Hip Structure Associated With Hip Fracture in Women: Data from the Geelong Osteoporosis Study (Gos) Data Analysis-Geelong, Australia

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ABSTRACT

Backgrounds	Aging leads to changes in bones to be highly fragile causing fractures. In this research, changes in the dimensions of the hip structure can be measured by using a computer program called 'Hip Structural Analysis (HSA)'. The objective of this study is to estimate the association between hip geometries in Femoral Neck (FN) and the risk of hip fracture in older women.
Methods	A case control study was performed to explore the objective respectively using the data of participants from population cohort and fracture cohort of the Geelong Osteoporosis Cohort Geelong, Southern Victoria, Australia. Simple and multiple logistic regressions were performed.
Results and Discussion	Of total of 598, comparing Fracture group (44 subjects) and non-fracture group (454 subjects) aged over 63 years, the odds of hip fracture increased by approximately 2 fold for each 1 SD increase in width (OR=1.70(1.18-2.45,p 0.005), endocortical diameter (OR=1.80 (1,23-2.62, p=0.002), and buckling ratio (OR=1.85(1.32- 2.61, p < 0.0001) and for each 1 SD decrease in BMD (OR=1.98(1.21-3.23, p.0.006) and average cortical thickness (OR=2.02(1.23-3.34), p.0.006) controlling for age, height, weight and menopausal status. Findings suggest that not only is BMD associated with hip fractures, but also other hip geometry dimensions, including WID, ENDO, AVCO and AVBR, independent of age, height, weight and physical activity.
Conclusions	These results provide additional insights that the geometries of FN is associated with fracture neck of femur in older women and strongly suggest its potential value, not only BMD, as clinical predictors for assessing the risk of hip fracture in older women. In addition to this, utilization of some combined parameters of bone geometries in FN might be a more effective method in screening than case findings to reduce the burden of hip fracture in the future. Further statistical methods is needed to analyze the combined hip structure to predict hip fracture.

INTRODUCTION
Background and Rationale

Hip fracture is a major public health problem and a leading cause of morbidity, hospitalisation and mortality in particular cases (Deng et al., 2002, Hannan, 2001, Wehren and Magaziner, 2003, Khasraghi, 2003). Hip fractures are also associated with certain medical complications, including electrolyte imbalance, urinary tract infection, respiratory failure and delirium in both men and women (Khasraghi, 2003). In the early twenty-first century, the estimated number of incident osteoporotic hip fractures was 1.6 million worldwide; with approximately 70 % of these occurred in women. The Disability Adjusted Life Years (DALYs) for hip fracture was 0.82 million in men and 1.53 million in women within the same year. Moreover, hip fracture contributed for 41 % of the global burden of osteoporosis in 2000 (Johnell and Kanis, 2006).

In Australia, hip fractures were predicted to increase for 36 % between 1996 and 2006 (from 15000 to 21000 cases) (Sanders et al., 1999a). This significant increase was due to the increased number of elderly aged 85 years and over as Australia faces the challenges of an aging population (Sanders et al., 1999a). Furthermore, hip fractures are projected to increase by twofold in 2026 and fourfold in 2051 (Sanders et al., 1999a) with hospitalization rate of almost 100 % (Pasco et al., 2005). A number of studies showed that women have a higher incidence of hip fractures than men (Sanders et al., 1999b, Seeman, 2002, Wehren and Magaziner, 2003).

Bone mineral density (BMD), a surrogate marker of strength of bone (Bonnick, 2007, Rivadeneira et al., 2007), has also been widely used in clinical bone research as the main diagnostic factors to estimate fracture risk (Heaney, 2005, Pulkkinen, 2004). Measurement of BMD using DXA only generate length and breadth (two dimensional), acting as a surrogate for three dimensional volume (length, breadth and depth of bone structure) (Heaney, 2005). Thus, other important elements, for instance the size, shape, geometries, and relative amounts of bone in cortical and trabecular compartments that are related to bone strength is not measured directly by conventional DXA (Black et al., 2008). On the contrary, HSA has been able to generate 3 dimensional measurement from 2 dimensional measurement of DXA scans results using specific principles developed by Beck and colleagues (Beck et al., 1990).

