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Study of sex differences in the association between hip fracture risk and body parameters by DXA-based biomechanical modeling

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ABSTRACT

There is controversy about whether or not body parameters affect hip fracture in men and women in the same way. In addition, although bone mineral density (BMD) is currently the most important single discriminator of hip fracture, it is unclear if BMD alone is equally effective for men and women. The objective of this study was to quantify and compare the associations of hip fracture risk with BMD and body parameters in men and women using our recently developed two-level biomechanical model that combines a whole-body dynamics model with a proximal-femur finite element model. Sideways fall induced impact force of 130 Chinese clinical cases, including 50 males and 80 females, were determined by subject-specific dynamics modeling. Then, a DXA-based finite element model was used to simulate the femur bone under the fall-induced loading conditions and calculate the hip fracture risk. Body weight, body height, body mass index, trochanteric soft tissue thickness, and hip bone mineral density were determined for each subject and their associations with impact force and hip fracture risk were quantified. Results showed that the association between impact force and hip fracture risk was not strong enough in both men ($r = -0.31, p < 0.05$) and women ($r = 0.42, p < 0.001$) to consider the force as a sole indicator of hip fracture risk. The correlation between hip BMD and hip fracture risk in men ($r = -0.83, p < 0.001$) was notably stronger than that in women ($r = -0.68, p < 0.001$). Increased body mass index was not a protective factor against hip fracture in men ($r = -0.13, p > 0.05$), but it can be considered as a protective factor among women ($r = -0.28, p < 0.05$). In contrast to men, trochanteric soft tissue thickness can be considered as a protective factor against hip fracture in women ($r = -0.50, p < 0.001$). This study suggested that the biomechanical risk/protective factors for hip fracture are sex-specific. Therefore, the effect of body parameters should be considered differently for men and women in hip fracture risk assessment tools. These findings support further exploration of sex-specific preventive and protective measurements to reduce the incidence of hip fractures.

1. Introduction

Low-trauma hip fracture has become a major health problem among the elderly over the world [1]. Socioeconomic impacts of hip fracture are two-fold. On one hand, hip fracture increases the morbidity and mortality in the elderly [2–4]; on the other hand, it is a substantial source of health care expenditure [5,6]. 18–33% of older hip fracture patients die within one year following their fracture [7–15], 15–25% require long-term nursing home care or institutionalization [16], and approximately 50% can neither walk independently nor achieve their previous level of independent living [8,16–18]. The incidence of hip fracture appears to be increasing all over the world [19]. It has been estimated that the number of hip fractures globally will rise from 1.3 million in 1990 to between 4.5 and 21.3 million by 2050 [20]. This underscores the importance of understanding the etiology of hip fracture. Knowledge of the dominant sex-specific risk factors for hip fracture can be used to identify high-risk men and women, so that they may benefit from in-time treatment to avoid fracture.

Clinical observations showed that more than 90% of hip fractures are caused by falls [21–26] and mainly by sideways falls from standing height [1,27,28]. A complex combination of body parameters affects the fall-induced impact force and hip fracture risk [29]. The impact force to the proximal femur increases directly with body weight (BW) [30,31]. BW itself is, in turn, positively associated with trochanteric soft tissue thickness (STT) [32] that is able to considerably attenuate the impact force [10,33]. Body height (BH) is also correlated to the impact velocity, and thus the impact severity [31]. In addition, body mass index (BMI) has been identified as a hip fracture risk indicator [32,34–36] which is, in turn, associated with BW, BH, and STT. Apart from the mentioned parameters, BMD, that is commonly used to assess the hip

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fracture risk in clinics [37–39], is inversely correlated to the age of the individual [40–42]. Complexity of the associations between the interdependent factors and hip fracture risk makes it difficult to diagnose patients with high risk of fracture. Therefore, there is a substantial need to quantify the effect of influential parameters on hip fracture risk. Furthermore, there are challenges whether body parameters identically affect the impact force and hip fracture risk in men and women. For example, some studies have suggested that men fracture at the same absolute BMD level as women do [43–46], and therefore, the same absolute BMD threshold should be used in determining the risk of fracture. Other studies suggested different correlations between BMD and hip fracture risk in men and women [37,47–49]. Also, the effect of impact force on hip fracture risk is not compared between men and women and it is unclear if the impact force can be considered as a similar indicator of hip fracture risk in men and women. Furthermore, several studies have discussed whether the association of hip fracture risk with STT [50,51], BMI [41,52,53], and other body parameters [54–56] is the same in men and women. Although higher mortality among male hip fracture patients than female ones has been observed [57], the majority of studies focused on women only [44] and hip fractures in men have received less attention [55,58]. The present study investigated the hip fracture risk in both men and women using a recently developed model [59].

The objective of this study was to identify how different body parameters affect the hip fracture risk in men and women by conducting a quantitative comparison of the associations between body parameters (BMD, BW, BH, STT, BMI), impact force, and hip fracture risk.

