and six slices) of bread were tested. The dose-response relationships observed at lower doses and a leveling off in glycemia after a load of four slices of bread suggests healthy individuals are able to control glycemia within narrow physiological boundaries by increasing the amount of insulin secreted (*24*). On the other hand, test meals in the present study were designed to be close to the daily intake in Vietnam. After converting the amount of rice into carbohydrate, 84 g and 66 g of carbohydrate were contained in meal A and B, respectively. These amounts were over 52 g carbohydrate, which was equivalent to the mentioned four slices of bread. The glycemic effect caused by different amount of carbohydrate seemed to be attenuated by other factors such as fat and protein contained in side dishes (*11*). However, the considerable difference observed in the subjects in their sixties might be caused by age or potentially by adipose tissue (*25, 26*). It has been indicated that abdominal fat and body fat percentage are increasing in Vietnamese, especially in females (*5*). It is also worth mentioning that decreasing insulin sensitivity due to body fat increased with age has been observed (*26*). However, it was the limitation of this study that the blood glucose used as an indicator and BMI used as the anthropometric criterion were inadequate to provide a further explanation.

Studies indicate that dietary fiber contained in vegetables delayed the absorption of carbohydrates and ameliorated the postprandial glycemic response (*17–20*). In this study we observed an interesting phenomenon. The favorable effect occurred only in the subjects in their forties and not in the subjects in their twenties and sixties. The results of the subjects in their twenties and sixties were also different. In the subjects in their twenties, the AUCs of meals A and C were similar and low but in the subjects in their sixties, the AUCs of both test meals were similarly high. The results may suggest that the young group had the ability to control blood glucose level regardless of the dietary vegetables. In the elderly group, the AUC was high even though they took the meal with vegetables (meal A); nevertheless, an increase in the AUC was not observed by taking the meal without vegetables (meal C). This observation needs further studies to elucidate the favorable effects of dietary vegetables in the elderly.

The GI might be of some help to patients with impaired glucose tolerance (*11, 12*). Nevertheless, the GI concept, especially considering its interpretation by health professionals or the general population, should not be the only, nor the most important, criterion to judge a food (*12*). A low dietary fat ratio and excess carbohydrate could also account for increased glycemic response, not only using rice as a staple food. Our observation was in line with the recommendation by the ADA which states that the amount of available carbohydrate is more important than the source (*27*), since most of the time individuals consume a mixed meal rather than a single food. A dietary guideline must be based on ordinary dietary habits, or it will be futile. The dietary pattern of consuming rice as a staple food with other side dishes might represent a good dietary habit of Asians, with total energy intake being taken into account. However, such test meals are probably not exactly representative of those in everyday life. Further studies involving a large number of young and elderly healthy subjects are needed to elucidate the effect of the dietary FC ratio in mixed meals.

In conclusion, the present study showed that postprandial glycemic responses were different among three age groups, despite the consumption of the same test meal. The diet with about 70% energy from carbohydrate, which is commonly consumed by Vietnamese, increased glycemic response, especially in the elderly subjects. Dietary vegetables may also be beneficial to prevent such an increase in glycemic response.

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REFERENCES

1) Ota T, Takamura T, Hirai N, Kobayashi K. 2002. Preobesity in World Health Organization classification involves the metabolic syndrome in Japanese. *Diabetes Care* **25**: 1252–1253.
2) Le Nguyen TD, Tran TM, Kusama K, Ichikawa Y, Nguyen TK, Yamamoto S. 2003. Vietnamese type 2 diabetic subjects with normal BMI but high body fat. *Diabetes Care* **26**: 1946–1947.
3) WHO Expert Consultation. 2004. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* **363**: 157–163.
4) Dickinson S, Colagiuri S, Faramus E, Petocz P, Brand-Miller JC. 2002. Postprandial hyperglycemia and insulin sensitivity differ among lean young adults of different ethnicities. *J Nutr* **32**: 2574–2579.
5) Le DS, Kusama K, Yamamoto S. 2006. A community-based picture of type 2 diabetes mellitus in Vietnam. *J Atheroscler Thromb* **13**: 16–20.
6) Shiwaku K, Hashimoto M, Nogi A, Kitajima K, Yamasaki M. 2004. Traditional Japanese dietary basics: a solution for modern health issues? *Lancet* **363**: 1737–1738.
7) Miller JB, Pang E, Bramall L. 1992. Rice: a high or low glycemic index food? *Am J Clin Nutr* **56**: 1034–1036.
8) Willett WC. 2001. Eat, drink and be healthy. The Harvard Medical School Guide to Healthy Eating. Simon & Schuster Source, New York, Free Press.
9) United States Department of Agriculture. 1992. Food Guide Pyramid Booklet, Center for Nutrition Policy and Promotion, United States Department of Agriculture, Washington, DC.
10) Khoi HH, Khan NC, Mai LB, Tuyen LD. 2003. General Nutrition Survey 2000. Medical Publishing House, Hanoi.
11) Flint A, Moller BK, Raben A, Pedersen D, Tetens I, Holst

JJ, Astrup A. 2004. The use of glycemic index tables to predict glycaemic index of composite breakfast meals. *Br J Nutr* **91**: 979–989.

12) Pi-Sunyer FX. 2002. Glycemic index and disease. *Am J Clin Nutr* **76**: 290S–298S.

13) Willett W, Manson J, Liu S. 2002. Glycemic index, glycemic load, and risk of type 2 diabetes. *Am J Clin Nutr* **76**: 274S–280S.

14) Indar-Brown K, Noreberg C, Madar Z. 1992. Glycemic and insulinemic responses after ingestion of ethnic foods by NIDDM and healthy subjects. *Am J Clin Nutr* **55**: 89–95.

15) Coulston AM, Hollenbeck CB, Swislocki AL, Reaven GM. 1987. Effect of source of dietary carbohydrate on plasma glucose and insulin responses to mixed meals in subjects with NIDDM. *Diabetes Care* **10**: 395–400.

16) Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. 2003. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* **26**(Suppl 1): S5–20.

17) Dror Y. 2003. Dietary fiber intake for the elderly. *Nutrition* **19**: 388–389.

18) Buyken AE, Toeller M, Heitkamp G, Vitelli F, Stehle P, Scherbaum WA, Fuller JH. 1998. Relation of fibre intake to HbA1c and the prevalence of severe ketoacidosis and severe hypoglycemia. EURODIAB IDDM Complications Study Group. *Diabetologia* **41**: 882–890.

19) Chandalia M, Garg A, Lutjohann D, von Bergmann K, Grundy SM, Brinkley LJ. 2000. Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. *N Engl J Med* **342**: 1392–1398.

20) Fukagawa NK, Anderson JW, Hageman G, Young VR, Minaker KL. 1990. High-carbohydrate, high-fiber diets increase peripheral insulin sensitivity in healthy young and old adults. *Am J Clin Nutr* **52**: 524–528.

21) National Institute of Nutrition. 2000. Nutritive Composition Table of Vietnamese Foods. Medical Publishing House, Hanoi.

22) Wolever TM, Jenkins DJ, Jenkins AL, Josse RG. 1991. The glycemic index: methodology and clinical implications. *Am J Clin Nutr* **54**: 846–854.

23) Abbott Laboratories. Clinical Performance of the TrueMeasure™ Technology Test Strip on Capillary, Arterial, Venous and Neonatal Blood Samples, P/N 487107 Rev. 0 11/02.

24) Brand-Miller JC, Thomas M, Swan V, Ahmad ZI, Petocz P, Colagiuri S. 2003. Physiological validation of the concept of glycemic load in lean young adults. *J Nutr* **133**: 2728–2732.

25) DeFronzo RA, Bonadonna RC, Ferrannini E. 1992. Pathogenesis of NIDDM. A balanced overview. *Diabetes Care* **15**: 318–368.

26) Basu R, Breda E, Oberg AL, Powell CC, Dalla Man C, Basu A, Vittone JL, Klee GG, Arora P, Jensen MD, Toffolo G, Cobelli C, Rizza RA. 2003. Mechanisms of the age-associated deterioration in glucose tolerance: contribution of alterations in insulin secretion, action, and clearance. *Diabetes* **52**: 1738–1748.

27) Franz MJ, Bantle JP, Beebe CA, Brunzell JD, Chiasson JL, Garg A, Holzmeister LA, Hoogwerf B, Mayer-Davis E, Mooradian AD, Purnell JQ, Wheeler M; American Diabetes Association. 2002. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. *Diabetes Care* **25**: 148–198.

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Resting Metabolic Rate of Elderly Vietnamese

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Key Words
Resting metabolic rate · Elderly Vietnamese · Predictive equation

Abstract
Background/Aims: To evaluate the FAO/WHO/UNU equations for predicting resting metabolic rate (RMR) in elderly Vietnamese. ***Methods:*** A cross-sectional study involving healthy and elderly subjects was carried out at the Basic Nutrition Department, National Institute of Nutrition, Vietnam. A total of 75 subjects who had a normal body mass index (BMI) were divided into two groups according to sex. The RMR was measured by indirect calorimetry and anthropometric indices were recorded. Equations derived by linear regression of RMR and body weight were compared to the FAO/WHO/UNU (1985) predictive equations. ***Results:*** The mean age of males and females were 65.03 ± 4.0 and 66.48 ± 4.61 years, respectively. Mean RMRs (MJ/kg/day) were 0.0963 ± 0.0121 for males and 0.0925 ± 0.0117 for females. Compared to the FAO/WHO/UNU equations, our findings were 10.9 and 11.1% lower in males and females, respectively ($p < 0.05$). ***Conclusion:*** Our findings suggest that the FAO/WHO/UNU equations may overestimate RMR in elderly Vietnamese. Further studies to find out the most appropriate equation or to establish new predictive equations for RMR in elderly Vietnamese should be conducted.

Introduction

Determining a person's energy requirements is essential for energy balance. Daily energy requirement is determined by measuring or predicting a person's basal metabolic rate (BMR), which normally constitutes 60–70% of daily energy expenditure, and multiplying by a factor that encompasses other daily energy needs, including the thermic effect of food and physical activity [1]. BMR is defined as the amount of energy expended by the body at rest in a fasted state at a thermoneutral temperature. BMR includes the energy expended in ventilation, blood circulation, intestinal contraction, the activities of internal organs, and maintenance of thermal equilibrium. Resting metabolic rate (RMR) is the energy expended while an individual is resting quietly in a supine position. Although there are some small differences between BMR and RMR, they are sometimes used interchangeably in community studies [2].

