3	211.8	-1.82	27.9	-0.74
		139	female	161.4	123.1	72.6	**	**	27.6	-0.75
		139	female	157.8	120.3	76.0	+	+	27.4	-0.76
Own work	1994	59	male	183.7	131.16	78.66	236.16	-2.1	29.20	-0.70
		164	female	179.3	130.04	80.79	228.54	-1.97	29.69	-0.65
		164	female	168.4	140.24	37.35	*	*	27.29	-0.72
		164	female	168.2	139.19	41.09	**	**	27.37	-0.72

* quadratic regression model
** cubic regression model
\+ double-breakpoint regressiom model

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The regression analysis model used to describe the changes in BMC pattern showed a reduction with age. The male group showed a uniform, or linear reduction. The female group on the other hand, showed an accelerated reduction in the postmenopausal period.

The cubic regression model gave a more exact information on the pattern of changes in BMC with age in the female group, which is reflected by the increase in the regression determination indicator (R^2). Through this model it can be seen that there was slight increase in BMC at the age of 20-30, followed by a slight decrease after the age of 40 and marked decrease after the age of 50. Although some authors suggest that a linear regression model within 2 standard errors can in practice be used as reference values, it is advised to apply the cubic regression model with an estimation area of 2 standard error as reference for BMC in women. The linear regression model can be applied to estimate the BMC of male subjects.

The double-breakpoint regression model of the female subjects, showed that BMC reduction was initially stable then followed by 2 accelerated reduction, after the age of 55 and 65. This differs from the findings of Kalender for Europeans, where the accelerated reduction occured over the age of 40 and 56. The decrease was 8.8 mg/ml per year for those over 55 and 3.95 mg/ml for those over 65 in the female Indonesian subjects, compared to 3.21 mg/ml for those over 40 and 1.57 mg/ml for those over 56 in Europeans.[7] This was probably due to differences in dietary patterns, physical activity, estrogen deficiency, or the use of postmenopausal supplementary drugs including estrogen. Further studies are needed on postmenopausal women in Indonesia, especially on the effects of those factors.

Comparisons between results of several studies can be seen in Table 3. In general, it can be noted that the pattern of change is the same. The rate of BMC

reduction may differ according to the regression model employed, and if only subjects of perimenopausal age is used.

CONCLUSIONS

1. The rate of BMC reduction with age in the female subjects was not uniform, there was an accelerated reduction in the perimenopausal period.
2. The rate of BMC reduction with age in the male subjects was uniform.
3. Average BMC values, based on the appropriate regression model, of both male and female subjects of various age groups can be considered as reference values for Indonesians.
4. The average BMC values of Indonesian males of various age groups and Indonesian females up to the age of 50 does not differ much from other studies; it was found to be different in Indonesian females over the age of 50.

SUGGESTIONS

Future studies on osteoporosis should cover :

* BMC studies using a wider cross-sectional design on different population samples.
* Longitudinal or follow-up studies to determine the rate of natural BMC reduction in Indonesians.
* Cross-sectional or longitudinal studies to determine the BMC where the risk of fractures increases (fracture threshold)
* Studies on the rate of BMC reduction of menopausal women and the effects of dietary patterns of calcium rich food, physical activity, supplementary estrogen and other factors.

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