2. Methods

2.1. Study population

Under a research ethics approval, 130 Chinese subjects, including 50 males, ranging in age from 16.0 to 86.0 years (39.8 ± 22.1 years), and 80 females, ranging in age from 20.1 to 87.8 years (mean age = 53.7 ± 19.9 years), were recruited in this study. None of the individuals had suffered a hip fracture. The subjects had varying body habitus, i.e., the body weight range of 29.5–133.8 kg (mean weight = 68.7 ± 18.6 kg) and body height range of 124.2–186.2 cm (mean height = 162.3 ± 11.6 cm), which was an advantage for investigating the effect of body parameters on impact force and hip fracture risk. However, the ages of the male and female subjects did not have a good match, which required a special consideration in the processing of results. The subjects were categorized into four BMI groups, i.e., underweight (BMI<18.5), normal (18.5<BMI<25), overweight (25<BMI<30) and obese (BMI>30), according to the WHO criterion [60].

2.2. Calculation of impact force and hip fracture risk

In our previous study [59], a two-level subject-specific biomechanical model was introduced to determine the hip fracture risk in sideways falls and its advantages over currently available methods were demonstrated by investigating the hip fracture risk among women. It is the first subject-specific biomechanical model that integrates both fall- and femur-related parameters in hip fracture risk assessment, including body segments anthropometric parameters, i.e., segments length, mass, mass center, and mass moment of inertia, kinematics of body segments during the fall, such as rotational and translational velocities of body segments, effect of trochanteric soft tissues on attenuating the impact force, load/constraint conditions of the proximal femur during the impact, femur bone quality, and bone geometry. This model is adopted in the present study to determine the hip fracture risk of 130 subjects. The procedure of determining subject-specific hip fracture risk is shown in Fig. 1(a) and explained in the following.

The inputs required by the model are the subject's body weight, height, whole-body and hip DXA (dual energy X-ray absorptiometry) image. First, length, mass, mass center, and mass moment of inertia of the shank, thigh, and trunk were determined for each individual, using body tissue mass estimation from the subject's whole-body DXA image [59,61]. In this method, the correlation between the pixel intensity in the DXA image and the tissue mass density was used to determine the pixel mass [61] and subsequently the required parameters. The obtained parameters were then used to construct a three-link human-body dynamics model, developed by the authors and validated by experiments [59,62], in order to simulate a lateral fall from standing height. The three links represent respectively the shank, the thigh, and the trunk. Lagrange's method was used to derive the equations of motion of the dynamics model considering the potential energy of the system (based on the distance between body segments mass center and the ground), the kinetic energy of the system (characterized by the linear and angular velocities of the body segments), and the action of joints [59,62]. The validated human body dynamics model [62] predicts the hip impact velocity and the body configuration at the impact moment.

The interaction between the body and the ground during the impact was then described by an impact model, which consisted of an effective mass, characterized by the body configuration at the impact instant, as well as a spring and a damper. In order to quantify the energy attenuation by hip soft tissues during the impact, stiffness (K) and damping (C) properties of the impact model for men and women were separately determined from experimental data [63], while in currently existing studies [51,64] the effect of STT is considered identical in men and women. Multivariate nonlinear least square fits of power functions were used to obtain the sex-specific correlation between stiffness/damping coefficient and the hip soft tissue thickness. The thickness of soft tissues overlying the greater trochanter was determined from the whole body scans by measuring the lateral distance between the greater trochanter and the air-soft tissue boundary [50]. The average soft tissue thickness of right and left sides was measured and used for subsequent analyses. Table 1 shows the anthropometric details and physical properties of the subjects across BMI groups. The impact model was used to determine the time history of the impact force applied from the ground to the greater trochanter. The impulse-momentum principle was also used to determine the joint force applied from the acetabulum to the femoral head in a sideways fall [59]. The determined fall-induced load/constraint conditions were then applied to the proximal femur finite element (FE) model (Fig. 1(d)) to calculate the stress/strain distribution in the femur bone.

For constructing the finite element model, geometric information and material properties were extracted from the proximal femur DXA scan. DXA scans of the proximal femur from the baseline visit were analyzed using in-house MATLAB codes. The codes were written to extract a pixel-by-pixel BMD map of the hip DXA scan. An image-processing algorithm, that combined edge detection and thresholding, was used to segment the proximal femur. A subject-specific thickness of the proximal femur was first derived as [65,66]:

$$t = \frac{3.5\pi W}{16} \tag{1}$$

where W is the width of the femoral neck from the DXA scan. The obtained thickness was then used to convert areal BMD to volumetric BMD as:

$$vBMD = \frac{BMD}{t} \tag{2}$$

assuming the plane-stress approach, i.e., considering that proximal femur is a plate with a constant thickness [65,66]. Then, isotropic inhomogeneous material properties were derived from $vBMD$ using the empirical equations of Morgan and colleagues [67,68]:

$$\text{Modulus of Elasticity (MPa)} = \left\{ \begin{array}{l} 15,010\rho^{2.18}\ if\ \rho \leq 0.280\text{g/cm}^3 \\ 6,850\rho^{1.49}\ if\ \rho \geq 0.280\text{g/cm}^3 \end{array} \right\} \tag{3}$$