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The Vietnam Osteoporosis Study: Rationale and design

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ABSTRACT

Objectives: Osteoporosis and fracture impose a significant health care burden on the contemporary populations in developing countries. The Vietnam Osteoporosis Study (VOS) sought to assess the burden of osteoporosis and its comorbidities in men and women.
Methods: The study was designed as a population-based family investigation in which families were randomly recruited from Ho Chi Minh City, Vietnam. Individuals were assessed for bone health, including bone mineral density (BMD) and body composition and trabecular and cortical bone properties by pQCT (peripheral quantitative computed tomography). Fasting blood samples were obtained for the analysis of plasma glucose, glycosylated hemoglobin, and bone turnover markers. Genomic DNA extraction from whole blood samples for further genetic and genomic analyses.
Results: We have recruited more than 4157 individuals from 817 families. The average age of participants was 51, with approximately 45% of the individuals aged 50 years and older. Approximately 3% of participants were obese (body mass index $\geq$ 30 kg/m^2), and 21% were overweight. Notably, 11% of participants aged 40 years and older were diabetic. Among those aged 50 years and older, approximately 14% of women and 5% of men had osteoporosis (i.e., femoral neck BMD T-scores ≤ -2.5). There were modest correlations between volumetric BMD and areal BMD.
Conclusions: VOS is a major bone research project in Vietnam aimed at comprehensively documenting the burden osteoporosis, its co-occurrence of chronic diseases, and their underlying etiologies. The Study will make important contributions to the literature of bone health worldwide.

1. Introduction

Osteoporosis and its consequence of fragility are increasingly recognized as a major public health burden in contemporary populations. It is highly prevalent among the elderly of both genders. In the Caucasian populations, the lifetime risk of fracture is about 50% for women and 30% for men [1]. In women, the lifetime risk of hip fracture is higher than the lifetime risk of having invasive breast cancer [2]. Moreover, for women aged 50 years, their risk of death related to a hip fracture is equivalent to their risk of death from breast cancer and 4 times greater than that from endometrial cancer [3]. Currently, due to lack of prospective studies, no data on the lifetime risk of fracture in Asian populations are available. However, it is expected that with the ongoing increase in ageing in Asian populations, the burden of osteoporosis is expected to increase in the near future.

Another important aspect of osteoporosis is that patients with a pre-existing fracture are at increased risk of refractures [4] and mortality [5]. Indeed, among individuals with an incident fracture, the risk of a refracture is increased by 30%–40% within 3 years [5]. However, more disturbingly, fracture is associated with reduced life expectancy or increased risk of premature mortality, with men having higher risk of death than women [6]. The 5-year post-fracture cumulative survival probability for men and women were 48% and 59%, respectively. Approximately one-fifth of patients with hip fracture die within 12 months after the event [7], and the 5-year cumulative survival probability was 63%. These data collectively indicate that osteoporotic fracture, particularly hip fracture, is a serious condition because it is associated with increased risk of death, a fact that is not well known within the primary care

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community.

Vietnam, a developing country in Southeast Asia, is an ideal setting for studying osteoporosis. The country has a population of 92 million, with per capita gross domestic product being ~2000 United States dollar. The population is undergone ageing, with increase in the proportion of people aged 60 years and above. The country is in the stage of rapid urbanization with significant changes in lifestyle factors. Thus, there is an increasing interest in the epidemiology of osteoporosis in Vietnam. In a recent study in Vietnam, we have estimated that approximately 29% of women aged 50 + years had osteoporosis [8] and about 28% of them have vertebral fractures [9]. These data show that the magnitude of osteoporosis in Vietnam is similar to that in other countries in Asia and in the West.

Osteoporosis has a complex pathophysiology. The susceptibility to osteoporosis and its consequence of fracture is determined by factors related to hormone, lifestyle, environmental exposures, and genetics. Osteoporotic patients usually have comorbidities that are mostly associated with osteoporosis such as obesity, diabetes, cardiovascular disease, metabolic syndrome and osteoarthritis. These complex noncommunicable diseases (NCDs) are characterized by deterioration in multiple dimensions also related to lifestyle, genetics and hormones. Thus, osteoporosis and these chronic diseases are linked in a networking manner through the genetic factors that can be referred to as “diseasome.” In the Wnt pathway alone, on average each disease shared ~15 neighbors with each other disease, indicating high comorbidity within the network [10].