Previous studies from the US (Kaptoge, 2008) and Netherland (Rivadeneira et al., 2007) population has shown that some parameters generated from HSA measurements, areal BMD, cortical thickness (AVCO) and buckling ratio (AVBR), were associated with increased risk of hip fracture. These results support the strong potential of BMD and other hip geometries to be used as risk predictors for future hip fracture (Kaptoge et al., 2008, Rivadeneira, 2007). However, there are indications that variation in BMD and other geometrical dimension of bone is largely influenced by ethnicity (Wang, 2005, Nelson, 2004, Peacock et al., 2009). Therefore, the utility of this method needs to be confirmed in terms of its consistency in a different setting across different age. The Objective of the research was to examine the association between hip geometries in Femoral Neck and the risk of hip fracture in older women.

METHODS
Study Design
A case control design was used to determine risk factors of fracture, in particular, measured from FN geometries.

Data Collection
This study was conducted using the data drawn from the large epidemiological project known as the Geelong Osteoporosis Study (GOS) with a population cohort (Henry et al., 2000) that commenced in 1994 and a fracture sample (Sanders, 1998) collected at the same time period. The date has been extracted and cleaned by Dr. Margaret Henry.

Study Area
The GOS, a population-based cohort study was based in a region surrounding Geelong in Southern Victoria (Henry et al., 2000). The region named Barwon Statistical Divisions, was defined by the Australia Bureau of Statistics (Henry et al., 2000). The region consists of stable urban and rural populations that may represent the Australian populations (Henry et al., 2000). A small number of radiological centres indicates a complete ascertainment can be attained by accessing all radiological reports (Pasco et al., 1999). There are two cohort data in the GOS; fracture cohort (Sanders, 1998) and population cohort (Henry et al., 2000).

This study used the population and sample from the GOS. The detail of GOS has been published elsewhere (Henry et al., 2000, Sanders, 1998). Study Sample in this research is that the eligible case and control sample was made up of participants in fracture cohort and population cohort of the Geelong Osteoporosis Study respectively in older group aged $\geq$ 64 years old. The inclusion criterion for case group was also that participants have sustained in the low trauma group of hip fracture. Low trauma group was defined by the GOS researchers as fracture due to accidental fall from less than standing height (lying/sitting), accidental fall from standing height, a spontaneous

fracture and other fracture except due to transportation accidents. Moreover, the inclusion criterion for the control group was that participants have not sustained any fracture based on self-reported data in population cohort of GOS. Participants who had previous hip fractures were excluded in fracture groups. The consideration of the exclusion was that hip structure in participants with previous fracture would be not similar with that in participants who never have hip fracture previously. Therefore, exclusion might reduce bias.
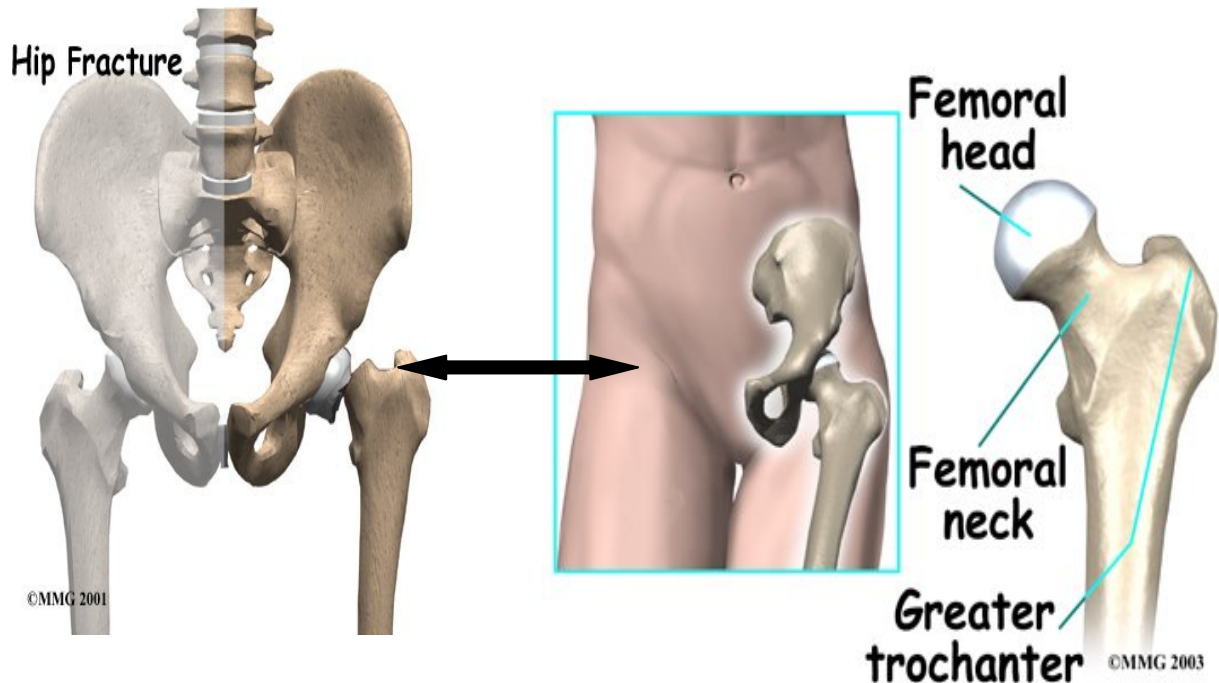