Standard physiological factors such as sex, age and body composition are related to BMR in man [3]. Indeed, differences due to age and sex exist when BMR values are expressed as calories per unit of body weight or body surface area [4]. Many equations for estimating the BMR of individuals have been formulated and used when actual metabolic measurements are not available [1, 5, 6]. FAO/WHO/UNU 1985 equations are formulas commonly used to estimate BMR [5]. These equations were derived

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from data from different ethnic groups, although 38% of the data were from white men and women [5, 7, 8].

Experts in energy metabolism have observed problems with equations used to predict energy expenditure [6, 7]. It is unclear whether predictive equations derived from one population can be applied correctly to a different population [9]. In a preliminary analysis of BMR and race using adult data, Henry and Rees [10] concluded that those people living in the tropics, such as Brazilian, Filipino, Indian, Chinese, Japanese and Malaysian, have a lower BMR than predicted by the Schofield equations which were adopted by the FAO/WHO/UNU 1985. Further analysis of data of adult people also came to a conclusion that the actual BMR of people in the tropics was on average 8% below that predicted by the FAO/WHO/UNU equations [6].

Many studies have concluded that race has an influence on metabolic rate [11–13]. For example, Indian subjects have a lower BMR than Northern European and North American subjects [12]. Asian and Siberian subjects have a lower BMR than North American [6, 7, 11]. It is reported that most equations from data from whites overestimated measured BMR in healthy Chinese [14]. There is a need to re-evaluate equations used to predict energy expenditure in Asians, because previously reported measurements of BMR may not be accurate or appropriate when applied to a modern population [15].

In Vietnam, a recent study on Vietnamese adults showed that the FAO/WHO/UNU equations overestimated RMR by 7.4, 9.0, 11.7, and 13.5% in males and females aged 18–29 and 30–60 years, respectively [16]. However, the RMR of elderly Vietnamese has not been reported. Therefore, this study was aimed to determine the RMR of elderly Vietnamese and to compare the values with those determined by the FAO/WHO/UNU 1985 predictive equations.

Methods

Participants

The study was carried out in Hanoi, a city of >2 million in the Northern region of Vietnam. 120 males and females aged 60–70 years were randomly selected from an urban commune for a screening study. Details of the study were explained carefully to all subjects. To recruit these subjects, a listing of people aged 60–70 years was constructed. From this list, the first subject was selected by randomly picking a subject's code. From the first subject, using the systematic random sampling method, we approached another subject and added subjects to obtain the 120 people [17]. In the screening, subject's height and weight were measured and a short questionnaire about disease history was filled in. After screening, a total of 75 healthy subjects (35 males, 40 females) who were without disabilities, hypertension, goiter, chronic diseases of the heart or lungs, and who had a normal body mass index (BMI) (18.5–24.9 kg/m^2) were selected. Informed consent was obtained from each participant. The protocol of this study was approved by the Scientific Board of the National Institute of Nutrition of Vietnam.

Anthropometric Measurement

Body weight and height were measured in light clothing and without shoes to the nearest 0.1 kg and 0.1 cm respectively. BMI was calculated as weight per square of height (kg/m^2). Body fat percentage was measured by bioelectrical impedance (Omron HBF-351, Kyoto, Japan).

Physical Activity

Energy expenditure was estimated by recording all activities of subjects for the preceding 24 h. Physical activity level (PAL) was calculated by total daily energy expenditure divided for basal metabolic rate over 24 h. The PAL was classified as light, moderate or high by following the WHO criteria [18].

Measurement of RMR

Subjects were familiarized with the equipment and given a briefing on the experimental protocol the day before the measurement. They were advised to avoid medications, coffee and other caffeine-containing beverages, smoking, heavy meals, alcohol and strenuous exercise the evening before testing. In order to check the adherence to instructions, local health staff came to each household the day before the measurement to obtain written consent from each subject, and reminded them to avoid nicotine, alcohol, caffeine, and food.

On the test day, subjects came to the Basic Nutrition Department in the early morning after a 12-hour fast, in a non-strenuous manner. Subjects lay quietly and relaxed for 30 min prior to measurement. All measurements were carried out between 06:00 and 09:00 h in a quiet room with an ambient temperature of 22–24°C and barometric pressure of 760–770 mm Hg. RMR was measured using an open-circuit indirect calorimeter (Oxycon Delta, Erich Jaeger BV, Bunnick, The Netherlands). Calibration of the calorimeter in the early morning was done according to the manufacturer's instructions. First, the test subject was adapted to a tight-fitting breathing mask with attached Triple V sensor, which measures volume. The gas exchange measurement was done via the extremely fast O_2 and CO_2 analyzers. RMR was determined over a 15-min period while resting with the ergospirometry measurement program 'Breath by Breath'. RMR was calculated from the oxygen consumption and carbon dioxide production from minutes 5 to 15 to avoid the unstable condition at the beginning of each measurement. In addition, in order to minimize the bias from measurement, any subject who had relatively high or low RMR, or deviations of RMR >10% or spontaneous movement was re-measured on the same day or on another day. RMR was derived using the Weir equations [19, 20]. In addition to the measured values, RMR was predicted using the equations of FAO/WHO/UNU 1985.

Statistical Analyses

Data are presented as means ± SD. Paired t test was used to test differences between measured and predicted values. Linear

Table 1. Physical characteristics of subjects

Age group	n	Age, years	Weight, kg	Height, m	BMI, kg/m^2	Body fat, %
Male >60 years	35	65.03 ± 4.0	60.66 ± 8.45	1.62 ± 0.49	22.89 ± 2.04	22.10 ± 4.24
Female >60 years	40	66.48 ± 4.61	51.89 ± 4.90	1.53 ± 0.41	21.90 ± 1.80	29.76 ± 3.56

regression equations were derived for groups of subjects according to sex and age. Correlation analysis was done to determine relationships between variables. A p value <0.05 was considered significant. All data were analyzed using the SPSS software (SPSS/Windows Version 9.0, Chicago, Ill., USA).

Results

Thirty-five males and 40 females took part in the studies. Anthropometric indices of the participants are presented in table 1. The mean age, mean body weight and mean height of males and females, respectively, were 65.03 ± 4.0 and 66.48 ± 4.61 years, 60.66 ± 8.45 and 51.89 ± 4.90 kg, and 1.62 ± 0.49 and 1.53 ± 0.41 m. There were significant differences ($p < 0.05$) in weight, height, BMI and body fat percent between male and female subjects.

The correlation coefficient between the measured RMR and various anthropometric variables is shown in table 2. The measured RMR were significantly correlated with body weight, BMI and body fat percent ($p < 0.01$) in both males and females. The correlation between physical activity and RMR was found significant only in males ($p < 0.01$). Body weight has the highest r-value in both males and females.

Table 3 shows the means, standard deviations and differences between the measured RMR and the predicted RMR by FAO/WHO/UNU equations. The mean of the measured RMRs (MJ/kg/day) were 0.0962 ± 0.0121 in males and 0.0925 ± 0.0117 in females, while that of predicted values were 0.1068 ± 0.0085 and 0.1028 ± 0.0065, respectively. Differences were not statistically significant between males and females ($p < 0.01$). In comparison to predicted RMR by FAO/WHO/UNU equations, the overestimation was 10.9% in males where 51.5% of the predicted values were within 10% of the measured RMR and 49.5% were greater than 10% of measurement. The maximum underestimation and overestimation was 6.2% and –25.6% in males. On the other hand, the measured values were 11.1% lower than the RMR predicted for females by FAO/WHO/UNU equations ($p < 0.05$). 47.5% of females had predicted values within 10% of measured RMR and in 52.5% it was >10% of measured RMR. The maximum underestimation and overestimation was 7.5% and –24.6% in females. Linear regression of RMR generated by the two methods shows that the measured values were lower than predicted values in both groups (fig. 1a, b).

Table 2. Correlation coefficients (r) between measured RMR and age and specific variables

Variables	Male	Female
Body weight, kg	0.694*	0.636*
Height	0.153	0.228
BMI	0.480*	0.379*
Body fat percent	0.356*	0.402*
Physical activity	0.439*	0.280

* $p < 0.01$.

Figures 2a and b show the individual differences between measured and predicted values of RMR plotted against the measured values using the technique of Bland and Altman [21] in males and females. The 95% limits of agreement of RMR were –2.0609 to 0.3839 and –1.7189 to 0.5615 MJ/day in the male and female groups, respectively. In addition, we used the standard errors and confidence interval (CI) to see how precise our estimates were. Hence, the 95% CI for the bias of RMR was 0.1098 and 0.0992 MJ/day in males and females, respectively. The standard error of limits (mean ± 2 SD) was 0.1901 and 0.1719 MJ/day for males and females, respectively. The 95% CI for the lower limit of agreement was –2.4639 to –1.6578 and –2.0833 to –1.3544 MJ/day for males and females, respectively. For the upper limit of agreement the 95% CIs were –0.0191 to 0.7869 and –0.1970 to 0.9259 MJ/day for males and females, respectively.

Table 3. Measured and predicted values of resting metabolic rate of elderly Vietnamese

Age group	Measured RMR		Predicted RMR by WHO		Difference, % (overestimation of WHO equations)
	MJ/day	MJ/kg/day	MJ/day	MJ/kg/day	
Male >60 years	5.7836 ± 0.7203	0.0963 ± 0.0121	6.4122 ± 0.4104	0.1068 ± 0.0085	10.9 ($p < 0.05$)
Female >60 years	4.7801 ± 0.6061	0.0925 ± 0.0117	5.3128 ± 0.1732	0.1028 ± 0.0065	11.1 ($p < 0.05$)

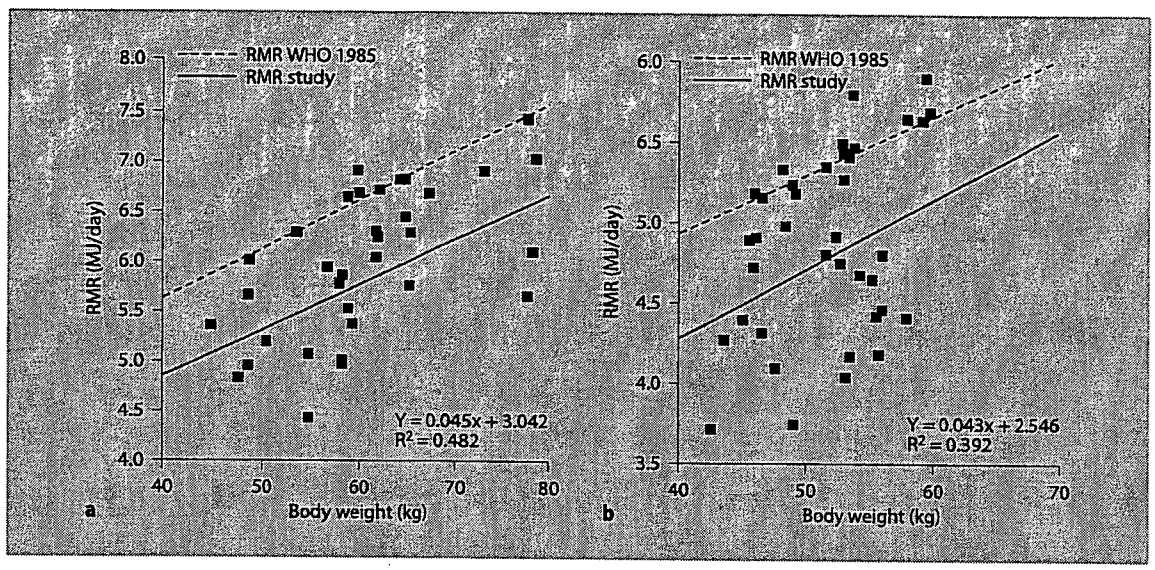

Fig. 1. Comparison between RMR of males (**a**) and females (**b**) aged 60–70 years and predicted RMR by FAO/WHO/UNU (1985).