Vietnam has also undergone remarkable changes in disease burdens parallel with the economic development. Indeed, the prevalence of NCDs is rapidly increasing. According to a recent report, NCDs collectively account for 71% of total burden of disease in Vietnam, including 60% of all-cause deaths [11]. Compared with two decades ago, the disease burden attributable to NCDs represents a 30% increase. As a result, osteoporotic fracture, which is usually associated with comorbidity NCDs, has an increase in mortality risk. However, the burden of and risk factors for osteoporotic fractures and comorbidity NCDs have not been well documented in Vietnam and a complete map of interassociations between chronic morbidities and osteoporosis has not been developed.

The hypothesis underlying the present study is that osteoporosis and its multimorbidity NCDs share genes, their encoded proteins and pathways that stratify patients in subgroups and their tendency to co-occur together. The overall goal of VOS is to map genetic and environmental factors that underlie the risk of fragility fracture and the co-occurrence of related chronic diseases (i.e., the so-called “diseasome”) in the Vietnamese people.

We pursue the following specific aims: (1) to assess the skeletal burden and its associated morbidities in the general population. We aim to estimate the prevalence of osteoporosis, osteoarthritis and multimorbidity, the incidence of fragility fractures and osteoarthritis in men and women by age group; (2) to determine the extent to which variation in osteoporosis, fracture and osteoarthritis susceptibility is determined by genetic factors. We also aim to identify genetic variants that are associated with osteoporosis, fracture and osteoarthritis; (3) to understand the interplay between genes and environmental factors in the determination of the association between osteoporosis and other chronic diseases, NCDs including osteoarthritis, sarcopenia, obesity, diabetes, metabolic syndrome, and cardiovascular disease.

This project will contribute significant new information on the genetic and environmental bases of osteoporosis and related chronic diseases. The project will also contribute to the knowledge on the specific genes that underline the between subject variation in skeletal parameters.

2. Methods

2.1. Study design

The study is designed as a population based family study. Participants were drawn from multiple families who were living in Ho Chi Minh City and rural areas. The study's procedure and protocol were approved by the research and ethics committee of the People's Hospital 115 on August 6, 2015 (approval number: 297/BV-NCKH). The Study was conducted according to the ethical principles of the Declaration of Helsinki, and all participants gave written informed consent.

We used 2 approaches to recruit participants. In the first approach, we contacted community organizations to solicit a list of members, and from the list we ran a computer program to randomly selected individuals who met the age and sex criteria. A letter was then sent to the selected individuals to invite them and their family members to participate in the Study. In the second approach, we recruited participants via television, the Internet, and flyers in universities. The flyers described (in Vietnamese) the study's purposes, procedures, and benefits of participants. Individuals agreed to participate in the study were then transported to the Bone and Muscle Research Laboratory at the Ton Duc Thang University for clinical assessment and evaluation. The participants do not receive any financial incentive, but they received a free health check-up, and lipid analyses.

The inclusion criteria were broad: men and women aged between 18 years and older, who agreed to participate in the study. We excluded individuals deemed to have impaired cognitive function or are not willing to give informed consent or were physically unable to complete clinical tests. The participants will then be followed for 10 years to record the incidence of fractures and chronic diseases.

2.2. Measurements

Extensive data were collected at baseline. Each participant was administered with a structured questionnaire by a trained interviewer. The questionnaire solicits information concerning their demographic factors, clinical history, medication use, lifestyle factors, physical activity, dietary habits, history of falls and fractures, and anthropometric factors.

2.2.1. Anthropometry

Height and weight were measured by an electronic portable, wall-mounted stadiometer (Seca Model 769; Seca Corp., CA, USA) without shoes or ornaments or hats or heavy layers of clothing. Body mass index (BMI) was derived as the weight in kilograms divided by the square of the height in meters. We classified the BMI into 4 groups as follows: underweight (if BMI < 17 kg/m^2); normal (BMI between 17 and 22 kg/m^2); overweight (BMI between 23 and 27.4 kg/m^2); and obese (BMI > 27.4 kg/m^2).

Waist circumference (WC) and hip circumference (HC) were also measured in each participant by using the World Health Organization (WHO) protocol [12]. HC was measured around the widest portion of the buttocks (in standing position) by using a measuring tape. WC was measured at the midpoint between lower margin of the least palpable rib and the top of the iliac crest. Waist to hip ratio (WHR) was derived as the ratio of WC over HC. Central obesity was defined as WHR > 0.85 for women or >0.90 for men.

2.2.2. Lifestyle data

Participants were also asked to provide information on current and past smoking habits. Cigarette smoking was classified into 2 broad groups: past smoking and current smoking. In addition, the