Figure 1   Hip Fracture picture and hip Anatomy **(Matt, 2002, Matt, 2003)**

Statistical Analysis
All analysis procedures were performed using a statistical computer program, STATA version 10. Initially, case and control definitions were re-checked to eliminate the possibility of misclassification due to statistical properties. Missing values and wrong coding were also properly checked and corrected as necessary.

The outcome, fracture status, was measured dichotomously, coded into 1 for cases (fracture group) and 0 for control (non fracture group). At the beginning, basic descriptive statistics were performed to review the description of each variable. Means, standard deviation or standard errors were generated for continuous variables with normal distribution and median and range for those with asymmetric distribution, while proportion was used for categorical variables.

Exposures were hip geometries and outcome was risk of fracture. Univariable analysis was performed to find a difference between participants' characteristics and the outcome. Student t-test was used for the continuous exposure, while Chi-Square test was performed for categorical exposure. Pearson's correlation was performed to find correlation value between two hip geometries. Subsequently, the association of hip geometries and risk of hip fracture was performed by using logistic regression. This estimated regression coefficients were expressed by odds ratio for the association between risk of fracture and hip geometries (dimensions). OR of hip fracture corresponds to 1 SD change (decrease or increase) in the Hip structural variables increasing risk of hip fracture, therefore the interpretation of possible hip predictors of fracture were able to be described clearly. Regression coefficient (the first objective), the Odds Ratio (the second objective), the 95 % confidence interval and p value were reported.

RESULTS
Association between hip geometries in Femoral Neck and risk of hip fracture Characteristics of sample

Table 1 Characteristics of Participants in Fracture and Non Fracture Group

Characteristics	Fracture group N=44	Non fracture group N=454	P value*
Steroid/Corticosteroid Hormone Use , n, (%) Yes	3 (4%)	49 (10%)	0.383
Smoking Status, n, (%) Yes	18 (40%)	142 (31%)	0.232
Menopause Status , n, (%) Yes	45 (100%)	454 (100%)	-
Calcium/Multivitamin D Use , n, (%) Yes	4 (9 %)	92 (20%)	0.07
Hormone Replacement Therapy, n, (%) Yes	4 (9%)	82 (18 %)	0.303
Physical Activity n, (%)			
Active	8(18%)	179 (40%)	
Sedentary	15 (34 %)	180 (40%)	<0.0001
Limited	21 (8 %)	95 (82 %)	
Family History , n, (%) Yes	1 (2%)	29 (6%)	0.26
Drinking status, n, (%) Yes	35 (13 %)	10 (4 %)	0.001
	Mean (SD)		**P Value****
Height ,cm	156.88 (6.28)	156 (6.17)	0.72
Current Age, year	79.1 (7.54)	75.65 (6.91)	0.001
Weight, kg	61.39 (11.17)	65.37 (12.64)	0.04
Bone mineral density, g/cm2	0.59 (0.14)	0.68 (0.14)	<0.0001
Cross sectional area, cm2	1.64 (0.40)	1.78 (0.36)	0.014
Cross sectional Moment of Inertia, cm4	1.52 (0.51)	1.43 (0.40)	0.0.16
Width, cm	2.90 (0.25)	2.73 (0.28)	0.0001
Section modulus, cm3	0.98 (0.30)	0.99 (0.23)	0.69
Endocortical diameter, cm	2.67 (0.26)	2.46 (0.30)	<0.0001
Average cortical thickness, cm	0.11 (0.03)	0.13 (0.03)	<0.0001
Buckling ratio	14.54 (4.35)	11.41 (3.33)	<0.0001
Centroid Position	0.48 (0.03)	0.49 (0.03)	0.04