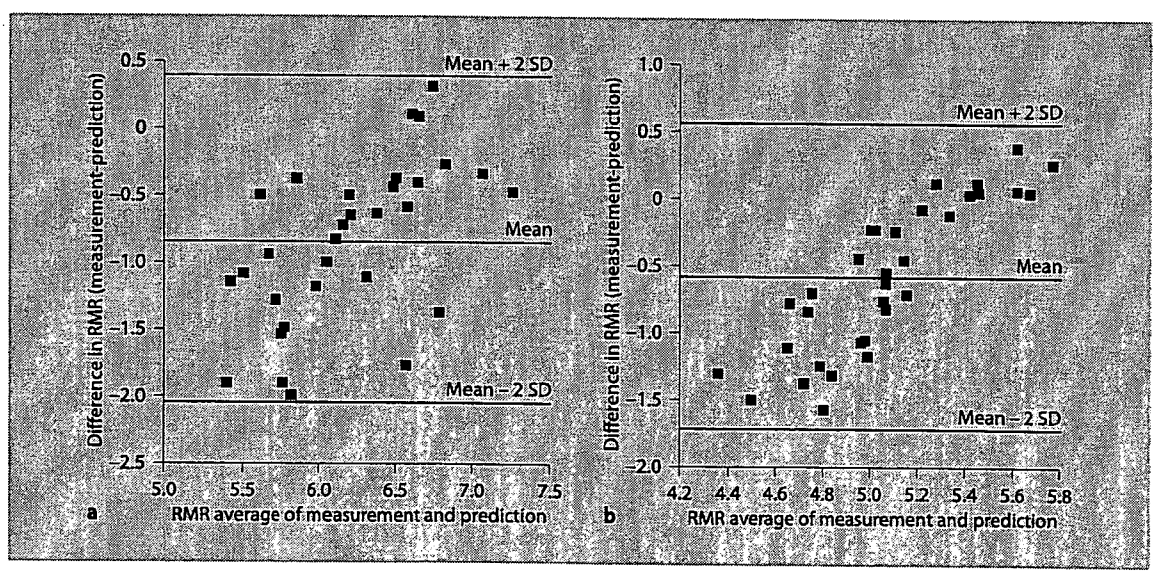

Fig. 2. Resting metabolic rate: difference between measurement versus prediction by FAO/WHO/UNU (1985) for males (**a**) and females (**b**) aged 60–70 years with 95% limits of agreement.

Discussion

Aging has been frequently associated with significant changes in body composition, body fat distribution, and RMR [22, 23]. Studies have shown that RMR decreases with age and that this reduction is dependent on the relationships among energy intake, energy expenditure, changes in body composition, and physical activity [4, 24]. On the other hand, aging is also associated with an increase in non-communicable lifestyle-related diseases such as obesity, type 2 diabetes, hypertension and coronary heart disease [25]. Therefore, to ensure energy balance in elderly people, and to prescribe nutrition therapy for persons with conditions associated with aging, such as overnutrition, physical dysfunction and malnutrition, energy expenditure must be determine accurately.

Several investigators have reported racial differences in RMR [6, 10]. Schofield [8] reported that the predicted RMR by his equations may overestimate measured RMR of different racial groups, especially Asian Indians. Henry and Rees [10] suggested that different ethnic groups may have different metabolic responses to climate and that differences may also be attributable to the varying degree of muscular relaxation during rest. Up until now there have been many studies that have re-evaluated the Schofield equations, but doubts still remain about the accuracy of the Schofield-FAO/WHO/UNU equations to predict BMR in all races and ages [7, 10].

The major finding of the present study was that the measured RMR in both males and females is lower than that predicted by the FAO/WHO/UNU 1985 equations. This is in good agreement with our recent findings of RMR in Vietnamese adults [16]. Such overestimation by these predictive equations has been reported in other papers [6, 7, 10]. The overestimation was first indicated in Schofield's data analysis report where the RMR of Asiatic Indians was overestimated by 10–11% by their equations [7, 8]. Henry and Rees [6] reported that the FAO/WHO/UNU predictive equations overestimated RMR of people living in the tropics by an average of 8, and by up to 11.5% for males >30 years of age. A study in Malaysians showed that these predictive equations overestimated RMR of adults by an average of 13% in males and 9% in females while differences of 4–5% were observed when compared to Henry and Rees [6] equations for people in the tropics. The same overestimation was found in Brazilian, Filipino, Chinese, Indian and Japanese [10]. The study in RMR of Asian women found that the measured values were lower than predictive values, and it has been suggested that caution must be taken when predicting RMR of Asian women using the FAO/WHO/UNU 1985 equations, and indirect calorimetry or an equation specific to Asians is recommended when an accurate estimate is required [26].

Various other equations for calculating RMR are available in the literature [6, 8, 15]. However, as in the WHO equations, the predictive equations for the elderly were also exclusively derived from studies with small samples. On the other hand, Schofield [8] did not consider diseases or medications in his analysis. Moreover, Schofield's equations were conducted under different experimental conditions with different types of devices and different procedures, and covered a very large period of times (1914–1983). Furthermore, a study in RMR of elderly Germans showed that, even within the elderly age group, a specific age still has an influence on RMR [27]. Therefore, age has to be considered when calculating RMR in the elderly. However, for subjects who were older than 60 years the WHO equation was not divided by age group [5].

A reduction in RMR with advancing age has been observed as an attribution to the decrease in RMR associated with aging to a change in body fat mass and a decrease in fat-free mass (FFM). It is suggested that in healthy subjects the age-related decline in RMR is not caused by a decreasing organ metabolic rate but is fully accounted for by a reduction in FFM and proportional changes in its metabolically active component [27]. There was increasing evidence that the associations between BMI, percentage of body fat and body fat distribution differ across populations. In particular, in some Asian populations a specific BMI reflects a higher percentage of body fat than in white or European populations, especially in females [25]. That might be a reason for the lower RMR of Asian people.

We applied Japanese [28] and Henry and Rees [6] predictive equations to our populations and found that there was no significant difference between measured and predicted values (tables 4, 5). It could be suggested that these equations might be more appropriate for elderly Vietnamese. However, a large-scale study should be conducted for confirming the accuracy of these equations.

The individual differences between measured and predicted values were in a normal range, as reported by other authors [29]. These individual differences may be too large to make any predicted formula for individual use. In circumstances where individual values are required, the measurement instead of the prediction of RMR is highly recommended.

Table 4. Measured and predicted values of resting metabolic rate from Japan 1999 [28]

	Measurement MJ/kg/day	Japan 1999 MJ/kg/day	Overestimation %
Males >60 years	0.0963 ± 0.0121	0.0928 ± 0.0043	-3.6 ($p > 0.05$)
Females >60 years	0.0925 ± 0.0117	0.0892 ± 0.0034	-3.5 ($p > 0.05$)

Table 5. Measured and predicted values of resting metabolic rate by Henry and Rees [6]

	Measurement MJ/kg/day	Henry and Rees MJ/kg/day	Overestimation %
Males >60 years	0.0962 ± 0.0121	0.0990 ± 0.0073	2.8 ($p > 0.05$)
Females >60 years	0.0925 ± 0.0117	0.0955 ± 0.0045	3.2 ($p > 0.05$)

The reasons why the FAO/WHO/UNU equations tended to overestimate the BMR in the elderly are still unclear. The RMR observed in our study is found to be relatively lower in comparison with the FAO/WHO/UNU equations. However, it may be due to the difference of PAL and lifestyle and body composition of the elderly in developed and developing countries.

We conducted our RMR measurements under carefully controlled conditions, taking many factors into consideration. However, due to the small sample size, the results might not be applicable for entire elderly population in Vietnam. Further studies on RMR are, therefore, highly recommended.

In conclusion, our study showed that the FAO/WHO/UNU equations overestimated RMR in elderly Vietnamese by 10.9% in males and 11.1% in females. The measured values were not significantly different to the estimated values by Japanese [28] and Henry and Rees [6] equations, suggesting that the equations generated for Asians may be more appropriate for Vietnamese. Further studies on energy metabolism and energy requirements of the elderly are needed.

References

1 Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO: A new predictive equation for resting energy expenditure in healthy individuals. Am J Clin Nutr 1990;51:241–247.

2 Krause MV, Mahand LK: Nutrition and Diet Therapy. Philadelphia, Raven Press, 1992.

3 John JC: A reanalysis of the factors influencing basal metabolic rate in normal adults. Am J Clin Nutr 1990;33:2372–2374.

4 Benedict F: Factors affecting basal metabolism. J Biol Chem 1915;20:263.

5 FAO/WHO/UNU: Energy and Protein requirements. Report of a Joint FAO/WHO/UNU Expert Consultation. Tech Rep Ser 724. Geneva, WHO, 1985.

6 Henry CJK, Rees DG: New predictive equations for the estimation of basal metabolic rate in tropical peoples. Eur J Clin Nutr 1991;45:177–185.

7 Shetty PS, Henry CJK, Black AE, Prentice AM: Energy requirements of adults: an update on basal metabolic rates and physical activity levels. Eur J Clin Nutr 1996;50(suppl 1):S21–S23.

8 Schofield WN: Predicting basal metabolic rate, new standards and review of previous work. Hum Nutr Clin Nutr 1985;39(suppl 1):5–41.

9 Durnin JVGA: Low energy expenditures in free-living populations. Eur J Clin Nutr 1990;44(suppl 1):95–102.

10 Henry CJK, Rees DG: A preliminary analysis of basal metabolic rate and race; in Blaxter K, Macdonald I (eds): Comparative Nutrition. London, Libbey, 1988, pp 149–158.

11 Benedict FG: The racial elements in human metabolism. Am J Physiol Anthropol 1932;16:463–473.

12 Quenouille MH, Boyne AW, Fisher WB, Leitch I: Statistical studies of recorded energy expenditure of man. Part I: Basal metabolism related to sex, stature, age, climate and race. Tech Commun No 17. Aberdeen, Commonwealth Bureau of Animal Nutrition, 1951.

13 Elia M: Energy expenditure in the whole body; in Kenney JM, Tucker HN (eds): Energy Metabolism: Tissue Determinants and Cellular Corollaries. New York, Raven Press, 1992, pp 19–59.

14 Liu HY, Lu YF, Chen WJ: Validity of predictive equations for the calculation of basal metabolic rate in healthy Chinese adults. J Chin Nutr Soc 1994;19:141–150.

15 Soares JM, Shetty PS: Predictive equations for basal metabolic requirements of Indian males. Eur J Clin Nutr 1993;47:389–394.

16 Nhung BT, Khan NC, Hop LT, Lien DTK, Le DSNT, Hien VTT, Kunii D, Sakai T, Nakamori M, Yamamoto S: FAO/WHO/UNU equations overestimate resting metabolic rate in Vietnamese adults. Eur J Clin Nutr 2005;59:1099–1104.
17 Levy PS, Lemeshow S: Sampling of Populations. Methods and Applications, ed 3. New York, Wiley, 1999.
18 William DM, Frank IK, Victor LK: Exercise Physiology, ed 3. London, Lea & Febiger, 1991.
19 Weir JBD: New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949;109:1–9.
20 Weir JBD: New methods for calculating metabolic rate with special reference to protein metabolism. Nutrition 1990;6:3.
21 Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;i:307–310.
22 Piers LS, Soars MJ, McCormack LM, O'Dea K: Is there evidence for an age-related reduction in metabolic rate?. J Appl Physiol 1998; 85:2196–2204.
23 Roberts SB, Fuss P, Evans WJ, Heyman MB, Young VR: Energy expenditure, aging and body composition. J Nutr 123:474–480.
24 Fukagawa NK, Bandini LG, Young JB: Effect of age on body composition and resting metabolic rate. Am J Physiol 1990;259:E233–E238.
25 WHO Expert Consultation: Appropriate body mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157–163.
26 Case KO, Brahler CJ, Heiss C: Resting energy expenditures in Asian women measured by indirect calorimetry are lower than expenditures calculated from prediction equations. J Am Diet Assoc 1997;97:1288–1292.
27 Bosy-Westphal A, Eichhorn C, Kutzner D, Illner K, Heller M, Muller MJ: The age-related decline in resting energy expenditure in human is due to the loss of fat-free mass and to alterations in its metabolically active components. J Nutr 2003;133:2356–2362.
28 Health Service Bureau, Ministry of Health and Welfare, Japan: Recommended Dietary Allowance for the Japanese, 6th Rev. Tokyo, Daiichi Shuppan, 1999, pp 32–47.
29 De Lorenzo A, Andreoli A, Bertoli S, Testolin G, Oriani G, Deurenberg P: Resting metabolic rate in Italians: relation with body composition and anthropometric parameters. Acta Diabetol 2000;37:77–81.

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ORIGINAL ARTICLE

Association of estrogen receptor alpha gene polymorphisms and lifestyle factors with calcaneal quantitative ultrasound and osteoporosis in postmenopausal Vietnamese women

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Abstract Genetic and lifestyle factors are important in the pathogenesis of osteoporosis. We investigated the relationships of *Pvu*II and *Xba*I polymorphisms of the estrogen receptor alpha (ER-α) gene, lifestyle factors with speed of sound at the calcaneus (calcaneal SOS) and osteoporosis in a population-based study of 140 healthy postmenopausal women. By an analysis of covariates, women with higher copies of P or X alleles had higher calcaneal SOS compared with others (P=0.012, PP vs. pp; P=0.045, Xx vs. xx). Women with lower copies of px or higher copies of PX haplotypes had higher calcaneal SOS compared with others (P=0.021, 0 px vs. 2 px; P=0.011, 1 PX vs. 0 PX). The px and PX haplotypes, age and years since menopause were found to be independent predictors of calcaneal SOS in multiple linear regression models. Using logistic regression, we found an increased osteoporosis risk with evidence for a px haplotype dose effect (OR=2.82, 95% CI=1.50–5.31, P=0.001) and for a PX haplotype dose effect (OR=0.42, 95% CI=0.19–0.93, P=0.033). An increased educational level was associated with a reduced risk of osteoporosis (P=0.035 in the model with px, P=0.044 in the model with PX). In conclusion, the present study suggests that *Pvu*II and *Xba*I polymorphims of the ER-α gene, age, years since menopause and educational level are associated with bone density, as assessed by calcaneal SOS, and osteoporosis in postmenopausal Vietnamese women.

Keywords Estrogen receptor-α gene · Lifestyle factors · Osteoporosis · Quantitative ultrasound · Postmenopausal Vietnamese women

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Introduction

Osteoporosis is a major health problem worldwide, particularly in the elderly. More than 40% of postmenopausal women, on average, will suffer at least one osteoporotic fracture (Spencer et al. 1986). It is also a common complex disorder that involves environmental and genetic factors and results in an increased risk of fracture. The environmental risk factors of osteoporosis have been reported in previous studies as low calcium intake, vitamin D deficiency, excessive alcohol, smoking and lack of physical activity (Anthony and Kristina 2003). Several studies have proved the dominant role of the genetic factors in the pathogenesis of osteoporosis. Studies in twins and parent–offspring have shown that additive genetic effects account for 60–80% of the population variance and stature (Giguere and Rousseau 2000; Nordström and Lorentzon

1999). Genetic linkage studies (Johnson et al. 1997; Devoto et al. 1998) and candidate-gene association studies have identified loci and candidate genes that are involved in the regulation of bone mass and the pathogenesis of osteoporotic fractures (Morrison et al. 1994; Kobayashi et al. 1996; Masi et al. 1998; Gennari et al. 2005). One such candidate gene is the estrogen receptor alpha (ER-α). The importance of ER-α in the regulation of bone mass has been indicated by the occurrence of osteoporosis in a man with mutations in the coding region of ER-α (Smith et al. 1994) and by the observation that the bone mineral density (BMD) of mice lacking a functional ER-α gene is 20–25% less than that of wild-type mice (Korach 1994). Several genetic variations in the ER-α gene have been described, and relationships of these polymorphisms with BMD and quantitative ultrasound (QUS) parameters have been reported, but the results have been inconsistent, pointing to the possibility that gene–gene and gene–environment interactions may present important confounding factors (Kobayashi et al. 1996; Han et al. 1997; Patel et al. 2000; Kim et al. 2001; Van Meurs et al. 2003; Koh et al. 2004; Albagha et al. 2005; Mitra et al. 2006). Moreover, there are few studies that have analyzed the relationship of both ER-α polymorphisms and environmental factors to osteoporosis. Here, we take into account anthropometric measurements and life style factors (such as weight, height, age, years since menopause, educational level, occupation, smoking and drinking alcohol) in analyzing the association of ER-α with osteoporosis.

To assess bone status, QUS of the bone has been proposed as an alternative method for noninvasive assessment of skeletal status, as it reflects not only the bone mass, but also the qualitative aspects of bone tissue such as elasticity, structure and geometry (Gluer 1997). The heritability estimates of the QUS parameters are also comparable with those of BMD, ranging between 53 and 74% at the calcaneus (Danielson et al. 1999; Howard et al. 1998). More importantly, the proportion of postmenopausal women classified as normal, osteopenic or osteoporotic was similar when using either BMD or QUS measurements (Frost et al. 2001; Huopio et al. 2004). However, in contrast to the many reports using BMD, genetic studies using QUS measurements are extremely rare. In addition, to the best of our knowledge, there is still a dearth of data on the genetic factors of osteoporosis in Vietnam. Therefore, we performed a population-based study to investigate the association of the *Pvu*II and *Xba*I genotype, haplotype of ER-α gene as well as environmental factors with osteoporosis and bone density assessed by SOS at the calcaneus in postmenopausal Vietnamese women.

Subjects and methods

Subjects

First, 500 postmenopausal women living in a rural area of the Hai Duong province were screened from two communes by questionnaire. Women who had one or more of the following factors were excluded from the study: (1) current cancer or hyperparathyroidism; (2) a kidney stone in the past 5 years, renal disease, or bilateral hip surgery; (3) therapy with a bisphosphonate, calcitonin, estrogen, tamoxifen, or testosterone in the past 6 months or fluoride in the past 2 years; (4) laboratory evidence of kidney or liver disease. As a result, 140 healthy postmenopausal women who met the criteria of the study were recruited for the study. None of the recruited subjects had ever used any bisphosphonates in their medical history. The Ethics Committee of the National Institute of Nutrition, Vietnam, and the Ethnical Committee of Tokushima University, Japan, approved the study. All participants provided written informed consent before entering the study.

Measurements

All participants completed a structured questionnaire. Data were collected on the anthropometric measurements, current age, age at menarche, age at menopause, ethnicity, educational level, occupation, medical and reproductive history, and smoking and drinking history. The lifelong occupation was defined as the occupation that the subject engaged in most frequently in her life. It was classified as heavy work (farmers; manual workers), office work (office clerks and other sedentary jobs) or domestic work (housewife). The educational level was categorized into three groups according to the number of years of schooling: low level (≤5 years), medium level (6–8 years) and high level (≥9 years).

Bone mass was assessed by speed of sound (m/s) at the calcaneus using a QUS device (CM–100; ELK Corporation, Tokyo, Japan) as described by Hien et al. (2005). The precision error (percent coefficient of variation) using the phantom technique was 0.15% and, in vivo, was 0.27% (Hien et al. 2005). The *T*-score for each subject was calculated by using the peak speed-of-sound value for a defined population of young adults, and its standard deviation, with the following equation (Cheng et al. 1999): $T\text{-score} = (\text{speed of sound}_{\text{subject}} - \text{speed of sound}_{\text{peak value for young adults}}) / \text{standard deviation}_{\text{peak value for young adults}}$. The peak speed-of-sound value for young adults ($\text{speed-of-sound}_{\text{peak value for young adults}}$) was found by estimating the

peak bone mass, which was itself defined as the average maximum bone mass achieved by young, healthy, sex- and race-matched adults (Frost et al. 1999). The speed-of-sound $_{\text{peak value for young adults}}$ and standard deviation$_{\text{peak value for young adults}}$ were used from a previous large population-based study (Hien et al. 2005). A person was classified as having osteoporosis if her *T*-score was ≤–1.8, and as normal if the score was >–1.8.