* Chi Square function   ** Student t-test function

Table 1 shows the basic characteristics of participants in this study according to fracture and non-fracture. There were 44 participants (8.8%) in fracture group and 454 participants (91.2%) in non-fracture group. Fracture group had lower weight, older age, and slightly higher height compared than non-fracture group. Furthermore, some hip geometry dimensions, including the average value of BMD, WID, ENDO, AVCO, and AVBR were considerably different among fracture and non fracture group ($p \leq 0.0001$). Differences of characteristics of study participants between fracture and non fracture group were also found in physical activity ($p <0.0001$) (table 1)

Association between hip structural analysis variables in Femoral Neck region and risk of hip fracture in older women

Table 2 shows the unadjusted and adjusted model of the association between HSA Parameters and hip fracture. In model 1, BMD, WID, ENDO, AVCO, and AVBR were strongly associated (all p <0.0001) and CSMI and SectMod were weakly associated with risk of hip fracture. After adjusting for age, height, weight and physical activity, most of these associations remain, however the strength of this association was reduced (model 2, table 1).

Table 2   Association of HSA parameters in NN region with hip fracture

Parameters (per 1 SD changes)	Direction of change^^	Model 1†		Model 2 §	
		OR (95% CI)	*P* value	OR	*P* value
Bone mineral density(BMD)	(-)	2.18 (1.5, 3.18)	<0.0001	1.98(1.21, 3.23)	0.006
Cross sectional area(CSA)	(-)	1.53(1.09, 2.15)	0.015	1.26(0.81, 1.96)	0.311
Cross sectional Moment of Inertia (CSMI)	(+)	1.22(0.92, 1.62)	0.164	1.43(1.02, 2.02)	0.04
Width (WID)	(+)	1.94 (1.39, 2.70)	<0.0001	1.70 (1.18, 2.45)	0.005
Section modulus (SECMOD)	(+)	1.06(1.46, 0.78)	0.685	1.19 (1.75, 0.81)	0.368
Endocortical diameter (ENDO)	(+)	2.14(1.52, 3.00)	<0.0001	1.80(1.23, 2.62)	0.002
Average cortical thickness (AVCO)	(-)	2.24(1.52, 3.29)	<0.0001	2.02 (1.23, 3.34)	0.006
Buckling ratio	(+)	2.03(1.54, 2.67)	<0.0001	1.85(1.32, 2.61)	<0.0001
Centroid Position (CENPOS)	(-)	1.44(1.01, 2.03)	0.041	1.25(0.89,1.76)	0.188

† Unadjusted

§ Adjusted for dimension age, height. weight, and physical activity

^^The direction of change is indicated as increase (+) or decrease (-) 1 SD of hip geometries.

DISCUSSION

This case control study also suggests that increased AVBR, WID, ENDO and a reduced BMD and AVCO in FN region are associated with an increased risk of hip fracture with independent effect of height, weight, age and physical activity. Findings suggest that not only is BMD associated with hip fractures, but also other hip geometry dimensions, including WID, ENDO, AVCO and AVBR, independent of age, height, weight and physical activity.