Genotyping

Peripheral blood samples were obtained from each woman, and genomic DNA was extracted from peripheral blood leukocytes, using the QIA amp DNA blood kit (Qiagen GmbH, Hilden, Germany). The *Pvu*II (rs2234693) and *Xba*I (rs9340799) polymorphisms are 45 bp apart and located approximately 400 bp upsteam of exon 2 of the ER-α gene. ER-α genotypes and haplotypes were determined with the restriction fragment length polymorphism (RFLP)-PCR analysis, as previously described (Van Meurs et al. 2003). The PCR products were digested at 37°C for 90 min with 5 units *of Pvu*II and 7 units *of Xba*I restriction enzymes (New England Biolabs). Haplotypes for the individuals carrying the PpXx genotype were determined by double digestion with both *Pvu*II and *Xba*I restriction enzymes. The digested products were analyzed by 3% agarose gel electrophoresis in 0.5× TBE buffer at 100 V for 40 min, and ethidium bromide staining was used. By convention, the small p and x denote the presence of *Pvu*II and *Xba*I restriction sites, respectively; the capital P and X indicate the absence of *Pvu*II and *Xba*I restriction sites, respectively. Four haplotype alleles for *Pvu*II and *Xba*I were encoded as px (1), PX (2), Px (3) and pX (4).

Statistical analysis

We used the general linear models (GLM) for univariate analysis to evaluate the relationships between calcaneal SOS and ER-α genotypes and haplotypes. The raw SOSs were adjusted by regression for covariates of the height, weight, age, years since menopause, and number of children. The educational level was entered in models as a random factor. Multiple group comparisons were made by one-way ANOVA. Group–group differences were then assessed by the post hoc test of Bonferroni. Binary logistic regression analysis was used to test several models for the associations of osteoporosis to the *Pvu*II and *Xba*I genotypes, haplotypes of the ER-α gene and other variables. Here, data are presented as the odds ratios with 95% confidence intervals (CI). Multiple linear regression was used to test for independent predictors for calcaneal SOS, entering the *Pvu*II–*Xba*I haplotypes, age, years since menopause, weight, height and educational level into the model. The independent distribution of errors was assessed by an analysis of residuals. The chi-square (χ^2) test was used to assess the distribution of *Pvu*II, *Xba*I genotypes and *Pvu*II–*Xba*I haplotypes for Hardy–Weinberg equilibrium. Associations were considered statistically significant at $P<0.05$ for all the analyses. All statistical procedures were performed using SPSS version 11.0 (SPSS, Inc., Chicago, IL).

Results

Characteristics of the subjects

Of the 140 subjects in the study, 137 (98%) were farmers and manual workers, and the others were office clerks. All subjects were healthy women who did not smoke and drink alcohol. The mean (±SD) of age, age at menarche and age at menopause of the study group were 55.6±3.8, 16.7±2.1 and 47.7±3.4 years, respectively. The characteristics of subjects according to the *Pvu*II and *Xba*I genotypes of the ER-α gene are shown in Table 1. We found no statistically significant differences among the three groups of either polymorphism in the weight, height, BMI, age, age at menopause, years since menopause and number of children.

ER-α genotype and haplotype frequencies

The frequencies of the *Pvu*II and *Xba*I genotypes of the ER-α gene were as follows: PP, 15.7% (*n*=22); Pp, 47.1% (*n*=66); pp, 37.2% (*n*=52); XX, 3.6% (*n*=5); Xx, 32.1% (*n*=45); xx, 64.3% (*n*=90). The frequencies of *Pvu*II–*Xba*I haplotypes were as follows: px, 60.7%; PX, 19.6%; Px, 19.6%; pX, 0%. The frequencies of *Pvu*II–*Xba*I diplotypes were: 37.1, 25.7, 24.1, 3.6, 6.4 and 5.7% for px–px, px–PX, px–pX, PX–PX, PX–Px and Px–Px, respectively. The distributions of the *Pvu*II, *Xba*I genotypes and the *Pvu*II–*Xba*I haplotype genotypes were compatible with a population in Hardy–Weinberg equilibrium.

Associations of the PvuII and XbaI polymorphisms, PvuII–XbaI haplotype and lifestyle factors with calcaneal SOS

To investigate the relationship between the individual *Pvu*II, *Xba*I polymorphisms and *Pvu*II–*Xba*I haplotype of the ER-α gene with calcaneal SOS, we used the

Table 1 Characteristics of the subjects according to the *Pvu*II and *Xba*I genotypes of the ER-α gene (n=140)

	*Pvu*II			*P* value	*Xba*I			*P* value
	PP (n=22)	Pp (n=66)	pp (n=52)		XX (n=5)	Xx (n=45)	xx (n=90)	
Age (years)	56.1±3.4	54.9±3.6	56.3±4.1	0.123	54.8±3.7	54.8±3.8	56.1±3.8	0.141
Age at menopause (years)	47.3±3.1	47.5±3.8	48.0±3.1	0.665	48.2±3.3	47.4± 3.6	47.8±3.4	0.780
Years since menopause	8.8±3.2	7.4±3.1	8.3±3. 6	0.162	6.6±1.1	7.4±3.2	8.3±3.5	0.195
Height (cm)	148.4±6.0	149.4±4.7	149.2±5.1	0.712	150.0±2.7	149.3±5.5	149.0±4.9	0.901
Weight (kg)	46.2±7.7	46.3±6.7	44.3±5.8	0.234	50.5±6.8	45.9±6.7	45.0±6.4	0.169
BMI (kg/m^2)	20.9±2.6	20.7±2.8	19.9±2.2	0.134	22.5± 3.0	20.6±2.6	20.2±2.5	0.151
No. of children	3.8±1.7	3.2±1.4	3.6±1.5	0.20	4.4±1.1	3.4±1.3	3.4±1.6	0.344

Data are presented as the mean ± SD. The number in parenthesis indicates the number of subjects in each genotype group
P values were obtained by the one-way ANOVA test

general linear model (GLM) univariate analysis in which calcaneal SOS was presented as the mean ± SE and adjusted for the weight, height, age, years since menopause, number of children, and educational level. As shown in Fig. 1, calcaneal SOS was higher in women with the PP genotype than in those with pp genotypes (P=0.012, ANCOVA). On the other hand, calcaneal SOS was lower in women with the xx genotype than in those with Xx genotypes (P=0.045, ANCOVA). The above analyses resulted in the hypothesis that there was an association between the number copies of PX and/or px haplotypes and calcaneal SOS. In view of this, we next evaluated the relation between each of the three haplotypes (px, PX and Px) and calcaneal SOS (Fig. 2). Calcaneal SOS was significantly lower in the 2-px and 0-PX groups compared to the 0-px group and 1-PX groups, respectively (P=0.021, 2 px vs. 0 px; P=0.011, 0 PX vs. 1 PX, ANCOVA). Carries with higher copy of px tended to have lower calcaneal SOS, while carries with higher copy of PX were prone to have higher calcaneal SOS. A similar analysis showed no association between number copies of the Px haplotype and calcaneal SOS. In addition, the calcaneal SOS was lower in the low educational level compared to the medium level and high level (P=0.038 and 0.002, respectively, one-way ANOVA). After adjusting for confounding factors, a significant difference remained between the low educational level and medium educational level (P=0.004 ANCOVA, data not shown).

Risk factors associated with osteoporosis and independent predictors for calcaneal SOS

To assess potential risk variables of osteoporosis, we used binary logistic regression in the models, including the copy number of the px or PX haplotype, age, years since menopause, number of children, weight, height and educational level (Table 2). As shown in the model 1, the copy number of the px haplotype and years since menopause were positively related to the risk of osteoporosis (P=0.007, 2 px vs. 0 px; P=0.045, respectively). We found an increased osteoporosis risk with evidence for a px haplotype dose effect with an odds ratio of 2.82 (95% CI=1.50–5.31, P=0.001). On the other hand, the model 2 showed that the copy number of the PX haplotype was negatively related to the risk of osteoporosis (OR=0.42, 95% CI=0.19–0.93, P=0.033). Increased years since menopause was associated with a significantly increased risk of osteoporosis in model 1 (OR=1.16, 95% CI=1.01–1.34, P=0.045), but not in the model 2 (OR=1.13, 95% CI=0.98–1.30, P=0.087). In

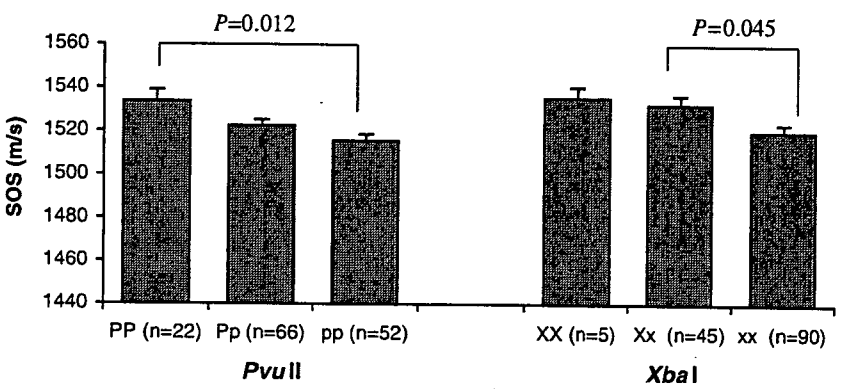

Fig. 1 Calcaneal SOS in postmenopausal women according to the *Pvu*II and *Xba*I genotypes of the ER-α gene. SOS values are the means ± SE and are adjusted for weight, height, age, years since menopause, number of children and educational level. *P* value obtained by ANCOVA

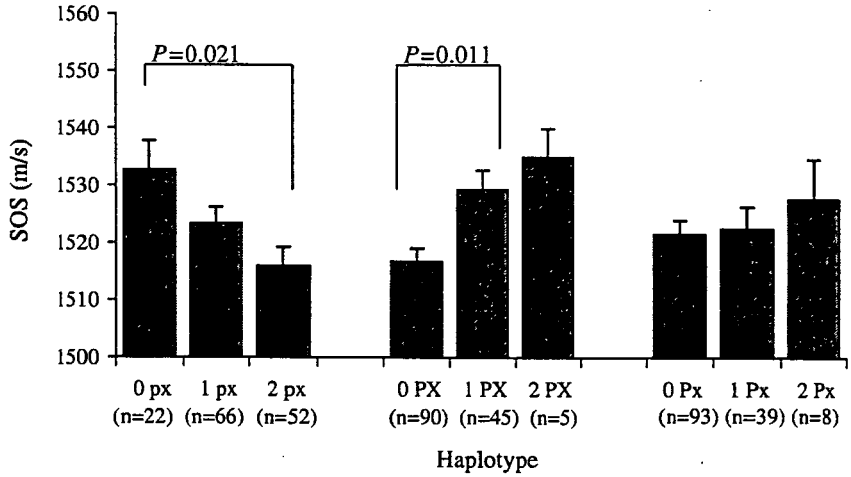

Fig. 2 Calcaneal SOS in postmenopausal women according to *Pvu*II–*Xba*I haplotypes of the ER-α gene. SOS values are the means ± SE, and are adjusted for weight, height, age, years since menopause, number of children and educational level. *P* value obtained by ANCOVA