Association between hip geometries and hip fracture have been widely studied. Zebaze (2007) concluded in their study in Lebanon that the result of failure to adapt bone's architecture to loading may lead to bone fragility, not just low bone mass. However, Zebaze used a different method called micro Computed Tomography. Zebaze et al (2005) argues that DXA is not a suitable method to measure FN (FN) depth and volume BMD (vBMD) because DXA assume a circular and a square cross section. However, Beck et. al (1990) have validated that HSA using DXA as accurate method in measuring geometric measurements and strength estimates. Pulkkinen P (2004) and El-Kaissi et al (2005) found the similar conclusions to Zebaze. However, both studies used manufacture rulers to measure hip geometries using a single observer. Hence, the results might have been impacted by observer bias and measurement bias that might weaken the validity of these studies.

Two studies on Hip Structural Analysis parameters were found. Firstly, a research by Rivadeneira et al (2007) with 2740 women aged ≥ 55 years old (106 hip fracture) found that an decreased BMD in FN is a strong predictor of hip fracture in women. However, this result is not mechanically clear because this findings suggests that BMD is capturing a strength aspect (Kaptoge, 2008). SectMod as an indicator for bone strength is not present in this study (Rivadeneira et al., 2007). However, Kaptoge (2008), a study with 635 hip fracture cases among 7474 participants, found that each dimension in FN adjusted by age, weight and height was associated with hip fracture (Kaptoge, 2008).

Both studies used cohort design that could minimize some limitations in case control design, including bias and confounders. In this study, cohort study design was not performed, because the population cohort in the GOS consisted of only approximately 700 participants aged over 50 years at baseline. Only a small sample size could be obtained if cohort designs had been used. Moreover, Kaptoge's and Rivadeneira's research was conducted in the USA and the Netherlands respectively with different ethnics groups comparing to Australia. The results might not directly equate to the Australian population, because different races and ethnics have different bone structures (Wang, 2005, Nelson, 2004, Peacock et al., 2009). However, the writers also

suggest that hip geometries in FN indicates strong evidence associated with risk of fracture regardless of the different research methods, study design and ethnics based on this research and previous research above. Moreover, the utility of HSA method has been confirmed in terms of its consistency in a different setting across different age in this study.

Australia, like other western countries, has to cope with the health problem related to ageing as early as possible, particularly osteoporotic hip fractures. This condition is more likely to be major component of the expected increased demand for acute-care hospital services in the future (Pocock et al., 1999). Case findings of hip fracture related osteoporosis, using measurements based on only BMD in WHO criteria for this high risk group (prior fragility fracture, corticosteroid use, family history, and low body mass index), could be underestimating the scope of the problem (Kanis et al., 2002). Therefore, additional hip geometries as independent factor of hip fracture could be considered a clinical assessment method to evaluate risk of hip fractures in high risk group in the population.

There are also some limitations in this study. Firstly, investigating possible confounder factors in this study was based on self reporting; therefore recall bias might have also been present. However, those residual measurements are difficult to be controlled in every research. Secondly, limitation of DXA is that it only produces a two dimensional image of bone to predict a three dimensional image. Projection images from 3-dimensional can be performed using quantitative computed tomography (QCT) application. However, this costly measurement requires much higher effective dose (Genant, 1993). Thirdly, the small sample size in fracture group is a potential limitation. Moreover, cervical fracture and trochanteric fracture were combined as hip fracture. Hence, our study result should be interpreted cautiously to detect due to less statistical power. However, the results of this study could be as baseline of description that the importance of hip geometries in predicting hip fracture.

Some future research is proposed. Sensitivity and specificity can be considered to explore the predictive power of this model as the following study after this research. Moreover, a cohort study with a larger number of samples in the baseline could be performed to reduce the limitation of case control design. Another study that is proposed is meta-analysis of some studies by pooling other research with the same research questions and variables in order to obtain results with high statistical power.

CONCLUSION

These results provide additional insights that the geometries of FN is associated with fracture neck of femur in older women and strongly suggest its potential value, as clinical predictors for assessing the risk of hip fracture in older women. In addition to this, utilization of some combined parameters of bone geometries in FN may be a more effective method in screening than case findings to reduce the burden of hip fracture in the future. However, more studies with stronger design are clearly needed to eliminate some limitations found in this study.

ACKNOWLEDGEMENTS

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