Table 2 Risk factors for osteoporosis assessed by calcaneal SOS in Vietnamese postmenopausal women

Model 1				Model 2			
Factors	Odds ratio	95% CI[a]	*P* value[b]	Factors	Odds ratio	95% CI[a]	*P* value[b]
Number of px	2.82	1.50–5.31	0.001	Number of PX	0.42	0.19–0.93	0.033
0 px	1.00	–	–	0 PX	1.00	–	–
1 px	1.51	0.42–5.45	0.527	1 PX	0.35	0.14–0.88	0.026
2 px	6.00	1.61–22.1	0.007	2 PX	0.35	0.03–3.98	0.401
Years since menopause	1.16	1.01–1.34	0.045	Years since menopause	1.13	0.98–1.30	0.087
Age	1.09	0.94–1.26	0.258	Age	1.09	0.95–1.26	0.229
Educational level	0.54	0.30–0.96	0.035	Educational level	0.57	0.33–0.98	0.044
Low level	1.00	–	–	Low level	1.00	–	–
Medium level	0.60	0.23–1.61	0.315	Medium level	0.70	0.28–1.79	0.459
High level	0.27	0.08–0.88	0.030	High level	0.29	0.09–0.93	0.037
Weight	1.02	0.95–1.09	0.683	Weight	0.98	0.93–1.07	0.951
Height	1.05	0.96–1.16	0.265	Height	1.07	0.98–1.17	0.152
Number of children	1.22	0.93–1.60	0.152	Number of children	1.22	0.94–1.58	0.142

[a] 95% confidence interval of odds ratio

[b] *P* value obtained by logistic regression

both models, an increased educational level was associated with a reduced risk of osteoporosis (P=0.035 in model 1 and P=0.044 in model 2), while there were no associations of the age, weight, height and number of children with a risk of osteoporosis.

To assess independent predictors for calcaneal SOS, we used multiple linear regression, entering the px or PX haplotypes, age, years since menopause, weight, height, number of children and educational level into the models. The models shown in Table 3 explained 23.8 and 25.8% of the total observed variance in calcaneal SOS according to the copy number of the px and PX haplotypes, respectively. However, the copy number of the px and PX haplotypes, age, and years since menopause were the most significant independent predictors of calcaneal SOS. Further stepwise multiple linear regression analyses showed that the px and PX haplotypes accounted for approximately 5 and 7% at the calcaneal SOS, while the age and years since menopause accounted for about 4 and 6%, respectively.

Discussion

In this study, we found a statistically significant association between calcaneal SOS and the ER-α *Pvu*II and *Xba*I polymorphisms when they were analyzed individually and by the copy number of the px and PX haplotypes in postmenopausal women.

ER-α appears to be the major receptor mediating estrogen action in bone, and it has a prominent effect on the regulation of bone turnover and the maintenance of bone mass (Gennari et al. 2005), but association studies to date have yielded inconsistent results. First, Kobayashi et al. (1996) reported no significant difference in BMD values in Japanese women in relation to individual *Pvu*II and *Xba*I polymorphisms.

Table 3 Multiple linear regression analysis of calcaneal SOS and independent variables

Model 3			Model 4		
Predictors	Coefficient	*P* value	Predictors	Coefficient	*P* value
No. of px haplotype	–9.074	0.002	No of PX haplotype	13.243	0.001
Years since menopause	–1.445	0.043	Years since menopause	–1.155	0.102
Age (years)	–1.722	0.011	Age (years)	–1.669	0.013
Educational level	4.629	0.092	Educational level	4.736	0.081
Weight (kg)	0.140	0.693	Weight (kg)	0.152	0.662
Height (cm)	–0.536	0.246	Height (cm)	–0.606	0.182
No. of children	–1.160	0.384	No of children	–1.399	0.289
Constant	1708.474	0.001	Constant	1697.579	0.001
Final adjusted R^2=0.238			Final adjusted R^2=0.258		

Subsequent studies of association between ER-α genotypes and BMD have showed mixed results. For instance, in postmenopausal Korean women, Han et al. (1997) failed to find any significant association between the ER-α genotypes and BMD in a hospital-based study, whereas Nam et al. (2005) observed the association of the *Pvu*II polymorphism of ER-α with BMD, and Kim et al. (2001) revealed the association of both *Pvu*II and *Xba*I polymorphisms with BMD in population-based studies. These controversial results may be explained partly by an insufficient sample size, population specificity and possible genetic effects masked by different gene–gene and gene–environment interactions.

Because osteoporosis is known as a lifestyle-related disease, we took into account the analysis of both genetic factors and environmental factors, including: (1) anthropometric measurements: weight and height; (2) reproductive status: age, age at menopause, years since menopause and number of births; (3) lifestyle factors: educational level and occupation. As all subjects were healthy women who did not smoke and drink alcohol and most of them (98%) were farmers and manual workers, we could eliminate the confounding factors of these variables in the all analysis models. It is the first report of the relationship between genetic factors, environmental factors and calcaneal SOS in Vietnam. To date, there have been few previous reports regarding to relationship between the ER-α *Pvu*II and *Xba*I genotypes and QUS parameters, although the QUS measurement has many advantages, such as noninvasive assessment of skeletal status, which is especially usefulness for pregnant women, low cost, portable tools and feasibility for a large population study. In agreement with the findings of Patel et al. (2000) and Koh et al. (2004), we found that the x allele of the ER-α gene was significantly associated with the reduced QUS parameter, while Albagha et al. (2005) observed no association. Interestingly, we also revealed the association of the P allele with increased QUS parameters, which is inconsistent with previous studies (Patel et al. 2000; Koh et al. 2004; Albagha et al. 2005). Our results can be explained by the hypothesis of Khosla et al. (2004) that the pp or xx genotype may be relatively estrogen insensitive and that subjects with the P or X allele may benefit more from the protective effects of estrogen on bone than subjects with the p or x allele. Thus, positive or negative associations may be dependent on circulating of the estrogen level.

With regard to the relationship between the *Pvu*II, *Xba*I genotype of the ER-α gene and BMD in postmenopausal Asian populations, some studies reported that women with the XX genotype had higher BMDs than those with the Xx and/or xx genotype (Koh et al. 2004 and Mitra et al. 2006), while others found the opposite results (Kim et al. 2001 and Thuy et al. 2003). Similarly, the P allele was also associated with a higher BMD in most of the reports (Nam et al. 2005; Kim et al. 2001; Mitra et al. 2006), whereas only one reported an opposite association (Huang et al. 1999). The recent meta-analyses in Caucasian women, Ioannidis et al. (2004) confirmed that XX homozygotes consistently had a higher BMD and also a decreased risk of fractures when compared with carriers of the x allele, whereas the *Pvu*II genotype was not associated with either BMD or fracture risk.

In terms of haplotype, we found that both px and PX haplotypes were associated with calcaneal SOS. Albagha et al. (2005), in the population-based cohort of 3,054 Scottish women, indicated that the px haplotype was associated with reduced calcaneal broadband ultrasound attenuation values. Surprisingly, our report is the first of an association between the PX haplotype and QUS parameter in postmenopausal women, while previous studies observed no association or did not carry out an analysis (Patel et al. 2000; Koh et al. 2004; Albagha et al. 2005). Other studies reported a haplotype analysis for the ER-α gene in relation to BMD,

deriving inconsistent conclusions concerning the effects of the different haplotypes among different ethnic populations. Some studies indicated that the px haplotype was associated with lower BMD (Van Meurs et al. 2003; Zhang et al. 2003), while others (Huang et al. 1999) reported the association of the PX haplotype with lower BMD and others demonstrated the association of the Px haplotype with higher BMD (Kobayashi et al. 1996; Albagha et al. 2001). These largely inconsistent results may derive from the diverse genotype and haplotype distributions and the differential degree of linkage disequilibrium of different haplotypes with underlying unknown functional mutations among ethnic groups. In this study, the distribution of *Pvu*II–*Xba*I haplotypes differed from that in several ethnic backgrounds of Asian and Caucasian women (Patel et al. 2000; Koh et al. 2004; Albagha et al. 2005). On the other hand, the controversial results can be explained by gene–gene interaction. For instance, Zhang et al. (2003) revealed that neither of the single polymorphisms of the ER-α *Pvu*II or *Xba*I and none of the four haplotypes were associated with BMD. However, with AA (or A allele) at the vitamin D-receptor locus, PP carriers had lower hip BMD than the non-carriers.

Predictors for reduced bone density and an increased risk of osteoporosis are very important to prevent a population from fracture effectively. The present data show that the copy number of the px and PX haploypes and the years since menopause are significant predictors of both calcaneal SOS and osteoporosis. Other studies reported that either the Px haplotype (Albagha et al. 2001) or px haplotype (Ioannidis et al. 2004) were independent predictors of BMD and osteoporosis in different ethnic populations. Increased age is a significant predictor of low SOS. This association was reported in previous studies (Thuy et al. 2003; Hien et al. 2005) and was also confirmed in our data. Our study also agreed with previous research reporting that an increased educational level was associated with a reduced risk of osteoporosis in Vietnamese women (Hien et al. 2005). It may be elucidated by the report of Woo et al. (1999) that showed that a higher level of education was associated with a healthier diet and a better education might directly influence bone health through the positive effect of better health knowledge on individuals' lifestyles and behaviors.

The present findings must be interpreted in the context of a number of potential limitations. First, using SOS measurements is not known as a "gold standard" to diagnosis osteoporosis in the hospital, but rather BMD measured by dual-energy X-ray absorptiometry. However, many studies have supported the view of using QUS to screen for osteoporosis at the community level (Gluer 1997; Danielson et al. 1999; Frost et al. 2001; Hien et al. 2005). The previous studies also applied a *T*-score threshold of ≤–1.8 to define osteoporosis by using QUS (Frost et al. 2001 and Hien el al. 2005). Thus, in the context of this study in developing countries at the public health level, we could only apply QUS and use a *T*-score threshold of ≤–1.8 to identify subjects with osteoporosis. Second, calcium intake of the subjects was not used in these findings to evaluate a potential effect of this variable in our results. Next, our exclusion criteria, including the use of bisphosphonates within 6 months, were inappropriate because the treatment with these drugs in the prior 6 months might affect the bone measurements (Stock et al. 1997). Nevertheless, none of the recruited subjects had ever taken any bisphosphonates in their medical history. Thus, we could eliminate this confounding factor in the present study. Lastly, our sample size was relatively small and might provide inflated estimates compared to reality (Ioannidis et al. 2001). Although it was designed to eliminate the effects of confounding factors and to detect the statistically significant difference among genotypes and haplotypes of ER-α,it did not have enough power to carry out further analysis by stratums and interactions between genetic and environmental factors. However, although it wassmall, this could be considered as a representative sample of postmenopausal women in rural Vietnam without other ethnic admixtures.

In conclusion, it is the first report to suggest that the *Pvu*II and *Xba*I genotypes and haplotypes of the ER-α gene, age, years since menopause and educational level have associations with bone density, as assessed by calcaneal SOS, and are significant predictors of osteoporosis in postmenopausal Vietnamese women.

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References

Albagha OME, Mcguigan FEA, Reid DM et al (2001) Estrogen receptor α gene polymorphisms and bone mineral density: haplotype analysis in women from the United Kingdom. J Bone Miner Res 16:128–134

Albagha OM, Pettersson U, Stewart A et al (2005) Association of oestrogen receptor alpha gene polymorphisms with postmenopausal bone loss, bone mass, and quantitative ultrasound properties of bone. J Med Genet 42(3):240–246

Anthony D Woolf, Kristina Åkesson (2003) Preventing fractures in elderly people. BMJ 327:89–95

Cheng S, Fan B, Wang L et al (1999) Factors affecting broadband ultrasound attenuation results of the calcaneus using a gel-coupled quantitative ultrasound scanning system. Osteoporos Int 10:495–504

Danielson ME, Cauley JA, Baker CE et al (1999) Familial resemblance of bone mineral density (BMD) and calcaneal ultrasound attenuation: the BMD in mothers and daughters study. J Bone Miner Res 14:102–110

Devoto M, Shimoya K, Caminis J et al (1998) First-stage autosomal genome screen in extended pedigrees suggests genes predisposing to low bone mineral density on chromosomes 1p, 2p and 4q. Eur J Hum Genet 6:151–157

Frost ML, Blake GM, Fogelman I (1999) Contact quantitative ultrasound: an evaluation of precision, fracture discrimination, age-related bone loss and applicability of the WHO criteria. Osteoporos Int 10:441–449

Frost ML, Blake GM, Fogelman I (2001) Quantitative ultrasound and bone mineral density are equally strongly associated with risk factors for osteoporosis. J Bone Miner Res 16:406–416

Gennari L, Merlotti D, De Paola V et al (2005) Estrogen receptor gene polymorphisms and the genetics of osteoporosis. Am J Epidemiol 161:307–320

Giguere Y, Rousseau F (2000) The genetics of osteoporosis: 'complexities and difficulties.' Clin Genet 57:161–169

Gluer CC (1997) Quantitative ultrasound techniques for the assessment of osteoporosis: expert agreement on current status. The international quantitative ultrasound consensus group. J Bone Miner Res 12:1280–1288

Han KO, Moon IG, Kang YS et al (1997) Non-association of estrogen receptor genotypes with bone mineral density and estrogen responsiveness to hormone replacement therapy in Korean post-menopausal women. J Clin Endocrinol Metab 82:991–995

Hien Vu TT, Nguyen CK, Yamamoto S et al (2005) Determining the prevalence of osteoporosis and related factors using quantitative ultrasound in Vietnamese adult women. Am J Epidemiol 161(9):824–830

Howard GM, Nguyen TV, Harris M et al (1998) Genetic and environmental contributions to the association between quantitative ultrasound and bone mineral density measurements: a twin study. J Bone Miner Res 13:1318–1327

Huang Q, Wang Q, Zhang L et al (1999) Relationship between bone mineral density and polymorphism of the estrogen receptor gene in healthy postmenopausal women in China. Chin Med J 112:832–835

Huopio J, Kroger H, Honkanen R et al (2004) Calcaneal ultrasound predicts early postmenopausal fractures as well as axial BMD. A prospective study of 422 women. Osteoporos Int 15(3):190–195

Ioannidis JP, Ntzani EE, Trikalinos TA et al (2001) Replication validity of genetic association studies. Nat Genet 29:306–309

Ioannidis JP, Ralston SH, Bennett ST et al (2004) Differential genetic effects of ESR1 gene polymorphisms on osteoporosis outcomes. JAMA 292(17):2105–2114

Johnson ML, Gong G, Kimberling W et al (1997) Linkage of a gene causing high bone mass to human chromosome 11 (11q12–13). Am J Hum Genet 60:1326–1332

Khosla S, Riggs BL, Atkinson EJ et al (2004) Relationship of estrogen receptor genotypes to bone mineral density and to rates of bone loss in men. J Clin Endocrinol Metab 89:1808–1816

Kim JG, Lim KS, Kim EK et al (2001) Association of vitamin D receptor and estrogen receptor gene polymorphisms with bone mass in postmenopausal Korean women. Menopause 8:222–228

Kobayashi S, Inoue S, Hosoi T et al (1996) Association of bone mineral density with polymorphism of the estrogen receptor gene. J Bone Miner Res 11:306–311

Koh JM, Nam-Goong IS, Hong JS et al (2004) Oestrogen receptor alpha genotype, and interactions between vitamin D receptor and transforming growth factor-beta1 genotypes are associated with quantitative calcaneal ultrasound in postmenopausal women. Clin Endocrinol 60:232–340

Korach KS (1994) Insights from the study of animals lacking functional estrogen receptor. Science 266:1524–1527

Masi L, Becherini L, Colli E et al (1998) Polymorphisms of the calcitonin receptor gene are associated with bone mineral density in postmenopausal Italian women. Biochem Biophys Res Commun 248:190–195

Mitra S, Desai M, Khatkhatay MI (2006) Association of estrogen receptor alpha gene polymorphisms with bone mineral density in postmenopausal Indian women. Mol Genet Metab 87(1):80–87

Morrison NA, Qi JC, Tokita A et al (1994) Prediction of bone density from vitamin D receptor alleles. Nature 367:284–287

Nam HS, Shin MH, Kweon SS et al (2005) Association of estrogen receptor-alpha gene polymorphisms with bone mineral density in postmenopausal Korean women. J Bone Miner Metab 23(1):84–89

Nordström P, Lorentzon R (1999) Influence of heredity and environment on bone density in adolescent boys: a parent–offspring study. Osteoporos Int 10:271–277

Patel MS, Cole DE, Smith JD et al (2000) Alleles of the estrogen receptor alpha-gene and an estrogen receptor cotranscriptional activator gene, amplified in breast cancer-1 (AIB1), are associated with quantitative calcaneal ultrasound. J Bone Miner Res 15(11):2231–2239

Smith EP, Boyd J, Frank GR et al (1994) Estrogen resistance caused by a mutation in the estrogen-receptor gene in a man. N Engl J Med 331:1056–1061

Spencer H, Kramer L (1986) NIH consensus conference: Osteoporosis, factors contributing to osteoporosis. J Nutr 116:319–322

Stock JL, Bell NH, Chesnut CH et al (1997) Increments in bone mineral density of the lumbar spine and hip and suppression of bone turnover are maintained after discontinuation of alendronate in postmenopausal women. Am J Med 103(4):291–297

Thuy VT, Chau TT, Nguyen TV et al (2003) Assessment of low bone mass in Vietnamese: comparison of QUS calcaneal ultrasonometer and data-derived T-scores. J Bone Miner Metab 21(2):114–119

Van Meurs JB, Schuit SC, Weel AE et al (2003) Association of 5' estrogen receptor alpha gene polymorphisms with bone mineral density vertebral bone area and fracture risk. Hum Mol Genet 12(14):1745–1754

Woo J, Leung SS, Ho SC et al (1999) Influence of educational level and marital status on dietary intake, obesity and other cardiovascular risk factors in a Hong Kong Chinese population. Eur J Clin Nutr 53:461–467

Zhang YY, Long JR, Liu PY et al (2003) Estrogen receptor α and vitamin D receptor gene polymorphisms and bone mineral density: association study of healthy pre- and postmenopausal Chinses women. Biochem Biophys Res Commun 308:777–783

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Review

A Community-based Picture of Type 2 Diabetes Mellitus in Vietnam

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There has been a significant increase in the prevalence of type 2 diabetes mellitus (T2DM) in Vietnam. We found that Vietnamese with T2DM had a normal body mass index (BMI), but high levels of total body fat and abdominal fat. Based on published reports together with our own findings, we believe that a sedentary lifestyle and an abundance of starchy foods and also Western style energy-rich foods are factors associated with disease. The staple food of the Vietnamese is still polished-rice which has high glycemic index values. In addition, a Westernized diet, and the chronic consumption of high-glycemic index foods together with a sedentary lifestyle result in insulin resistance and diabetes. The average BMI of T2DM patients is ≤ 23 kg/m², greater than that 20 years ago. In addition,these patients have high levels of body fat, especially abdominal fat, measured as the waist to hip ratio (WHR ≥ 0.90). We therefore, tentatively suggest a BMI of 23 kg/m² together with a WHR of 0.90 for males and 0.85 for females as new cutoff values for the risk of T2DM in Vietnamese. These findings have important implications for primary prevention because they indicate that screening and intervention should focus on high-risk populations. *J Atheroscler Thromb, 2006; 13: 16–20.*

Key words: Type 2 diabetes, Prevalence, BMI cut-off, Percent body fat, Vietnamese

Introduction

Type 2 diabetes mellitus (T2DM) is one of the major non-communicable diseases in the world. The incidence and prevalence of diabetes are increasing not only in industrialized countries but also in developing and newly industrialized countries. According to the World Health Organization (WHO), the number of cases of diabetes will rise to 366 million by the year 2030, more than 270 million of which will occur in developing countries (1). The increase is primarily the result of lifestyle changes known as the "Nutrition Transition," characterized by over-consumption of food, increased consumption of total fat, animal fat, and protein, and decreased physical activity (2). The relationship between T2DM and dietary intake and physical activity has been examined in several recent studies (3, 4). However, the features of diabetes were characterized in each country (5). The purpose of this review was to highlight some of the characteristics of T2DM in Vietnam.

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The increase in prevalence of diabetes: a significant health problem

During the two last decades, socioeconomic conditions and lifestyle have changed profoundly in Vietnam. These changes have had marked effects on disease patterns in the population. The prevalence of non-communicable chronic diseases such as obesity, hypertension and cardiovascular diseases has been increasing (6, 7). The prevalence of diabetes has also been significantly increasing. In 2001, the results of a study conducted in adults in Ho Chi Minh City, southern Vietnam, indicated that the prevalence of diabetes was approximately 2.5

times higher (6.9%) than that recorded 8 years ago (2.5%) (8). Recently, Binh TV *et al.* published a report showing that the prevalence of diabetes in adults in Hanoi City, northern Vietnam, has increased remarkably from 1.2% to 5.8% (9). In addition, a study on middle age Vietnamese indicated that the proportion with high blood glucose levels had increased from 1.6% in 1997 to 6.1% in 2003 (10, 11). Although the prevalence of diabetes in Vietnam is still not very high, the rate of increase is higher than in countries such as China (12), Singapore (13) and the United States (14). These trends suggest that diabetes will be a major health problem in Vietnam.

Anthropometric characteristics and dietary habits of Vietnamese in relation to diabetes

Obesity is so far the most important risk factor for T2DM. Furthermore, its relationship with the disease was confirmed by intervention studies (15, 16). The degree of obesity and the distribution of body fat are very important in the development of diabetes. The distribution of body fat can be evaluated from anthropometric measurements such as height and weight for body mass index (BMI); waist, hip circumference or using bioelectrical impedance (BIA), dual-energy X-ray absorptiometry (DEXA), computerized tomography (CT), etc.

In the early 1990's, studies on diabetes in Vietnam indicated that most diabetic patients had a normal or low BMI (17, 18). The same findings were found in studies conducted from 1995 to 1999. According to a study on 241 hospitalized diabetic patients, the mean BMI of type 2 diabetic patients was 22.3 ± 5.0 kg/m^2 (males) and 21.1 ± 4.5 kg/m^2 (females) (19). Another study on 504 type 2 diabetic patients found that their BMI was in the normal range (22.6 ± 3.5 kg/m^2 for males and 22.7 ± 3.9 kg/m^2 for females) but waist-hip ratio (WHR) was high (0.96 ± 0.07 for males and 0.94 ± 0.08 for females) (20). A low BMI (20.5 ± 0.3) but high WHR (0.88 ± 0.05) in insulin-resistant individuals was also reported in study of Minh HV (21).

One report on middle-aged women in northern Vietnam found that subjects with high plasma glucose levels had a normal to low BMI but high WHR (10). Since 2000, the socio-economy has undergone rapid changes. The quality of life has improved. The mean BMI of Vietnamese which was constant from1985 to 1997 (22, 23), increased from 18.6 kg/m^2 to 20.3 kg/m^2 for males and from 20 kg/m^2 to 20.5 kg/m^2 for females (24). However, the BMI of diabetic patients was normal range based on WHO criteria. Our study (8) indicated that the mean BMI of patients with diabetes was 22.7 ± 3.8 kg/m^2 for males and 23.3 ± 4.1 kg/m^2 for females and WHR was 0.90 ± 0.07 in both genders; it also described an association between obesity, a high WHR and an increase in the prevalence of diabetes. The same findings of a normal BMI and high WHR in Vietnamese diabetics were confirmed in two articles (9, 11). In addition, percent body fat (BF%) was mentioned as a factor associated with diabetes. Tomisaka *et al.*, found that BF% was associated with the development of diabetes and Vietnamese had a higher percentage of body fat than Japanese (25). In 2001, a case-control study on newly diagnosed cases of diabetes using BIA to determine percent body fat, indicated that Vietnamese with type 2 diabetes had a normal BMI but high percent body fat (26). Additional studies indicated that abdominal fat and percent body fat are increasing in Vietnamese, especially in females (10, 11, 27). It is widely accepted that abdominal fat and total body fat are closely associated with insulin resistance. In addition, a role for insulin resistance in the pathogenesis of T2DM was well illustrated. Thereby, it might contribute to the increase in the prevalence of diabetes in Vietnam.

Furthermore, a lack of adaptation to dietary and lifestyle changes may be another possible explanation. In previous decades, the Vietnamese have spent long periods of time without enough food, and their bodies had to adjust to difficult conditions (especially from 1975 to 1985). As mentioned above, with the increase in development and industrialization in Vietnam from the 1990's, socio-economic conditions have improved. As a consequence, a shift from a traditional lifestyle (high levels of occupational and leisure time, lower fat meals) to a more Westernized one is taking place. According to a national general nutrition survey (23), protein and fat intake in Vietnamese increased remarkably (52.4 g vs. 62.0 g and 12.8 v.s 24.9 g, respectively) from 1985 to 2000. Increases in protein and fat intake and consumption of red meat were also observed in a case-control study (28). Interestingly, the traditional meal of Vietnamese, characterized by consumption of huge amounts of rice, coexists with a westernized diet. Although the consumption of rice is decreasing due to westernization (457 g/capita/day in 1985 vs. 452 g/capita/day in 1990 vs. 397 g/capita/day in 2000) (24), rice is still the staple food and provides more than 50% of daily energy intake. However, Vietnamese rice has high glycemic index values (GI: 86–109) (29). It is well recognized that the chronic consumption of high-GI foods which result in recurring, large postprandial fluctuations in blood glucose and insulin levels, can worsen insulin resistance in susceptible populations (30).

What is the cut-off value of BMI for observe risk in Vietnamese?

Body mass index cut-off values have been used internationally to classify overweight and obesity. The relationship between BMI and risk of comorbidities was well demonstrated (31). Recently, there is more and more evidence of a high prevalence of diabetes and coronary artery diseases emerging in Asian populations where the average BMI is lower than the WHO BMI cut-off for being overweight (32–34). In addition, the association be-

tween BMI, BF% and body fat distribution differ across populations. According to previous studies, Asians have a lower BMI but higher BF% than age-matched Caucasians (35–38). This strongly corroborates the need for specific cutoffs of BMI and abdominal fat for Asian populations. According to WHO, the BMI cut-off point for observed risk in different Asian populations varies from 22 kg/m^2 to 25 kg/m^2; for high risk it varies from 26 kg/m^2 to 31 kg/m^2. Lowering cut-off values (by three units) seems appropriate for Hong Kong Chinese, Indonesians and Singaporeans (39). Snehalatha *et al.* (40) gave a cutoff value for a normal BMI for Indian men and women of 23 kg/m^2. Wildman RP *et al.* also suggested that a BMI value of 24 and a waist circumference value of 80 in both genders were appropriate for use in the identification of high-risk Chinese patients (41). In addition, a BMI cut-off of 22–24 and waist circumference cutoff of 75–80 cm for women and 80–85 cm for men were suggested for being overweight and having central adiposity in Asian populations (32–34, 42–44).

Regarding the data on Vietnamese, the same phenomenon was observed: the mean BMI of Vietnamese type 2 diabetic patients was normal (22–23 kg/m^2), but percent body fat and abdominal fat, measured as WHR was high (19, 20, 26). The mean WHR of diabetic patients in those studies ranged 0.90–0.96. Furthermore, according to findings, newly diagnosed cases of diabetes had normal BMI (23.5 kg/m^2 for males and 21.9 kg/m^2 for females) but high WHR (0.93 for males and 0.90 for females) (28). Similar values were seen in the impaired fasting glucose (high risk group) (8). In addition, a normal BMI but high percent body fat and abdominal fat were also found in Vietnamese who suffered from metabolic syndrome (45).Using findings on Vietnamese and the WHO definition of central obesity (31), we tentatively suggest a BMI of 23 for both genders together with a WHR of 0.90 for males and 0.85 for females as the appropriate cutoffs for the risk of T2DM in Vietnamese. These cutoffs need to be re-evaluated based on the relative risk of other obesity-related diseases and their sensitivity and specificity.

Conclusion

The remarkable increase in the prevalence of diabetes has become a priority health problem in Vietnam. Understanding the characteristics and suggesting new cutoffs for BMI (23 kg/m^2 for both genders) together with WHR (0.90 for males and 0.85 for females) for T2DM will help in establishing a screening and intervention program in Vietnam.

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References

(1) Wild R, Roglic G, Green A, Sicree R, and King H: Global prevalence of diabetes. Estimates for the year 2000 and projections for 2030. Diabetes Care, 27: 1047–1053, 2004

(2) Khoi HH: Problems of Nutrition in Transition Period. In: "Problems of nutrition in Transition Period in Vietnam" by Khoi HH, pp 153–226. Hanoi: Medical Publisher, 1996

(3) Ramachandran A, Snehalatha C, Latha E, Manoharan M, and Vijay V: Impacts of urbanization on the lifestyle and on the prevalence of diabetes in native Asian Indian population. Diabetes Res Clin Pract, 44: 207–213, 1999

(4) van Dam RM, Rimm EB, Willet WC, Stampfer MJ, and Hu FB: Dietary patterns and risk for type 2 diabetes mellitus in U.S men. Ann Intern Med, 136: 201–209, 2002

(5) Bajaj M and Banerji MA: Type 2 diabetes in South Asians: a pathophysiologic focus on the Asian-Indian epidemic. Curr Diab Rep, 3: 213–218, 2004

(6) Loan TTH and Hung NTK: The overweight and obesity status in demographic strata in Ho Chi Minh City, The technical, public health and preventive medicine symposium, Ho Chi Minh City 2002: 28–36

(7) Hanh TTM, Komatsu T, Hung NT, Chuyen VN, Yoshimura Y, Tien PG, and Yamamoto S: Blood pressure, serum cholesterol concentration and their related factors in urban and rural elderly of Ho Chi Minh City, J Nutr Sci Vitaminol, 47: 147–155, 2001

(8) Duc Son LN, Kusama K, Hung NT, Loan TT, Chuyen NV, Kunii D, Sakai T, and and Yamamoto S: Prevalence and risk factors for Diabetes in Ho Chi Minh City, Vietnam, Diabetic Med, 21: 371–376, 2004

(9) Binh TV: Epidemiology of diabetes, risk factors and some issues in relation to diabetic management in 4 big cities of urban areas of Vietnam. Medical Publisher, Hanoi, 2003

(10) Lien DTK, Anh NTL, Khoi HH, and Chuyen NV: Screening test research of diabetes, dietary intake and everyday life of 50-59 year old subjects in 2 urban quarter of Hanoi. In Actual nutrition problems of Vietnam and Japan, pp 172–186. Hanoi: Medical Publisher, 1998

(11) Lien DTK, Anh NDV, Khang NV et al.: Investigate the nutritional status and related factor to high plasma sugar in middle age subjects (40–60y) in an urban district of Hanoi city. Vietnam Journal of Physiology, 8: 7–13, 2004

(12) Gu D, Reynolds K, Duan X, Xin X, Chen J, Wu X, Mo J, Whelton PK, and He J; Inter ASIA Collaborative Group: Prevalence of diabetes and impaired fasting glucose in the Chinese adult population: In-